



## RESEARCH ARTICLE

### A REVIEW ARTICLE: RISK FACTORS AND PREVENTION OF DEMENTIA.

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#### Manuscript Info

##### Manuscript History

Received: 08 July 2019

Final Accepted: 10 August 2019

Published: September 2019

##### Key words:-

Dementia, MCI, AD, risk factors, prevention.

#### Abstract

**Background:** Dementia is a disorder that has an increasing rate of incidence, according to that, this article demonstrated multiple risk factors of dementia and their effects in the progression of the disorder. In addition, this review article pointed to some prevention methods of dementia which can reduce the risks and protect the brain.

**Objectives:** To brief the risk factors by outlining them relying on evidence-based studies and also to clarify and summarize the methods of prevention of dementia.

**Methods:** Studies published from 2005 up to 2016 have been selected for this review, from Cochrane Database, PubMed, BMJ, NIMH and SDL.

**Conclusion:** The findings were the risk factors of dementia: aging (the strongest risk factor), genetic factors (presented in AD genetic predisposition), DM, CVD, hypertension, smoking, diet and level of education, and the methods help in the protection of the brain and the prevention of dementia by reducing the risk of the previous risk factors.

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#### Introduction:-

Dementia is a disorder that is recognized by an impairment of cognition including memory and another cognitive domain at least (language, executive function or visuospatial skills). It is not a disease by itself and it develops when the brain functioning areas related to the cognition functions are affected by an infection or a disease. The decline in cognitive functions progressively affects the person's daily life. Dementia has many types and causes; Alzheimer disease is the most common cause of dementia and is responsible for 50 to 70 % of the cases according to Cleveland clinic<sup>1</sup>. The second common type of dementia is the vascular dementia which occurs after stroke.

The topic of dementia is important because the studies show that the prevalence of dementia is increasing such as the study of the Newcastle University which reported that in the next 3 decades the prevalence of the dementia would significantly increase worldwide<sup>2</sup>. In addition, the lifespan of the people is getting longer and accordingly, the prevalence of late life - >65 years old- dementia is increasing in the developed countries where the dementia rate is doubling each five years while in the developing countries it tends to rise the double each seven years<sup>3</sup>. According to that, dementia is considered to be an aging disorder which is important to know the risk factors of its development and subsequently how to prevent.

The review aims to brief the risk factors of dementia by outlining them relying on evidence-based studies and also to clarify and summarize the methods of prevention of dementia.

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## Methodology:-

The objectives behind this review are: to brief the risk factors of dementia which is increasing in prevalence worldwide and to identify the ways of prevention to reduce the incidence of dementia.

The risk factors reviewed here are: Aging, genetic factors, diabetes, cardiovascular diseases, hypertension, smoking, lifestyle and diet.

Before starting the review article I had to study dementia, its types, clinical features and prevalence. To reach that amount of knowledge, I researched many websites such as Alz.org and Up To Date by typing the word Dementia in the research box of those websites.

The resources of my review article include many data bases such as: Cochrane Database, PubMed, BMJ, National Institute of Mental Health, science direct and Saudi digital library. The key words for searching are dementia, risk factors of dementia, prevention of dementia, genetic predisposition of dementia, diabetes and dementia, cardiovascular diseases and dementia, cognitive impairment, hypertension and dementia, aging and dementia, dietary supplementation and cognitive function, vitamin D and risk of dementia. The results I have used were articles and reviews published from 2005 up to 2016 and most of them were published in 2011, 2012 and 2013.

The way that I used to minimize the huge amount of results is to search in the previous 6 years and look for older results if that was needed. To manage the resources, I specified 10 resources for the introduction, 5 for each risk factor and 5 for the part of prevention.

## Review of literature:

### Risk factors of dementia:

According to the increasing incidence of dementia, which is a disorder that is characterized by an impairment of the cognitive functions especially in elderly population, this study aims to focus on the risk factors and methods to prevent dementia. The risk factors vary between strong and weak factors, some of them are associated with one type of dementia and others are common risk factors among all types of dementia <sup>1,4</sup>.

There are many factors enhancing dementia including aging, genetic factors, diabetes, cardiovascular diseases, hypertension, smoking, diet and drugs ®.

As mentioned before, Alzheimer is the commonest form of dementia. According to that, the majority of Alzheimer's risk factors are risk factors of dementia <sup>5</sup>.

### Aging:

Aging is the most common and the strongest risk factor of dementia. As the person gets older, the incidence of having dementia increases. It's an important risk factor because of the highest prevalence and incidence of dementia in the oldest age. Women have the tendency to develop dementia more than men, because their life expectancies are more than those of men. Aging is associated with diminished physical activity. Studies showed that the physically active people had resistance to the adverse changes which in turn initiated development of dementia <sup>5</sup>.

### Genetic factors:

the multiple neurodegenerative pathways lead to MCI (mild cognitive impairment) which is the primary form and subsequently converts to dementia; this is the AD (Alzheimer disease) pathway. The AD genetic predisposition is the most common genetic factor associated with dementia <sup>6</sup>. In a meta-analysis, the APOE-ε4 allele (rs429358 C allele) showed an association with the rate of MCI to AD dementia progression in all cohort studies analyzed. APOE-ε4 allele is implicated in MCI to AD dementia progression (HR = 2.20 (1.88–2.53) for subjects carrying APOE-ε4 allele). In the study of Hieab H. et al [2016], the progression rate of MCI to AD dementia increased continuously with age, whereas the effect of the allele APOE-ε4 on AD dementia progression decreased after the age of 80 years. However, a previous research has shown that both the incidence of AD and the AD risk effect of APOE-ε4 decreased in the elderly. The observation of a reduced association between APOE-ε4 and MCI to AD dementia progression was consistent with the survivor effect, as APOE-ε4 was a risk factor for both a shorter lifespan and dementia <sup>7</sup>.

**Hyperglycemia and diabetes:**

"Diabetes is one of the most common metabolic disorders". The prevalence of diabetes has been increased globally. Studies showed that diabetes was independently implicated in the development of dementia. Diabetes was assessed for 15 years in a study and the findings were that diabetes was a significant risk factor for all types of dementia. In addition the 2 hours PG (post-prandial glucose) level assessment showed a relation between the elevated PG levels and the higher risk of all subtypes of dementia<sup>8</sup>. Several studies have measured the level of glycated hemoglobin and assessed the results of glucose tolerance tests, those studies showed the relation between the elevated glycated hemoglobin and outcomes related to dementia such as changes in hippocampal volume on neuroimaging or rates of cognitive decline<sup>9</sup>. Over 20 years diabetes in midlife was associated with significantly greater cognitive decline. Among persons with pre-diabetes, cognitive decline was significantly greater (HbA1c 5.7- 6.4%) than those without diabetes (HbA1c < 5.7%). Participants with poorly controlled diabetes (HbA1c  $\geq$  7.0%) had a larger cognitive decline compared to persons whose diabetes was controlled. Longer duration of diabetes was also associated with greater late-life cognitive decline (p-value-for-trend  $\leq$  0.001)<sup>10</sup>.

**CVD (Cardiovascular diseases):**

The findings of a study on postmenopausal women regarding the relation between CVD and cognitive decline suggested that CVD was associated with cognitive decline in postmenopausal women. A history of myocardial infarction doubled the risk for MCI or AD compared with women without myocardial infarction. Hypertension and diabetes, but not adiposity, were associated with a higher risk for cognitive decline. As dementia is an increasingly significant problem in developed countries, more research is warranted on the potential of CVD prevention for the preservation of cognitive health<sup>11</sup>.

In addition, the results of a study conducted on adults aged 45 years old and older, to examine vascular risk factors, as measured by the "Framingham Stroke Risk Profile (FSRP)", to predict incident cognitive impairment, suggested that the vascular risk factors measured by the FSRP, elevated blood pressure and its long-term consequence, left ventricular hypertrophy, may provide a simple and efficient means of identifying adults who are at risk for future cognitive impairment and lent support to the notion that increased attention to prevention and treatment of high blood pressure may be effective in preserving Cognitive health<sup>12</sup>.

**Hypertension:**

high blood pressure is a common condition and, similar to diabetes, its prevalence increases worldwide. Many studies were concerned about the relation between hypertension and dementia, some of them confirmed that there was no association between them but the recent evidence based studies showed that there was positive association between hypertension and dementia. By examining old hypertensive persons without dementia but with MCI and Alzheimer disease, the results showed that hypertension was associated with cognitive phenotype characterized by "executive functioning, slower processing speed and poorer attention". So, according to those results, patients with MCI and hypertension were more susceptible to faster cognitive decline than the normotensive persons<sup>13</sup>. Erik Joas et al., [2012] conducted their study to clarify the mechanism by which hypertension accelerates progression to dementia, the main findings of the study were related to SBP (systolic blood pressure). High SBP was an indication of large artery stiffness, which increased the risk of dementia. High DBP (diastolic blood pressure) as a marker of peripheral resistance was related to ischemic white matter lesion<sup>14</sup>.

**Smoking:**

a meta-analysis of 37 studies of non- smokers and smokers and the risk of dementia showed that smokers had increased risk of all types of dementia. The risk increased with the increasing number of cigarettes smoked per day and among people aged between 65 and 75 and there was no significant difference according to sex or race<sup>15</sup>.

**Diet:**

Diet and lifestyle habits can be risk or protective factors of AD and dementia. Less intake of antioxidants e.g. vitamins C and E, polyunsaturated fatty acids and poly phenolic compounds can be a risk factor for AD and dementia<sup>16</sup>.

Vitamin D has an important role as an autocrine and paracrine agent and functionally it contributes as a neuroprotector by many modulating roles<sup>17</sup>. Low level of vitamin D was found to be associated with elderly cognitive function decline; vitamin D deficiency was associated with increased risk of dementia. Based on these results prevention of dementia could be performed by maintaining the normal level of vitamin D<sup>17,18</sup>.

**Literacy and level of education:**

Cross-sectional studies of older adults have shown that there are positive relationships between literacy and global cognition, memory, working memory, speech fluency and other executive skills. Results of many studies found that individuals with lower literacy showed greater decline in executive functioning, memory and language. According to those results, Limited literacy was an important risk factor for likely dementia <sup>19</sup>.

**Prevention of Dementia:**

There is no definite way to prevent dementia but there are ways to reduce the risks and protect the brain.

Prevention can be achieved by managing the modifiable risk factors such as diabetes, hypertension, smoking, diet habits and lifestyle.

Many studies evaluated the effect of antihypertensive drugs in reducing the risk of dementia, there were not any direct effects of these drugs on dementia. They just could help by controlling hypertension <sup>4,20</sup>.

The same result was found in a study of the evaluation of aspirin in prevention of MCI which is the predictor of dementia; Long term use of low dose aspirin did not provide overall benefits for cognition among generally healthy women aged 65 or more <sup>21</sup>.

Vitamin C and E: Vitamin E is a fat-soluble antioxidant vitamin, which can maintain the integrity and stability and eliminate lipid peroxidation of membranes and scavenge oxygen free radicals efficiently. Furthermore, vitamin E can reduce the toxicity of A $\beta$ , inhibit the deposition and promote the clearance of the peptide, and alleviate the dysfunction of the brain. Regarding vitamin C, as the major extracellular antioxidant, it is the only factor that is capable of preventing the lipid peroxidation induced by water-soluble free radicals. Furthermore, vitamin C has been found to restore the impaired activity of oxidized VE via the clearance of free radicals. The antioxidant defense system can be strengthened by a combination of VE and VC. Decreased in vivo concentrations of VE and VC can result in cellular structural and functional damage, affecting the cognitive function. In the elderly population it has been previously shown that the combination of vitamin E and vitamin C improved cognitive function <sup>22</sup>.

There is lacking of direct evidence on the effect of omega-3 on incident dementia. No benefit of omega-3 supplementation on cognitive function in cognitively healthy old people showed in the available trials. Omega-3 PUFA supplementation is generally well tolerated with common side-effects being mild gastrointestinal problems <sup>23</sup>.

Physical activity can help in the prevention of functional decline associated with age and promote global health status. Recent studies suggested that physical activity could prevent cognitive decline and progression to dementia, including Alzheimer disease <sup>24</sup>.

**Conclusion:-**

Over all, the findings of this review article consider aging, Alzheimer's disease genetic factors, hyperglycemia, diabetes, cardiovascular diseases, hypertension, smoking, lifestyle and diet habits as significant risk factors for dementia.

In addition, the review article approved that there is no definite way to prevent dementia but there are many ways that may help prevent or delay the onset of dementia such as managing the modifiable risk factors and choosing a healthy lifestyle and controlling diet habits.

**Acknowledgment:-**

I thank Dr. Rehab Eltahlawi for being my supervisor and for her willingness to allocate her time to help me doing this article.

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