



Dementia, Onset, Development of The Disease, Prevention

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SUMMARY

Introduction: Dementia is a chronic, progressive condition characterized by the irreversible decline of cognitive and other neurological functions. This article discusses how certain comorbidities, particularly those occurring during midlife, are associated with an increased risk of developing dementia. Both theoretical models and empirical studies support this link. Research suggests that up to 24% of individuals under the age of 50 may already exhibit early risk factors for dementia. This risk increases significantly with age and appears to be more pronounced in women, who are also more frequently affected by diseases with diverse clinical presentations that may contribute to cognitive decline.

Methodology: This article aims to critically examine relevant data and literature in order to draw informed conclusions relevant to the topic.

Topic: There are several types of dementia, but what is important to emphasize is that prevention remains the most effective strategy in reducing the risk of dementia. L-ascorbic acid has been shown to play a potential role in prevention due to its antioxidant properties. Additionally, certain hormones such as estrogen specific pharmacological agents may offer protective effects particularly when their related substances are found to be deficient in the bloodstream. There are several types of dementia, but vascular dementia and Alzheimer's dementia stand out in particular.

Conclusion: This article highlights the relative contributions of genetic predispositions and lifestyle habits to the development of dementia. It emphasizes the critical role of prevention both in reducing the risk of diseases that can lead to dementia and in potentially delaying or mitigating the progression of dementia itself.

Keywords: Dementia, Prevention, Vitamins

INTRODUCTION

Dementia has become an increasingly common disease in recent decades. Certain comorbidities such as obesity are among the risk factors. There is statistically significant evidence that dementia develops significantly in middle age. A meta-analytic study, which examined

the correlation between obesity and dementia, showed through 14 studies that had as many as 77,890 participants that obesity in middle age is a percentage-wise higher risk factor for the development of various forms of dementia [1].

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METHODOLOGY

This article aims to critically examine relevant data and literature in order to draw informed conclusions relevant to the topic.

TOPIC

While some studies have focused on general obesity, others have specifically examined central obesity, the key focus of this paper. Central obesity was assessed by measuring waist circumference and waist-to-hip ratio. One such meta-analysis, which included over 5 million participants from 16 studies, clearly demonstrated that individuals with larger waist circumferences had a statistically significant higher risk of developing dementia compared to those with smaller waist circumferences. Interestingly, this risk was more pronounced in individuals over the age of 65 than in those under 65 [1]. Two groups of foods hypothesized to improve and slow the progression of dementia and to worsen the progression of dementia. Nutrients such as omega-3 fatty acids, vitamin D, vitamin B12, and folic acid have shown a significant protective effect against the development of dementia. On the other hand, poorly controlled diabetes mellitus, hyperinsulinemia, and unhealthy dietary habits are associated with an increased risk of dementia. Hyperglycemia contribute to accumulation of amyloid beta in brain lesions, worsens oxidative stress, neuroinflammation and mitochondrial dysfunction, impairs the integrity of neurons and causes neurodegeneration [2].

A 2020 meta-analytic of 58 studies, clearly demonstrated strong association between physical activity and dementia. It is believed that physical activity helps preserve cognitive reserve and other protective mechanisms that delay or prevent the onset of dementia. It is believed that the mechanisms that form a protective barrier against the onset of this disease involve the preservation and strengthening of protective factors such as cognitive reserve [1].

Glucotoxicity can lead to structural and functional damage to brain cells and nerves, bleeding in cerebral blood vessels and increased accumulation of beta amyloid. These are potential mechanisms underlying diabetes-related dementia. Nutrients and natural food compounds are being investigated

as preventive and/or interventional strategies. Among the candidate components, resveratrol, curcumin and their analogs may be useful for preventing cognitive impairment associated with diabetes [2]. The etiology of diabetes and dementia is quite complex. The risk factors for these two diseases tend to overlap somewhat. Examples of overlapping mechanisms of diabetes and dementia are: inflammation, oxidative stress, and mitochondrial dysfunction. The mechanisms for these associations remain to be elucidated, but may involve cerebrovascular and nonvascular mechanisms. Increased adiposity in middle age is associated with a higher risk of dementia. Evidence linking adiposity in old age with dementia is conflicting. Several studies have shown that hyperinsulinemia, a consequence of higher adiposity and insulin resistance, is also associated with a higher risk of depression. Hyperinsulinemia is a known risk factor for type 2 diabetes, which itself has been linked to a higher risk of dementia. Particularly vascular more so dementia more so than Alzheimer's disease [3]. Although, Cognitive cognitive decline and dementia are typically seen in older adults, as prevention of cognitive decline may require intervention earlier in middle age. We described the association between hyperinsulinemia and the change in cognitive function over time independent of diabetes over 6 years in a middle-aged cohort. This study provides evidence that cognitive decline in a cohort of middle-aged adults without prior dementia, possible stroke/transient insulin attack, or residential type 2 diabetes with higher codes [4].

Protective substances that prevent the development of dementia

Vitamin E, and specifically its most important biologically active form alpha-tocopherol is a potent antioxidant with strong neuroprotective properties. It helps neutralize free radicals, not only in the extracellular space but also within cells. Foods rich in vitamin E include nuts such as hazelnuts and walnuts, as well as cold-pressed olive oil, sesame seeds, pumpkin seeds, and other nuts. The recommended daily intake of tocopherol (vitamin E) is between 7 and 15 milligrams [5]. Vitamin A is another powerful antioxidant that protects against free radicals and plays a role in preventing Alzheimer's disease. Like vitamin E, it is a fat-soluble antioxidant absorbed through

cell membranes and nuclei. It also binds to proteins in the cytoplasm and blood. Dietary sources of vitamin A include dark yellow and orange fruits and vegetables such as carrots and apricots, dark green leafy vegetables, and animal-based foods such as eggs, milk, and various types of fish. The recommended upper limit for vitamin A supplementation, based on the calculated half-life of retinol, is 900 µg RAE per day [6]. Vitamin C (L-ascorbic acid), although water-soluble rather than fat-soluble, also plays a key protective role. It not only neutralizes free radicals directly but also regenerates oxidized vitamins A and E, restoring them to their active forms. However, L-ascorbic acid is highly unstable in neutral and basic environments, where it can convert to D-ascorbic acid, which lacks antioxidant properties [7]. Certain foods may help prevent dementia. For example, salmon, flax seeds, egg yolks, and milk contain vitamin D, a fat-soluble vitamin known to protect against the onset of dementia. These foods are also rich in omega fatty acids, which play an important neuroprotective role. Shellfish, animal liver, eggs, and fortified foods provide significant amounts of vitamin B12, while dark green and other leafy vegetables are high in vitamin B9 (folic acid) [8]. Vitamin D, in particular, deserves emphasis. It not only offers protection against dementia but also plays a broader role in preventing various neurodegenerative and systemic diseases [9]. Since vitamin D receptors are present in nearly all human cells, its deficiency whether mild (hypovitaminosis) or severe can disrupt health and contribute to disease development [10]. The protective mechanisms of these nutrients are diverse. They include reducing inflammation in the brain and cerebral capillaries, protecting neuronal membranes, lowering amyloid plaque levels, modulating immune responses, and maintaining DNA repair proteins. They are also known to reduce homocysteine levels, which is associated with a lower risk of cognitive decline. Other beneficial foods include berries such as blueberries, and sugar-free dark chocolate with high flavonoid content. Turmeric, which contains the active compound curcumin, assists in clearing amyloid plaques from neurons. Green tea, with its strong antioxidant properties, also helps protect neuronal membranes [8]. Prebiotics are indigestible dietary fibers for humans, absorb water and harmful substances in the gut while serving as food for probiotic bacteria.

Prebiotic-rich foods include bananas (among fruits), garlic and onions (among vegetables), and whole grains. Cereals, in particular, contain inulin, a substance with known prebiotic effects [11]. Recent research highlights a significant correlation between a healthy intestinal microbiota and mental health. These findings suggest that microbiota products, not only reduce inflammation in the brain but also positively influence human cognitive and emotional functions through multiple mechanisms [11].

Foods That Can Worsen and Accelerate Dementia

Certain foods are known to contribute to elevated blood glucose levels, hyperinsulinemia, insulin resistance, chronic inflammation, the development of diabetes mellitus. These conditions are linked to impaired brain function and increase the risk of dementia. Simple sugars, especially those added to foods and beverages such as carbonated soft drinks, pastries, sweets, and artificially sweetened products can impair memory and promote inflammation in the brain's microcirculation [12,16]. Processed meats, such as bacon, salami, sausages, and other deli meats, often contain nitrites that convert into nitrates in the body. These compounds are associated with nerve damage and are also implicated in gastrointestinal diseases [11]. Moreover, processed meats rich in chemical additives may disrupt the gut-brain axis by altering the intestinal microbiota, thereby increasing cerebral inflammation. Fried food, commonly found in fast food meals such as French fries, fried meats, and salty snacks, are significantly associated with vascular damage heightened inflammation, and a higher risk of developing depression and dementia. Excessive use of alcohol consumption can damage GABA receptors in the brain. Chronic exposure may lead to brain atrophy, often accompanied by progressive memory loss [12,16]. In addition, poorly managed diabetes mellitus and chronic hyperinsulinemia are strongly associated with an increased risk of dementia. The proposed mechanisms include: beta amyloid accumulation, oxidative stress, mitochondrial dysfunction, and cerebral insulin resistance [11,12,16].

Medicines in the Treatment of Dementia

Alzheimer's disease is a chronic and progressive neurological disease. The stages of dementia are typically assessed by evaluating cognitive function, as well as through the patient behavior and the ability to perform activities. One of the earliest drugs used in Alzheimer's treatment is tacrine, an acetylcholinesterase inhibitor [13]. More recent cholinesterase inhibitors include donepezil, rivastigmine, and galantamine, which reduce the breakdown of acetylcholine in the cerebral cortex, thereby helping to preserve memory and cognitive function [15]. Another important medication is memantine, which belongs to the class of NMDA (N-methyl-D-aspartate) receptor antagonists. Memantine has been shown to significantly slow the progression of Alzheimer's disease, although it does not halt the condition entirely [13]. Selegiline a monoamine oxidase B (MAO-B) inhibitor, has long-lasting effects and has a mild beneficial effect on Alzheimer's disease, especially affecting the prevention of memory loss. Compared to placebo, selegiline has been associated with better preservation of neuronal integrity. The different results of subjects on drawing a clock - a special test used to evaluate this type of pathology, gave results that drawing a clock was proportional to the degree of dementia [14]. Among all current treatment options, cholinesterase inhibitors specifically donepezil, galantamine, and rivastigmine are the most effective in slowing cognitive decline. These drugs work by increasing acetylcholine levels in the brain, thereby stabilizing cognition and slowing the decline in memory and other higher neurological functions [15]. In cases of comorbid conditions, it is useful to employ drugs with direct antioxidant activity, which can protect cells from oxidative stress. This represents a significant scientific advancement, as such medications may help prevent damage to the membranes of red blood cells and neurons [17,18,19]. It is also important to note that some non-antioxidant vitamins may provide indirect protection by reducing levels of homocysteine, a substance associated with an increased risk of stroke and myocardial infarction. According to findings from a retrospective study, vitamins B9 (folic acid) and B12 significantly lower homocysteine levels an effect that cannot be achieved by antioxidants alone. This highlights the importance of these two vitamins in reducing vascular risk factors

that may contribute to dementia and cardiovascular disease [20].

CONCLUSION

Dementias have long been classified into several types, including vascular, Alzheimer's dementia, dementia with Lewy bodies, frontotemporal dementia, and hydrocephalus-related dementia. Among these, Alzheimer's disease and vascular dementia are the most prevalent and clinically significant. The goal of this article was to raise public health awareness and provide clinical insight into the importance of early recognition, prevention, and management of these debilitating conditions. Prevention strategies should not be underestimated, particularly in relation to dietary habits and environmental exposures. For example, attention should be paid to cooking utensils and food preparation methods, as aluminum ions potentially leached from cookware may contribute to beta-amyloid accumulation, a hallmark of Alzheimer's pathology, balanced and varied diet is essential for maintaining brain health, primarily due to its supply of vital vitamins and minerals, including those highlighted in this article. Individuals can take proactive steps to monitor and address micronutrient deficiencies, especially deficiencies in B-complex vitamins such as B1, B6, and B12, which have been shown to support cognitive function and potentially slow the progression of existing dementia. However, it is crucial that any therapeutic approach whether pharmacological, supplemental, or nutritional—is undertaken under the supervision of a qualified healthcare professional, who can tailor recommendations to the patient's individual medical condition.

CONFLICT OF INTEREST

The author declares no conflict of interest.

REFERENCES

1. Livingston G, Huntley J, Liu KY, Costafreda SG, Selbæk G, Alladi S, Ames D, Banerjee S, Burns A, Brayne C, Fox NC, Ferri CP, Gitlin LN, Howard R, Kales HC, Kivimäki M, Larson EB, Nakasujja N, Rockwood K, Samus Q, Shirai K, Singh-Manoux A, Schneider LS, Walsh S, Yao Y, Sommerlad A, Mukadam N. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *Lancet*. 2024 Aug 10;404(10452):572-628. doi: 10.1016/S0140-6736(24)01296-0. Epub 2024 Jul 31. PMID:

39096926.

2. Lee HJ, Seo HI, Cha HY, Yang YJ, Kwon SH, Yang SJ. Diabetes and Alzheimer's Disease: Mechanisms and Nutritional Aspects. *Clin Nutr Res*. 2018 Oct;7(4):229-240. doi: 10.7762/cnr.2018.7.4.229. Epub 2018 Oct 23. PMID: 30406052; PMCID: PMC6209735.

3. Luchsinger, J.A. (2009). Type 2 Diabetes, Related Conditions, and Dementia. In: Biessels, G., Luchsinger, J. (eds) *Diabetes and the Brain*. Contemporary Diabetes. Humana Press. https://doi.org/10.1007/978-1-60327-850-8_13

4. Young SE, Mainous AG 3rd, Carnemolla M. Hyperinsulinemia and cognitive decline in a middle-aged cohort. *Diabetes Care*. 2006 Dec;29(12):2688-93. doi: 10.2337/dc06-0915. PMID: 17130206.

5. Koprivica M, Miljković A. Uticaj vitamina E na različite organske sisteme. *Sanamed*. 2024;19(2):215-9. doi: 10.5937/sanamed0-49398

6. Koprivica M, Bjelanović J. Značaj vitamina a u ishrani. *Medicinski časopis*. 2021;55(3):99-103. doi: 10.5937/mckg55-31633

7. Orrell RW, Lane RJ, Ross M. Antioxidant treatment for amyotrophic lateral sclerosis / motor neuron disease. *Cochrane Database Syst Rev*. 2007 Jan 24;2007(1):CD002829. doi: 10.1002/14651858.CD002829.pub4. PMID: 17253482; PMCID: PMC8985756.

8. Leonardo Sepúlveda, Monica L. Chávez-Gonzalez, Nathiely Ramirez-Guzmán, José Sandoval-Cortes, Cristóbal N. Aguilar, Chapter 28 - Pomegranate and berries as source of bioactive compounds for neurodegenerative disorders, Editor(s): Raj K. Keservani, Rajesh K. Kesharwani, Mila Emerald, Anil K. Sharma, *Nutraceutical Fruits and Foods for Neurodegenerative Disorders*, Academic Press, 2024, Pages 561-569, <https://doi.org/10.1016/B978-0-443-18951-7.00030-X>.

9. Koprivica M, Bjelanović J. Vitamin D u ishrani i njegova dejstva na nervni sistem. *Medicinski časopis*. 2022;56(4):158-60. doi: 10.5937/mckg56-40957

10. Koprivica M, Miljković A. Javnozdravstveni aspekti vitamina D. *Srpski arhiv za celokupno lekarstvo*. 2025;153(1-2):103-6. doi: 10.2298/SAR-H241123012K

11. Arumugam Vignesh, Thomas Cheeran Amal, Ariyan Sarvalingam, Krishnan Vasanth, A review on the influence of nutraceuticals and functional foods on health, *Food Chemistry Advances*, Volume 5, 2024, 100749, <https://doi.org/10.1016/j.focha.2024.100749>.

12. Suraj Kumar, Rishabha Malviya, Sonali Sundram, *Nutritional neurology: Unraveling cellular mechanisms of natural supplements in brain health*, *Human Nutrition & Metabolism*, Volume 35, 2024;200232, <https://doi.org/10.1016/j.hnm.2023.200232>.

13. Chen Y, Lai M, Tao M. Evaluating the efficacy and safety of Alzheimer's disease drugs: A meta-analysis and systematic review. *Medicine (Baltimore)*. 2024 Apr 19;103(16):e37799. doi: 10.1097/MD.00000000000037799. PMID: 38640313; PMCID: PMC11029996.

14. Filip V, Kolibás E. Selegiline in the treatment of Alzheimer's disease: a long-term randomized placebo-controlled trial. Czech and Slovak Senile Dementia of Alzheimer Type Study Group. *J Psychiatry Neurosci*. 1999 May;24(3):234-43. PMID: 10354658; PMCID: PMC1189014.

15. Hansen RA, Gartlehner G, Webb AP, Morgan LC, Moore CG, Jonas DE. Efficacy and safety of donepezil, galantamine, and rivastigmine for the treatment of Alzheimer's disease: a systematic review and meta-analysis. *Clin Interv Aging*. 2008;3(2):211-25. PMID: 18686744; PMCID: PMC2546466.

16. Tannu SI, Nahid HM, Hoque MM. Uticaj prerađene i ultrapreradađene hrane na zdravlje. *Hospital Pharmacology - International Multidisciplinary Journal*. 2025;12(2):1664-73. doi: 10.5937/hpimj2502664T

17. Kastratović DA, Vasiljević ZM, Spasić MB, Perunić JP, Matić M, Blagojević DP, Mijalković DN, Antonijević NM, Marković SZ, Gojković-Bukarica L, Stojiljković MP, Lasica RM, Jones DR, Nikolić-Kokić AL. Carvedilol increases copper-zinc superoxide dismutase activity in patients with acute myocardial infarction. *Basic Clin Pharmacol Toxicol*. 2007 Aug;101(2):138-42. doi: 10.1111/j.1742-7843.2007.00094.x. PMID: 17651317.

18. Amirshahrokhi K, Abzirakan A. Carvedilol attenuates acrylamide-induced brain damage through inhibition of oxidative, inflammatory, and apoptotic mediators. *Iran J Basic Med Sci*. 2022 Jan;25(1):60-67. doi: 10.22038/IJBMS.2021.58808.13063. PMID: 35656449; PMCID: PMC9118273.

19. Yao J, Chen SRW. R-carvedilol, a potential new therapy for Alzheimer's disease. *Front Pharmacol*. 2022 Nov 24;13:1062495. doi: 10.3389/fphar.2022.1062495. Erratum in: *Front Pharmacol*. 2023 Jan 12;13:1125890. doi: 10.3389/fphar.2022.1125890. PMID: 36532759; PMCID: PMC9756136.

20. Koprivica M, Miljković A, Mikov M. Vitamin B12 and folic acid levels in the general population. *Scripta Medica*. 2025;56(4):699-705. doi: 10.5937/scriptamed56-60104

Demencija, početak, razvoj bolesti, prevencija

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KRATAK SADRŽAJ

Uvod: Demencija je hronična progresivna bolest koja dovodi do trajnog propadanja kognitivnih ali i ostalih moždanih funkcija. Ovaj članak nam prikazuje kako ostale bolesti imaju povećan rizik od razvoja demencije, naročito ukoliko se ta oboljenja jave u srednjem životnom dobu, za šta postoje kako teorijske tako i apstrakne šanse. Određene studije pokazuju da čak do 24% osoba starosti do 50 godina, ali i starije osobe od 50 godina imaju još veći procentualni rizik i imaju izraženu sklonost bolesti koje poseduju velik spektra manifestacija date bolesti, koja je češća kod osoba ženskog pola.

Metodologija: Ovo kratko saopštenje ima za cilj da prikaže prethodna i nova istraživanja Demencije, a zatim da se izvuku zaključci koji su ključni za ovaj zdravstveni problem.

Tema: Postoje različiti tipovi demencija ali ono što je značajno istaći je to da je ključ uspeha u sprečavanju demencije prevencija. Koja se ogleda kroz različite vidove prevencija koje uključuju higijensko-dijeteski režim. Poznato je da alfa tokoferol i L-askorbinska kiselina utiču u prevenciji demencija. Mada neki hormoni kao što je estrogen dovode do toga kao i neki (lekovi koji mogu prevenirati demenciju samo ukolu su supstance datih lekova deficitarne u krvi. Postoje više vrsta demencija ali posebno se ističu vaskularne demencije i Alchamerova demencija.

Zaključak: Ovaj članak jasno pokazuje značaj i zastupljenosti genetskih predispozicija, kao i uticaj lošeg higijenskog dijetetskog režima, koji dovode do demencije. Autori ukazuju na važnost preventive u sprečavanju nastanka drugih bolesti koje dovode do demencije ali i pokazuje kako se može sprečiti nastanak ili zaustaviti razvoj same demencije.

Ključne reči: demencija, preventiva, vitamini

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