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Research Article

Correlation between vitamin D and carotid artery intima media thickness in patients with ischemic stroke

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ABSTRACT

Background: This study aimed to investigate the relationship between serum vitamin D level and carotid artery intima-media thickness in ischemic stroke patients. The correlation of vitamin D and carotid artery intima media thickness in ischemic stroke patients had conflicting results in different parts of the world.
Methods: 217 patients with CVA infarct were selected for analysis between ages 45 and 80 years admitted at our hospital from January 2014 to December 2015. Measurements of serum vitamin D concentration and Carotid-IMT were made by electrochemiluminescence immunoassay and B-mode ultrasound, respectively. Confounding variables like diabetes, hypertension, smoking, alcohol, tobacco, dyslipidemia, BMI, CRP, Serum uric acid, duration of sunlight exposure, prior history of drug intake or fracture and Serum calcium were considered. 200 age and sex matched controls were taken. Questionnaires were used for data collection and multiple linear regression analysis and correlation analysis were used.
Results: The mean serum level of vitamin D was 19.14±9.45 SD ng/mL and average IMT was 0.78±0.09 SD mm with pearson coefficient of (-0.36) significant at 0.01 level. The R^2 value was 0.13.
Conclusions: Correlation analysis found an inverse relationship between serum vitamin D level and carotid-IMT in ischemic stroke patients.

Keywords: Vitamin D, Cerebral infarction, Carotid intima-media thickness

INTRODUCTION

Carotid atherosclerosis is a progressive multifactorial artery disease associated with high risks of morbidity and mortality.[1] Subclinical carotid atherosclerosis is an acknowledged challenge in primary stroke prevention.[2] Several underlying environmental and modifiable factors such as elevated systolic blood pressure (SBP), dyslipidemia, smoking and increased body mass index (BMI) play a significant role in the progression of the atherogenic process.[2] Carotid intima-media thickness (IMT) and plaque assessment by cervical ultrasonography is a noninvasive, feasible, and accurate method for detecting asymptomatic carotid atherosclerosis.[3] It is also largely used for risk assessment in primary prevention and in clinical trials as a surrogate endpoint for cardiovascular and cerebral events.[3] Both IMT and total plaque area (TPA) are associated with an increased risk of ischemic stroke and coronary heart disease.[4] It is well established that the presence of carotid plaques represents advanced carotid atherosclerosis, often symptomatic, whereas IMT can be assessed in the absence of focal plaques and symptoms.[5]

Altered calcium homeostasis, including vitamin D deficiency, was found to be associated with subclinical atherosclerosis and low bone mineral density.[6] Vitamin D insufficiency has been linked to cardiovascular diseases, infections, and even cancer in recent large epidemiological studies.[7] Low serum levels of 25-

hydroxyvitamin D (25(OH)D) is also shown to be associated with insulin resistance.[8]

Studies have also demonstrated that 25-hydroxyvitamin D deficiency is a novel CV risk factor, predicting both CV events and mortality.[9] Vitamin D deficiency is associated with changes in PTH, calcium, phosphorus, and 1,25-dihydroxyvitamin D levels (1,25(OH)2D).[10] The mechanisms by which vitamin D deficiency affects cardiovascular health are being investigated.[11]

Carotid atherosclerosis leading to increased carotid artery initma media thickness is an important factor in ischemic stroke patients.[12] Low vitamin D levels have been associated with increase in intima media thickness.[6] This correlation has conflicting results in various studies in different parts of the world.[13]

METHODS

A Case control study where all cases of ischemic stroke admitted from Neurology clinic, OPD and Medicine wards of LLR and Associated Hospitals, Kanpur, India from January 2014 to December 2015 and age and sex matched controls not having ischemic stroke were taken after informed consent.

Age group >30 years irrespective of sex with diagnosis of ischemic stroke by CT scan or MRI brain were included in the study and patients with valvular heart disease, cardiomyopathy, congenital heart disease and connective tissue disorders were excluded.

Detailed history and clinical examination focusing on carotid bruit, BMI & BP were taken. Serum vitamin D (25-hydroxy vitamin D) level was measured by chemiluminescence method by Architect i1000SR Machine (Abbott laboratories, Abbott park, IL 60064 USA) from morning fasting sample. Serum 25-hydroxy vitamin D <20ng/ml was considered as deficient and >30ng/ml as adequate.[14] Serum uric acid, serum calcium, CRP, complete blood count, serum creatinine, BUN, Liver function tests, serum electrolytes, blood sugar (Fasting, Post prandial) and lipid profile were measured by automated analysers. CT scan of head (plain) was done. Doppler ultrasound of carotid arteries (using MEDISON Sonoace X8 ultrasound machine) (Medison Co Ltd, 1003 Daechi-dong, Gangnam-gu, SEOUL 135-280 Korea) was done. EEG (wherever feasible and indicated) and MRI Brain (wherever feasible and indicated) were done.

Carotid Doppler ultrasound

In the supine position neck of the patient was slightly extended and rotated in the direction opposite to the probe. A multiple frequency (5 to 12MHz) linear array transducer attached to a MEDISON Sonoace X8 ultrasound machine was used to acquire images by a single-sonographer blinded to clinical status of the subjects. The intima media thickness was measured in a plaque free region 20mm from the bifurcation and an average of three measurements from each side was recorded according to Mannheim Carotid Intima-Media Thickness Consensus (2004–2006) (Figure 1).[15]

Figure 1: Measurement of carotid artery intima media thickness.

RESULTS

12.9% cases had adequate vitamin D levels whereas 70.04% cases had vitamin D deficiency. 22% controls had adequate vitamin D levels whereas 43% controls had vitamin D deficiency the average IMT was highest in 50-60 years (0.82±0.08 SD mm) followed by 60-70yrs (0.77±0.12 SD mm) and 40-50yrs (0.77± 0.06 SD mm). The association between age and IMT was found to be significant. Vitamin D deficiency was higher in cases (87%) as compared to controls (78%) and this association was found to be statistically significant(Chi square = 5.409, df=1, P = 0.02 and Odds Ratio=0.5253(95% CI:0.3125 to 0.8828) (Table 1).

Table 1: Comparison of deficiency of vitamin D in cases and controls.

Vitamin D (ng/ml)	Cases	Controls	Total
<30	189 (87%)	156 (78%)	345
>30	28 (12.9%)	44 (22%)	72
Total	217	200	417

Mean vitamin D level in cases was 19.142+/- 9.453 SD ng/ml whereas in controls it was 23.974 +/- 13.125 SD ng/ml. This association was found to be statistically significant (t = 4.338 df=415 P=<0.0001). Mean IMT in cases was 0.7894 +/- 0.09 SD mm whereas in controls it was 0.4937 +/- 0.07 SD mm. This association was found to be statistically significant (t= 34.899 df= 415 P <0.0001). There is a significant negative association between average IMT and vitamin D levels in cases but the correlation coefficient is -0.3624(r= -0.3624, P<0.0001) (Figure 2).

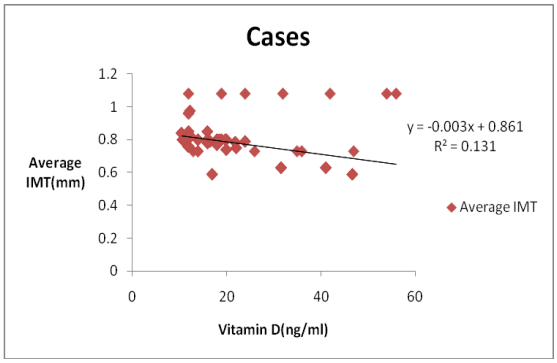

Figure 2: Correlation of vitamin D with Average IMT in cases.

There is a significant negative association between average IMT and vitamin D levels in controls but the correlation coefficient is -0.3322 (r =-0.3322, P =<0.0001) (Figure 3).

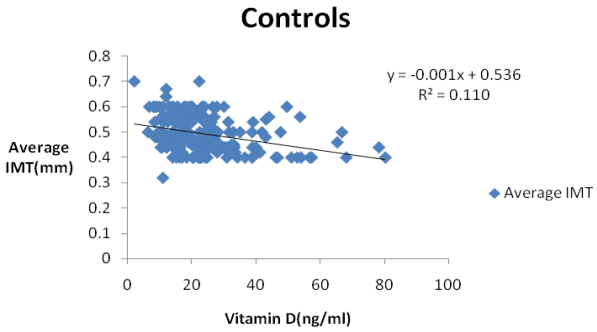

Figure 3: Correlation of vitamin D with average IMT in control population.

DISCUSSION

Our study was a case control based study where we found significant negative association between vitamin D and carotid artery intima media thickness in patients with ischemic stroke similar to the study of Carrelli AL et al.[6] We also considered other confounding variables like diabetes, hypertension, smoking, alcohol, tobacco, dyslipidemia, BMI, CRP, S. uric acid, duration of sunlight exposure, prior history of drug intake or fracture and S. calcium.

Majority of the subjects were deficient in vitamin D in our study similar to that stated by Lips P et al where serum 25(OH) D was lower with higher latitudes and with darker skin types. They showed that India and China had more prevalence of vitamin D deficiency (serum 25(OH) D<25 nmol/l) as compared to Japan and South-East Asia.[16]

Verdoia M et al included patients undergoing elective coronary angiography whereas we included all patients with ischemic stroke and non stroke individuals.[17] In our study hypovitaminosis D was observed in 83% of 417 subjects whereas in their study hypovitaminosis D was observed in 70.4% of 1484 patients.

Our study had the mean carotid IMT higher in patients with ischemic stroke similar to that of Freitas D et al who found increased CCA intima-media thickness was associated significantly and on an approximately linear way with ischemic stroke but not with hemorrhagic stroke.[18]

In our study also there is inverse correlation between vitamin D and carotid IMT. Zittermann A et al suggested vitamin D exerts a biphasic dose response curve on vascular calcification with deleterious consequences not only of vitamin D excess but also of vitamin D deficiency.[19] Hsu JJ et al found that there is a narrow range of vitamin D levels in which vascular function is optimized.[20] Levels above or below this range seem to confer a significant increase in risk for cardiovascular disease.

CONCLUSION

From this study it can be concluded that serum vitamin D level is inversely correlated with carotid artery intima media thickness in patients with ischemic stroke as well as in general population. Majority of the population is deficient in vitamin D levels. The average Intima media thickness was higher in CVA infarct patients than the general population.

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