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A CORRELATIVE STUDY OF CALCIFEROL WITH HOMOCYSTEINE, FOLIC ACID, AND COBALAMIN IN THE PATIENTS OF ALZHEIMER'S DISEASE: A CASE-CONTROL STUDY

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Abstract:
Background: Alzheimer's disease is a degenerative irreversible brain condition that gradually damages memory, reasoning, and abilities, and ultimately the ability to effectively carry out the most basic tasks. Low level of vitamin D might be the risk factor of Alzheimer's disease. Insufficient levels of folic acid may cause hyperhomocysteinemia, which may lead to oxidative stress in brain tissue and harm neurons.
Aim: The motive of the study was to find out the association and correlation of Vitamin level with folic acid, vitamin B12 and homocysteine in the subjects with Alzheimer's disease.
Method: This study was included 112 participants, out of these 56 cases and 56 control group. Patients having dementia were included in this study after taken ethical clearance certificate from IEC committee of BHU. Vitamin D, Homocysteine, folic acid and vitamin B12 were estimated for both group (Cases and control).
Result: This study observed negative correlation of vitamin D with Homocysteine and folic acid and positive correlation with vitamin B12, which was found statistically not significant (p-vale >0.05).
Conclusion: Vitamin D and folic acid deficiency is leading cause of Alzheimer's disease, which can reduced homocysteine level and harm brain tissues.

Keywords: Alzheimer's disease, Vitamin D, Vitamin B9, Vitamin B12 and Homocysteine.

Introduction:

Alzheimer's disease is also characterized by degenerative changes in specific brain regions, such as the temporal and parietal lobes, as well as confined areas of the frontal cortex and cingulate gyrus. Specific characteristics of Alzheimer's dementia may be attributed to the deterioration of these systems[1,2]. Previous studies demonstrate that low blood vitamin D levels are related with widespread Alzheimer disease (AD), dementia, and cognitive impairment[3]. The human brain has both the 1,25-dihydroxyvitamin D3 receptors and the enzyme 1α-hydroxylase, which synthesizes the bioactive form of vitamin D[4,5]. Vitamin D stimulates macrophages to improve phagocytic clearance of amyloid plaques and decreases amyloid-induced cytotoxicity and death in primary cortical neurons[6,7]. Vitamin D insufficiency has also been associated to vascular dysfunction, increased risk of ischemic stroke,

and brain shrinkage[8]. Folate deficiency may cause hyperhomocysteinemia, which can worsen oxidative stress in brain tissue and harm neurons. FA may reduce homocysteine levels in brain tissue, lowering oxidative stress and increasing cognitive function[9]. Homocysteine (Hcy) is a sulfur-containing amino acid that helps transfer methyl groups during cellular metabolism. High circulating levels of Hcy are a modifiable risk factor for dementia and Alzheimer's disease[10,11]. The B-group vitamins (B-2, B-6, folic acid, and B-12) have a role in Hcy metabolism. Deficiencies in folate and vitamin B-12 have been linked to elevated plasma homocysteine levels. Hyperhomocysteinemia may be utilized as a biomarker of these vitamin deficiencies[12,13].

Aim of study: The motive of the study was to find out the association and correlation of Vitamin level with folic acid, vitamin B12 and homocysteine in the subjects with Alzheimer's disease.

Method:

This study was conducted at the Institute of Medical Sciences, BHU, Varanasi, in the Department of Biochemistry in collaboration with the Department of Psychiatry. 56 control subject and 56 cases of Alzheimer disease-related senile dementia are included in this research. Between December 2014 and May 2016, the study included senior citizens between the ages of 60 and 75 who have been diagnosed with Alzheimer's-type senile dementia. Before starting the research, ethical approval was obtained from the Institute Ethics Committee, and informed permission was obtained before blood samples were collected in each case and control. Blood sample was analyzed for serum vitamin D, vitamin B9, vitamin B12 and Homocysteine for both the groups (case and control).

Inclusion criteria: All the patients are diagnosed by the consultant of psychiatry according to DSM IV and NINCDS-ADRDA criteria. Patients having dementia as rated on clinical dementia rating scale.

Exclusion criteria: Patient suffering from any significant co-morbid physical illness. Patient suffering from any of clinically diagnosed DSM V psychiatric illness. Patient suffering from any nutrition deficient status. Patient not accompanied by any caregiver.

Statistical analysis:

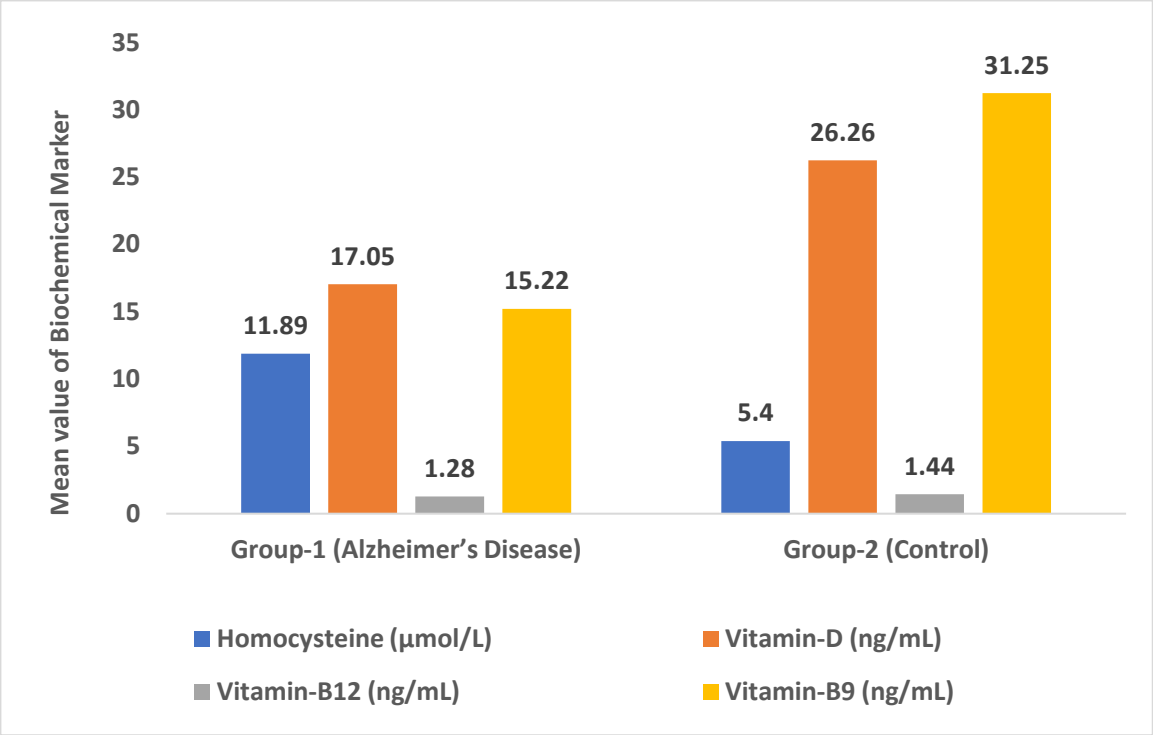
All the collected data were entered in MS office Excel Sheets and analyzed data with the help of SPSS 29.0 software. Descriptive analysis was used to calculate mean and standard deviation value. Pearson tool was applied to find out the correlation in between variance and calculate r value. Paired t-test for equal variance was applied to find out the statistical mean difference in two groups. P-value was calculated with the help of t-test value and r value (<0.05 considered as significant, <0.01 considered as highly significant and >0.05 considered as statistically not significant).

Result:

This study observed statistically significant association of vitamin D, folic acid and homocysteine in the patient of Alzheimer's disease. Table 1 and chart 1 is showing the decreased concentration of calciferol (17.05± 16.04), vitamin B12 (1.28 ± 1.12) and Vitamin B9 (15.22 ±14.85) in Alzheimer's subjects as compared to control group. t-test value for HCY is 4.04 (p-value: <0.01), for Vitamin B9 is 1.89 (p-value: 0.032), for calciferol is 2.67 (p-value: 0.0049) and for vitamin B12 is 0.87 (p-value: 0.87 (p-value: 0.194, which is found statistically not significant).

Biochemical Marker	Group-1 (Alzheimer's Disease)		Group-2 (Control)		t-test	p-value	Significance
	Mean	± Sd	Mean	± Sd			
Homocysteine (µmol/L)	11.89	8.01	5.40	4.62	4.04	0.000084	HS
Vitamin-D (ng/mL)	17.05	16.04	26.26	25.12	1.89	0.032	S
Vitamin-B12 (ng/mL)	1.28	1.12	1.44	0.74	2.67	0.0049	HS
Vitamin-B9 (ng/mL)	15.22	14.85	31.25	28.89	0.87	0.194	NS

Table-1: Comparison of Vitamin-D, Vitamin B12, Vitamin-B9 and Homocysteine level in between cases and control.

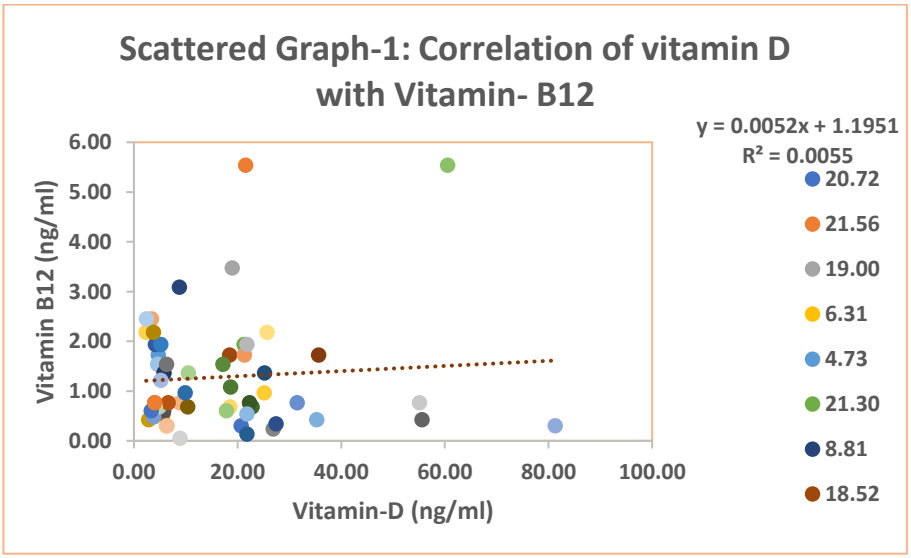


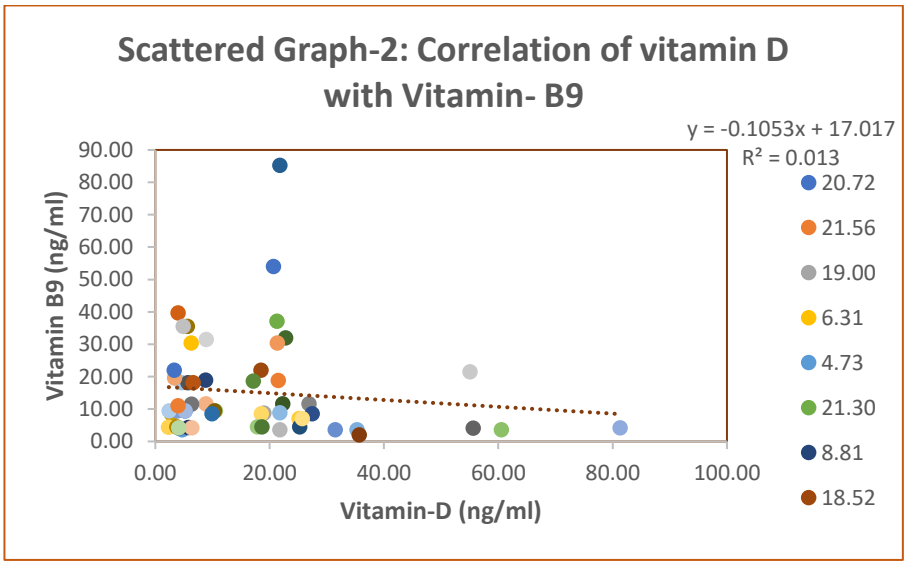
Graph Chart-1: Comparison of Vitamin-D, Vitamin B12, Vitamin-B9 and Homocysteine level in between cases and control.

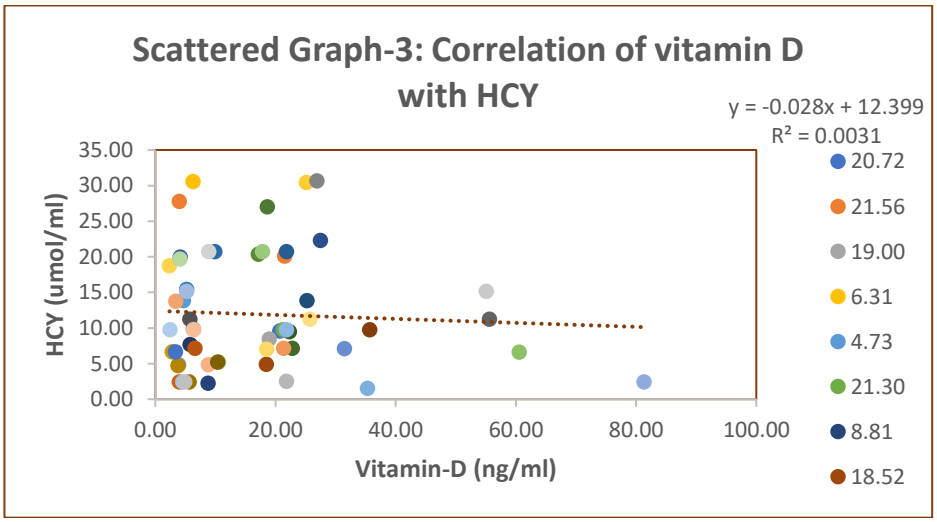
Table 2 is showing the correlation of Vitamin D with HCY, vitamin B9 and vitamin B12 in cases. Vitamin D has negative correlation with HCY (r-value: -0.056, r square value-0.003, p-value-0.68), and Vitamin B9 (r-value: -0.113, r square value-0.013, p-value-0.41), which is found statistically not significant. Vitamin D has positive relation with Vitamin B12 (r-value: +0.074, r square value-0.005, p-value-0.59), which is also statistically not significant.

Correlation Table		r-value	r square	p-value	Significancy
Vitamin-D	**Homocysteine**	-0.056	0.003	0.68	NS
	Vitamin-B9	-0.1138	0.013	0.41	NS
	Vitamin-B12	+0.074	0.005	0.59	NS

Table-2: Correlation of Vitamin D with HCY, vitamin B9 and vitamin B12 in cases.







Discussion:

In this research, we have found negative correlation of vitamin D with homocysteine, vitamin B9 and positive correlation with Vitamin B12, but relation of these marker is statistically not significant. Vitamin D level is decreased in cases as compared to healthy control. Vitamin B9 is also found in lower range, which is the major risk factor of imbalance homocysteine level and harm brain tissue to cause Alzheimer's disease. Vitamin B9 is also required to metabolized cobalamin and homocysteine, which are used to synthesized various neurotransmitters and helps in one carbon pool. Zuliani G et.al; found statistically significant higher level of homocysteine in dementia. He suggests that hyperhomocysteinemia may harm the neurological system by increasing the risk of vascular disease[14]. Litu W. et.al; were explain that, vitamin D has negative relation with homocysteine and folate in Alzheimer's patients. His study suggests the intake of vitamin D and folate to address vitamin D deficiency may enhance the performance of the nervous system[15]. Clark R. et.al; were said that Alzheimer's disease was linked to low blood folate and vitamin B12 levels, as well as high tHcy levels. The stability of tHcy levels over time, as well as the absence of a link with the length of symptoms, rule out these results being a result of illness and call for more research to determine the clinical implications of these relationships for AD[16].

Conclusion:
Vitamin D and folic acid deficiency is leading cause of Alzheimer's disease, which can affect homocysteine level and harm brain tissues. Vitamin B9 is also required to metabolized cobalamin and homocysteine, which are used to synthesized various neurotransmitters and helps in one carbon pool.

Conflict of interest: Nill.

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