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KEY WORDS:

ASSOCIATION OF VITAMIN D3 LEVELS AND PREVALENCE OF CARDIOVASCULAR MORBIDITY IN TYPE 2 DIABETES IN A PERIPHERAL HEALTH INSTITUTION

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ABSTRACT

A number of previous studies reflect a close association of low levels of l25-hydroxyvitamin D3 [25(OH)D] and diseases like insulin resistance (1)metabolic syndrome (2,3), type 2 diabetes(4-6), and cardiovascular disease(CVD) (7). However the exact relation of vitamin D3 levels with the development of cardiovascular morbidity needs to be evaluated. There has been biased data in the past and many studies have varied conclusions regarding the association of the two entities (8,9). Since prevalence of Vit D3 deficiency as well as type2 diabetes is quite high in our setting, we tried and carried out this single centre prospective study to look into the association of cardiovascular morbidity and the levels of vitamin D3 at our peripheral health institute.

RESEARCH DESIGN ANDMETHODS—

This is a single centre, cross-sectional, carried out at civil hospital Nagrota Bagwan, district Kangra, Himachal pradesh. The patients were enrolled in July 2019.We enrolled 50 consecutive routine patients having type 2 diabetic outpatients attending our diabetic clinic. 50 age and sex matched control patients were also enrolled who did not have type2 diabetes. A well informed written consent was obtained from the patients.

The following exclusion criteria were followed:

1. Recent illness
2. Advancedliver or renal disease
3. Cancer patients
4. Patients on anti seizure medications, steroids or any other drug interfering withVitD3 metabolism

Laboratory investigations were carried out by standard laboratoryprocedures. The levels of serum Vit D3 were measured using an automated immunoassay. Adult Treatment Panel III criteria (10) were used for classifying the metabolic syndrome. All the patients were thoroughly examined in our clinic for the presence of cardiovascular diseases like coronary artery disease, peripheral vascular disease, stroke etc. The cardiovascular disease status was confirmed both by examination and further by appropriate biochemical, disease specific investigations.

The statistical analysis was done using statistical package for social sciences 23.0 (SPSS) for windows. The demographic data was tabulated in Microsoft Excel. Measures of central tendency (mean, median) were calculated for all quantitative variables along with measures of dispersion (standard deviation, standard error) are presented as mean, median, range, etc. Comparison between discrete variables will be done by Chi square test, while continuous variables will be compared using Non parametric tests such as Mann Whitney test. The categorical variables were compared by Fisher's exact test. Risk ratio was calculated to denote the risk of various factors.

P value of ≤ 0.05 will be considered as statistically significant. The final aggregate end point was taken as presence of CVD taking into account minimum of one atherosclerotic. The cut off definition of low vit D was taken as a value of serum 25(OH)D concentration of 20 ng/ml (11,12).

RESULTS—

The mean (_SD) 25 (OH)D concentrationswere 25 ± 8.1 ng/ml among control subjects and 18.6± 10 ng/ml (17,3–76) among diabetic patients. The ageandsex-adjusted prevalence of hypovitaminosisD was higher in diabetic patients than in control subjects (56 vs 44%, *P* _0.001).As shown in Table 1, females having diabetes have increased prevalence of hypovitaminosis

Also the patients who were on insulin therapy as well as other agentslike lipid-loweringdrugs;antiplateletsdrugs had more prevalence of low vitD3 levels

Overall, 18(36%) of 50 patients had CVD. Of these, 9patients had coronary heart disease,2 had cerebrovascular disease and 2hadperipheral vascular disease. As shownin Table 1, the prevalence of CVD wasgreater among those with hypovitaminosisD. The duration of diabetes also have some significance (p=.05) with low vitamin D3 levels.

Table.1 Baseline patient characteristics

Variables	Without Low vitamin D3 (28.6±7ng/ml)	With low vit D3 (16.2±3 ng/ml)	p-value
N	19	31	Ns
Sex			
Male	5	9	0.001
Female	12	24	0.001
Age(years)	62±5	61±7	Ns
BMI(kg/m2)	26±3.2	27±2.1	Ns
Diabetes duration(years)	6±3	8±4	0.05
Insulin therapy	2	8	0.01
Oral hypoglycaemic drugs	19	31	0.01
Statins/ antiplatelets	9	16	0.01
HbAIC	7±1.3	7.6±1.5	0.01
Cardiovascular diseases	4	14	0.01
Aggregate End point			
Coronary heart disease	3	6	0.01
Cerebrovascular disease	0	2	0.001
Peripheral vascular disease	1	1	Ns

CONCLUSIONS— in this small study we found that there is increased prevalence of low vit D3 levels in patients with type 2 diabetes and a strong association between the presence of cardiovascular events in those patients. Similarly it can be concluded that the duration of diabetes also carries the risk of development of adverse cardiovascular events. Interestingly the prevalence of low vitD3 levels was also associated with the

longer disease duration. These findings suggest that there is potential role of vitamin D3 supplementation in the patients in order to prevent the adverse CVD outcomes. The available data also suggests the inverse relation of low vitamin D3 levels and the presence of calcifications in coronary micro vasculature (13,14). Many past by experimental studies reflect the influence of low vitamin D3 level and the natural activity of(15-19)macrophages and lymphocytes in atherosclerotic plaques. Further these chronic inflammatory changes paves the pathway in the development chronic inflammation in the coronary arteries. There is some data to suggest the potential benefits of vitamin D3 supplementation in preventing cardiovascular events

(20,21) where vitamin D supplementationmarkedly reduced serum levelsof CRP, interleukin-6, and tissue matrixmetalloproteinases. Similarly low vitamin D3 levels induced secondary hyperparathyroidism have been linked to insulin resistance (22). All these findings guide us to the conclusion that low level of vitD3 is a potential risk factor for the development of cardiovascular events particularly where type2 diabetes is the prime comorbidity. However our study has some limitations. Becauseour study was a cross-sectional one,the causative nature of the associationscannot be established. Additionally the number of patients involved was small and to establish the exact association we need to further investigate with a larger sample size of the patients. Also the levels of parathyroid hormones were not done. So to conclude we definitely have evidence to suggest the role of low vitamin D3 with the occurrence of adverse CVD events especially in patients with Type2 diabetes. However we need further detailed set of studies to know the exact association.

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