



# Vitamin B12 Deficiency Mediated Oxidative Stress and Its Effect on Cognitive Ability in Elderly Individuals

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## I. INTRODUCTION:

The world population is growing old and in many developed countries the fastest growing group of population is over 60 year age group. Almost all countries of the world are experiencing the growth of older people in terms of the number and proportion. According to data from world population prospects: the 2017 Revision shows that the population of old people (60 years or over) is expected to get double or more than that by 2050 and to more than triple by 2100, rising from 962 million globally in 2017 to 2.1 billion in 2050 and 3.1 billion by 2100. Globally, population aged 60 or over is growing faster than all younger age groups. The population of elderly people is growing at a rate of about 3 percent per year and the number of persons aged over 80 or over is projected to triple by 2050 from 137 million in 2017 to 425 million in 2050 in all over the world.

The greatest percentage of people aged 65 years or older is in Japan with 26.3% and it is predicted that by 2030 nearly a third of the Japanese people (32.2%) will be senior citizen. This is followed by Italy, with 22.4% of its population being 65 years of age or older.

As population of senior citizens are increasing, the growth of labor force is decreasing which is affecting economies in many ways – the deceleration in GDP, people of working age are paying more to support the older population and due to the higher expenditure on health and retirement programs, elderly people public budget is getting affected. Along with this, the end of baby boom also leads to decline in population of younger age group which in turn leads to the deceleration of economic growth.

According to Guardian by Nuffield Trust (1 Feb 2016)- it is estimated that more than two-fifth of National Health Spending is devoted to people over 65 in UK. The data (2016) depicts that on average a person in his late 30s costs the NHS (National Health Service) 7 times less than 85 year old man. After the age of 50, the health expenditure on per person increases abruptly, with people aged 85 and over costing the NHS an average of £7000 a year. Average health spending per person in the UK in 2013-14 was highest for people aged 85 and

over; it was £7,274 for women and £7,917 for men. Every year, there is inflation on spending money on health maintenance by 1% to 2% despite of sky touching price of new drugs and there is no sign of stopping.

Vitamin b12 is a water soluble vitamin which is required for the various metabolic reactions in the body. In its free form vitamin binds to transcobalamin I (carrier protein) and it is secreted by both salivary glands and mucosal cells of stomach. On other hand, if ingested in its protein bound form than it has to undergo a proteolytic cleavage in the stomach before binding to an R-binder. After this, for more cleavage it enters into the duodenum. In duodenum R-binders holding onto the vitamin b12 get destroyed by the proteases which are secreted by the pancreas. At this point this vitamin gets bound to the intrinsic factor and enters into the ileum of small intestine for the absorptions.

The signs and symptoms of severe and long term vitamin b12 deficiency and irreversible loss of cognitive functions have been recognized for decades. 90% of vitamin B12 deficient patient's shows irreversible neurological functions. 20% of people aged 50 years or over shows low levels of vitamin b12 and this deficiency is more common in elderly population. This is so, because vitamin B12 absorption tends to decrease with the age as senior citizens develop acidic problems and stomach enzymes needed to process the vitamin. Person with the deficiency of this vitamin may develop anemia, nerve cells may not work properly and the brain function gets impaired leading to memory problems, irritability and even dementia.

Both vitamin b12 and folate are required for the synthesis of monoamines such as dopamine and serotonin. These monoamine neurotransmitters are important in the pathophysiology of neuropsychiatric disorders such as depression and psychosis. For the synthesis of S-adenosylmethionine (SAM) vitamin b12 is required and this SAM acts as a methyl donor in certain methylation reactions in nervous system. As SAM shows antidepressant properties so disruption in formation of SAM leads to depression.



Deficiency also leads to nerve damage as normal levels of vitamin b12 in the body helps to keep the myelin sheath intact with protects the nerves from toxins and free radicals. Absence of myelin sheath may damage the nerves and the nerves may even die which ultimately lead to some nerve – related conditions. Myelin sheath is also absent in patients with Alzheimer’s disease. Apart from this, vitamin b12 helps to maintain DNA’s health thereby keeping cells younger. Moreover, good levels of vitamin b12 helps to keep levels of Homocystiene down which is very essential to keep the heart healthy as high levels of Homocystiene damages arteries leading to inflammation and heart disease. Not only higher levels of Homocystiene affect the heart but also lead to osteoporosis.

#### OBJECTIVE:

1. To assess the B12 status in elderly individuals.
2. To identify the B12 mediated oxidative stress markers and their quantification in such individuals.
3. To assess the cognitive ability of such persons.

#### II. REVIEW LITERATURE:

- Battacharjee et al (2016) reported that in rats vitamin B12 and folic acid prevents nicotine mediated oxidative stress in pancreatic cells.
- Bito et al (2017) reported that B12 deficiency in worms leads to severe oxidative stress, which significantly impaired memory retention. Unpublished data indicate that B12 deficiency causes the accumulation of S-adenosylhomocysteinine in worms and mammals which resulted in severe oxidative stress. Results indicate that vitamin B12 deficiency disrupts cellular redox homeostasis to induce severe oxidative stress.
- Lee et al (2016) stated that vitamin B12 status is significantly negatively correlated with the levels of blood glucose, oxidative stress and positively correlated with antioxidant enzyme activity in diabetic vegetarians.
- Obeid and Herrmann (2006) reported that hyperhomocysteinemia can be acquired in case of cofactor deficiency that is vitamin B12, B6 and folate, certain medications and diseases.
- Qureshi et al (2008) stated that vitamin B12 may have roles in the prevention of disorders of the CNS development, mood disorders and dementia. Deficiency of vitamin B12 in pregnancy leads to elevated levels of Homocystiene in foetus and increases the incidence of developmental defects in its nervous system. Free radicals can damage cells

directly through oxidation of biological molecules thus promoting a cascade of events leading to neuronal degeneration.

- Parker et al (2017) stated one explanation for the increased prevalence of autism is that increased exposure to acetaminophen, exacerbation by inflammation and oxidative stress, is neurotoxic in babies and small children. Excessively high levels of maternal vitamin B12 and vitamin B9 are additional risk factors linked to autism.
- Schiavone et al (2013) reported that oxidative damage leads to neurodegenerative diseases such as Alzheimer’s disease, Parkinson’s disease and psychiatric disorders in both animal models and patients. Accumulation of reactive oxygen species leads to increased Blood-Brain barrier permeability, alteration in brain morphology and neuronal death.
- Rizzo et al (2016) reported that vitamin B12 deficiency could be related to oxidative stress markers like plasma glutathione, serum total antioxidant capacity which could contribute to a neurophysiological disturbance.
- Black M.M (2008) reported that deficiency in cobalamin or folic acid have also been related to symptoms of depression in adults.
- Solomon (2015) reported that vitamin B12 responsive neuropathies are thus:
  1. Common even when confounding disorders are present
  2. Dissociated from presence of hematological abnormalities
  3. Dissociated from the presence of vitamin B12-responsive metabolic abnormalities
  4. Associated with the presence of oxidant risk when vitamin B12 levels are normal
- Deans (2016) stated that vitamin B12 is essential to brain health. It is vital for nerves to work properly. Deficiency of this lead to nerve death with other symptoms including depression and anxiety and is not found in vegan’s diet. Overall oxidative stress increases with inflammation and our ability to recover decreases.
- Qureshi et al reported that deficiency of vitamin B12 might increase the risk of having Parkinson’s disease. Therefore, higher dietary intake of folate, vitamin B12 and vitamin B6 might decrease the risk of Parkinson’s disease through decreasing plasma Homocystiene. Memory deficits and slowing of mental processes are the most commonly reported cognitive disturbances in cobalamin deficiency, but organic mental changes



resulting in hallucinations and delirium have also been reported.

#### TECHNICAL PROGRAMME OF WORK:

##### EXPERIMENT—1

**Name of the experiment-** Evaluation of dietary habits, cognitive functions and estimation of levels of oxidative stress markers in blood

**Methodology:** In this study, 50 each male and female senior citizen will be taken from local community and from different ethnic groups. They will be surveyed for their dietary habits and cognitive functions will be measured. To know the daily intake of vitamin B12, the diet analysis will be done. Blood analysis will be done to measure the level of vitamin B12 (Hunaiti and Mustafa 2016) and oxidative stress markers in vitamin B12 deficiency like plasma glutathione (Fitri et al 2016), serum total antioxidant capacity (TAC) and malondialdehyde (MDA) (Hunaiti and Mustafa 2016)

##### Observations to be recorded:

- Dietary habits
- Cognitive functions
- Vitamin B12
- Plasma glutathione
- Serum total antioxidant capacity
- Malondialdehyde

**Statistical Analysis:** Data will be analyzed by using SPSS software using suitable statistical design

##### EXPERIMENT—2

**Name of the experiment-** Evaluation of selected individuals after the administration of vitamin B12

**Methodology:** After, half of the individuals will be selected. The individuals will be supplemented with a required amount of vitamin B12. The brain functioning will be recorded. The level of oxidative stress markers like plasma glutathione, serum total antioxidant capacity (TAC) and malondialdehyde (MDA) will be measured in the blood of the controls.

##### Observations to be recorded:

- Brain function
- Plasma glutathione
- Serum total antioxidant capacity
- malondialdehyde

**Statistical analysis:** Data will be analyzed by using SPSS software using suitable statistical design.

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