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## Review On Dietary Factors In Alzheimer's Disease.

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### ABSTRACT

Alzheimers disease is the progressive neurodegenerative disorder that results in dementia affecting both the cognition and behavior with no known cause or cure. Alzheimers disease (AD) is the most common type of dementia. The conventional risk factors that responsible for AD are obesity, hypertension, diabetes, vitamin D deficiency, folate deficiency, hyperhomocystenemia, high C reactive protein concentration, hyperhomocystenemia, dietary saturated fats, cholesterol, alcohol consumption, smoking, physical activity, presence of atrial fibrillation, atherosclerotic disease and plasma concentration of hemostatic factors showed more risk for AD. A growing body of evidence suggests that certain dietary components (e.g., antioxidant nutrients, fish, dietary fats, and B-vitamins) may play a protective role in the risk of age-related cognitive decline and AD. Minimize intake of saturated fats and trans fats. Vegetables, legumes (beans, peas, and lentils), fruits, and whole grains should replace meats and dairy products as primary staples of the diet. Vitamin E should come from food sources such as seeds, nuts, green leafy vegetables, and whole grains. The recommended dietary allowance (RDA) for vitamin E is 15 mg per day. A reliable source of vitamin B12, such as fortified foods providing at least the recommended daily allowance (2.4 mg per day for adults), should be part of your daily diet. If using multiple vitamins, choose those without iron and copper and consume iron supplements only when directed by your physician. These are the guidelines are followed in alzheimers disease.

**Keywords:** Alzheimers disease, dementia, dietary factor, effect of food and beverages, effect of dietary patterns

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## INTRODUCTION

Alzheimer's disease is the progressive neurodegenerative disorder that results in dementia affecting both the cognition and behavior with no known cause or cure. Patients eventually lose all cognitive, analytical and physical functioning and the disease is fatal.<sup>1</sup> Alzheimer's disease (AD) is the most common type of dementia. Dementia is the gradual decline in cognitive function or thinking ability. It affects the person's ability to do the normal function. About 60- 80% of people were associated with dementia. According to the World Alzheimer Report 2015, million people worldwide were living with dementia in 2015. The estimated incidence of dementia in 2015 was 9.9 million new cases every year, which means one new case every 3.2.<sup>2</sup> AD destroys the neurons in the cortex and limbic structure responsible for the cognitive, memory and non-cognitive function. At diagnostic stage of AD, there will be a presence of neurofibrillary tangles and neuritic plaque. Neuritic plaques also called amyloid plaques are extracellular and composed of beta amyloid protein. The cleavage of protease enzyme in beta amyloid protein will results in the formation of neuritic plaque.<sup>3,4</sup> Increased apo lipoprotein level can also cause AD. The conventional risk factors that responsible for AD are obesity, hypertension, diabetes, vitamin D deficiency, folate deficiency, hyperhomocystenemia, high C reactive protein concentration, hyperhomocystenemia, dietary saturated fats, cholesterol, alcohol consumption, smoking, physical activity, presence of atrial fibrillation, atherosclerotic disease and plasma concentration of hemostatic factors showed more risk for AD.<sup>5</sup> Patient with habit of moderate alcohol, smoking, physical activity and healthy diet showed lesser risk for AD.<sup>6</sup> The clinical presentation of AD includes cognitive loss such as memory loss, aphasia, apraxia, disorientation. The non-cognitive symptoms include depression, psychotic symptoms, behavioral disturbances and functional loss includes inability to care for self (dressing, bathing, toileting and eating). Apart from pharmacological therapy, the non-pharmacological therapy will help the patient with AD. So much attention has been paid to disease modifying factors and risk factors. The studies showed the AD was often showed the complication of malnutrition and frequent weight loss. The calorie restriction in the early age may reduce the developing AD in old age.<sup>7</sup> Uncontrollable diet, excess calorie intake and overweight in early age increase the developing AD in old age. A growing body of evidence suggests that certain dietary components (e.g., antioxidant nutrients, fish, dietary fats, and B-vitamins) may play a protective role in the risk of age-related cognitive decline and AD. Thus, the potential role of nutrition in the development of AD is necessary.<sup>8</sup>

The seven guidelines that should be followed in alzheimer's disease are as follows:

1. Minimize your intake of saturated fats and trans fats.
2. Vegetables, legumes (beans, peas, and lentils), fruits, and whole grains should replace meats and dairy products as primary staples of the diet.
3. Vitamin E should come from food sources such as seeds, nuts, green leafy vegetables, and whole grains. The recommended dietary allowance (RDA) for vitamin E is 15 mg per day.
4. A reliable source of vitamin B12, such as fortified foods providing at least the recommended daily allowance (2.4 mg per day for adults), should be part of your daily diet.
5. If using multiple vitamins, choose those without iron and copper and consume iron supplements only when directed by your physician.
6. Aluminum's role in Alzheimer's disease remains a matter of investigation, those who desire to minimize their exposure can avoid the use of cookware, antacids, baking powder, or other products that contain aluminum.
7. Include aerobic exercise in your routine, equivalent to 40 minutes of brisk walking 3 times per week

The research articles from the year of 1997 -2018 were searched from the pubmed database and were used in this study. This review focused on the role of dietary factors in cognitive improvement in patient with alzheimer's.

### DIETARY FACTORS IN AD

#### Role of dietary fats:

The presence of epsilon 4 allele of the Apo lipoprotein E increased the risk for AD. This protein was encoded by APOE present in the plasma, cerebrospinal fluid and it serves as ligand for low density

lipoprotein receptors as suggested by some studies.<sup>9</sup> Through this receptors the transport of cholesterol and lipids were transferred between neurons. Metabolic studies showed that use of polyunsaturated or monounsaturated fats results in poor plasma lipid concentration. As a result high level of low density lipoprotein and decreased high density lipoprotein cholesterol will result in hypercholesteremia and cognitive aging. It was evidenced by the animal experimental study showed that apolipoprotein epsilon 4 allele proteins are responsible for the transport of cholesterol in the brain and causes a betaapoprotein deposition. So, the use of higher monounsaturated fatty acid showed better cognitive function is better than saturated fatty acid showed worse cognitive function.<sup>10</sup>

#### **Role of antioxidants:**

The numerous laboratory studies evident that antioxidant will protect the brain from oxidative and inflammatory changes. Experimental animal studies showed that AD will cause damage and inflammation of brain neurons. Antioxidant such as vitamin E and vitamin C plays a major defense mechanism in our body against the oxidation. Vitamin E breaks the chained oxidation and vitamin C helpful in restoring the vitamin E. So, the patient who are having the stroke and cardiovascular disease can be prevent from AD by increased consumption of vitamin E and C.<sup>8,11</sup>

#### **Role of vitamins:**

##### **Vitamin A:**

Vitamin A contain a group of compounds such as retinol, retinoic acid and b- carotene. The studies said that b-carotene have a beneficial effects on cognitive functions. The dietary deficiency of retinoic acid will decrease the DNA methylation in the hippocampus region in the brain.<sup>12</sup> Nutritional data on vitamin A in vivo was not available. But however experimental in vitro animal studies showed that vitamin A have a role in alzheimers disease prevention due to the presence of anti oligomerization chain that prevents the deposition of beta apolipoprotein in the brain.<sup>2</sup>

##### **Vitamin B**

Vitamins such as folic acid, vit B6 and vit B12 involved in inhibiting the oxidative stress in the brain.<sup>5</sup> The patient with AD showed increased homocysteine level.<sup>13</sup> The vit B6, vit B12, folate lowers the homocysteine level in AD. It was evidenced by the cohort study of 816 subjects showed low folate supplements increase the risk of AD where as a group with high folate supplements reduce the risk of AD.<sup>2,14</sup>

##### **Vitamin C and E**

Vitamin C has a role in reducing the apolipoprotein oligomer in the brain and Vitamin E is a lipid soluble antioxidant that acts as a neuroprotection by inhibiting oxidative stress and scavenging of  $A\beta$  associated free radicals.<sup>2</sup> The studies showed that vit c is necessary for recycling alpha tocopherol and beneficial effects of vitamin E depends on the concentration of vitamin C. The non-alpha forms of tocopherol showed decreased risk for AD as it exhibit high neuroprotection then the alpha tocopherol.<sup>15</sup>

##### **Vitamin D**

Vitamin D showed a little association with  $A\beta$  mechanism and involve in other pathways such as antioxidation, vascular, inflammatory or metabolic pathways. A meta-analysis of 10 studies showed that AD cases had lower serum vitamin D concentrations than matched controls.<sup>16,17</sup>

#### **Role of metals**

Dysfunctional homeostasis of transition metals is believed to play a role in the pathogenesis of AD by forming reactive species through metal amyloid complexes. Copper, zinc, iron are some of the metals that play a role in alzheimers disease. Increased dietary intake of metals will mediate the pathophysiology of AD.<sup>18,19</sup> It involve in the oxidative stress and free radical formation in the brain cells. So, limited intake of

dietary metal will reduce the risk of AD in old age people.<sup>20,21</sup>

Zinc deficiency will increase the risk for cognition loss in patient with alzheimers disease. It was found that the zinc will reduce the both  $A\beta$  and tau protein in the brain hippocampus and delays the hippocampus dependent memory deficits.

Increase in iron consumption will improve the attention and concentration. it mediates the oxidative stress process in patients with AD and its imbalance will results in imbalance of iron homeostasis. But however diet excessive in diet should be avoided in elder people.

### **Role of polyphenols**

Brain aging and neurodegenerative mechanism where characterized by oxidative damage and impaired hemostasis mechanism. Studies have demonstrated that polyphenols inhibited by  $A\beta$  formation and attenuated cognitive deterioration.<sup>22</sup> Polyphenols are secondary metabolites of plant sources. Depending on the plant structures they are classified into flavinoids , anthocyanins, flavones, flavanones, catechins present rich in turmeric, grapes, red wine, red wine, fruits, legumes etc. The use of polyphenols reduce the oxidative stress has been showed by in vitro study.<sup>20</sup>

## **EFFECT OF FOOD AND BEVERAGES IN AD**

### **Role of carbohydrates**

Patient with type 2 DM increase the risk of AD due to lack of insulin signal pathway in the brain, insulin resistance, insulin expression results in cellular damage that occur in cerebral neurons.<sup>9</sup> High carbhohydrate diets are well known to increase glucose and insulin level in human and this elevated insulin signaling may lead to raped aging of susceptible tissue. The mammalian brain is well supplied with insulin receptors where insulin appears to signal abundant food and not trigger glucose uptake as it does in muscles and fats. Therefore the post prandial blood sugar and insulin level were induced by high carbohydrates diet may continuously signal that nutrients are plentiful and accelerate the aging of susceptible neurons. So therefore the change in diet with decreased dietary carbohydrates will prevent AD.<sup>23</sup>

### **Fish**

The American stroke association guideline already recommended eating fish twice a week will improve the vascular health and can add cognitive health. Intake of fish will reduce the risk of AD due to its positive link of omega 3 fatty acid, EPA and DHA which was evidenced by the prospective and randomized trials.<sup>24</sup> Due to presence of PUFA acts as the protective role in the brain. People who eat a diet reduce with PUFA will show increased risk to AD due to lack of low fatty acids in their brain. Use of seafood meal a week over a 12 month will reduce the risk of AD.<sup>25</sup>

### **Fruits and vegetables**

Consumption fruits and vegetables will lowers the AD risk due to its presence of vitamins such as vitamin C, vitamin E, vitamin A, vitamin D due to its antioxidant and neuroprotective properties in the brain. The cohort study which included 2,613 participants with age group of 43–70 years old shows that the total intakes of fruits, legumes, and juices were not associated with changes in cognitive cognition, while higher intakes of some subgroups (e.g. nuts, cabbage, and root vegetables) may diminish age- related cognitive decline in middle-aged individuals.<sup>26</sup> Higher intake of fruits and vegetables showed neuroprotection effect in patient with apolipoprotein epsilon 4 allele and delays the onset of alzheimers disease.

### **Dairy products**

Increased in consumption of dairy and dairy products will increase the cognition due to its presence of magnesium, vitamin D, and phosphorous. The drinking of coffee and tea also reduce the risk of cognitive

decline which was supported by the study. The presence of caffeine in the coffee has a neuroprotection in the brain. Presence of polyphenols in the tea will modulate the oxidative stress pathways and improve the cognition function as supported by the study.<sup>27</sup>

## **EFFECT OF DIETARY PATTERNS**

### **Western diet**

The studies showed that western diet will increase the risk for AD due to its dietary pattern. The diet consists of high consumption of red meats, processed meats as well as fatty and fried foods. Due to presence of high fatty substance as it may responsible for the deposition of the beta amyloid deposition results in neuropathological changes in the brain and has been linked to cognitive decline and dementia.<sup>28,29</sup>

### **Japanese diet**

A traditional Japanese diet consists of more fish than red meat, plenty of vegetables, pickled and fermented foods and a small portion of rice. These types of diet possess low calories and were extremely nutritious. The type of foods in this diet possesses beneficial bacteria, enzymes, antioxidants and important vitamins and minerals. The study showed that the intake of Japanese diet will reduce the AD risk. Japanese diet contains the low carbohydrates, animal fats and increased intake of vegetables and fish. Due to the presence of omega 3 fatty acid, DHA, EPA in fish will modulate the pathway of APOE deposition and presence of vitamins will produce the antioxidants as well as the neuroprotection in the brain.<sup>30,31</sup> Presence of polyphenols in vegetables delays the alzheimers risk by its neuroprotective action.

### **Mediterranean diet**

The Mediterranean diet may play a major role against age-related changes in cognitive function, pre-dementia syndromes, slower cognitive decline (particularly the one related to the aging brain), reduced risk of developing MCI, reduced risk of conversion of MCI to Alzheimer's disease, reduced risk of Alzheimer's disease, and symptomatic relief. The traditional Mediterranean diet consists of high intake of plant-based foods (fruit as the typical daily dessert, vegetables, legumes, breads, and other types of grains and nuts), olive oil as the major source of monounsaturated fatty acids (used in cooking and salad dressing), low intake of saturated fat, moderately high intake of fish, depending on proximity to the sea, as a source of omega-3 Polyunsaturated Fatty Acids (PUFA), low to moderate intake of dairy products (mostly cheese and yogurt), low to moderate intake of poultry, regular low to moderate intake of wine (normally during meals), low intake of red meat, and a maximum of four eggs weekly.<sup>32</sup> Adherence to mediterranean diet will reduce the risk of developing MCI and prevent the conversion of MCI to alzheimers disease. The higher intake of vegetables, higher saturated and unsaturated fatty acids ratio will reduce the risk of MCI by 8% as reported by some study.

### **Healthy diet**

A healthy diet was defined as one positively related with consumption of fruit, whole grains, fresh dairy products, vegetables, breakfast cereal, tea, vegetable fat, nuts, and fish and negatively related with meat, poultry, refined grains, animal fat, and processed meat and showed better cognitive function.<sup>33</sup>

### **DASH-Style Diet**

The Dietary Approaches to Stop Hypertension (DASH) diet contains a high intake of plant foods, fruits, vegetables, fish, poultry, whole grains, low-fat dairy products, and nuts, while minimizing intake of red meat, sodium, sweets, and sugar-sweetened beverages and showed neuro cognitive improvement.<sup>34</sup>

## **Conclusion**

Alzheimer's disease is the neurodegenerative disorder that results in dementia. It affects the cognitive function of the individuals and make them to withdrawal from the normal activity. Increased age, patient with diabetes, cardiovascular disorder and other co-morbidities shows more risk to the Alzheimer

disease. Apart from pharmacological therapy, dietary modification will reduce the risk in Alzheimer's disease. As the study concludes, the use of foods that rich in vitamins, minerals, antioxidants, unsaturated fats will provide beneficial effects and improve the cognitive function.

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