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Does Vitamin D deficiency silently increase risk for cardiovascular disease? A cross sectional study in the population of West Bengal, India.

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Abstract:
Background: *Vitamin D deficiency is quite common worldwide, as well as in our population. It has been indicated in some recent studies, that Vitamin D deficiency is associated with some of the well known risk factors of cardio Vascular Diseases, like BP, Cholesterol, Blood Glucose, Blood Insulin level etc. There is very little data among the Indian population in this regard, inspite of wide prevalence of Vitamin D deficiency in the population. The Present study was aimed at bridging some of that gap.*
Materials and Methods: *In this cross sectional, observational study, 68 participants, all coming to the Biochemistry Department for Blood Vitamin D estimation, without any prior Cardio Vascular Disease history, were included. Their Blood Pressure were measured and fasting Blood samples were collected followed by estimation of Plasma Glucose and serum Cholesterol, Insulin and Vitamin D. The participants were divided into three groups dpending on their Vitamin D levels (Vitamin D sufficient, insufficient and deficient) and the other parameters were compared among three groups. The parameters indicating cardiovascular risk were also analyzed for correlation with Vitamin D levels.*
Results: *Systolic BP, Cholesterol and Insulin, all were found to be significantly different (P<0.001) among the three groups and these parameters also showed significant correlation (P<0.001) with Vitamin D. Fasting blood glucose levels however did not show any significant difference among groups or correlation with vitamin D (P>0.05).*
Conclusion: *The evidence from present study indicates higher risk of Cardiovascular Disease in the Vitamin D deficient patients in the population of West Bengal too. Since Vitamin D deficiency is quite prevalent and often undiagnosed in this population, it is very important to regularly check for the risk factors of Cardio vascular diseases in the Vitamin D deficient patients.*
Key words: *Vitamin D deficiency, Cardio Vascular Disease, Insulin, Cholesterol, Systolic BP*

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I. Introduction:

The major biologic function of Vitamin D in humans is to maintain serum calcium and phosphorus concentrations within the normal range by enhancing the efficiency of the small intestine to absorb these minerals from the diet[1]. Vitamin D deficiency is widely prevalent in the India and world-wide[2]. Low levels of 25-hydroxy vitamin D [25(OH) D], the principal circulating storage form of vitamin D, are present in one third to one half of otherwise healthy middle-aged to elderly adults[2-4]. Vitamin D metabolites also play an integral physiological role in no skeletal tissues and have been implicated in a wide range of chronic pathology, including skin and autoimmune disease, cancer, diabetes mellitus, hypertension, and cardiovascular disease (CVD). Although most consequences of vitamin D deficiency involve the musculoskeletal system, there is a growing body of evidence suggesting that low levels of vitamin D may adversely affect the cardiovascular system[5]. Vitamin D deficiency, which is affected by multiple factors, appears to have an association with diverse cardiac diseases starting with its direct effect on the cardiac cell, its association with coronary artery disease (CAD), and its risk factors such as diabetes and hypertension (HTN). Vitamin D is believed to help

improve the body's sensitivity to insulin - the hormone responsible for regulating blood sugar levels – and thus reduce the risk of insulin resistance, which is often a precursor to type-2 Diabetes. Vitamin D may help regulate the production of insulin in the pancreas. Vitamin D has in vitro & in vivo effects on pancreatic β cells & Insulin sensitivity[6]. Insulin resistance represents a major underlying abnormality driving CVD, the major cause of CV morbidity & mortality in much of the world. Insulin resistance may increase the risk of CVD mortality in both men and women. There is lack of data in Indian population regarding vitamin D deficiency and its association with CVD risk factors. The present study is an effort to find out any possible relationship between Vitamin D deficiency with CVD and insulin resistance.

II. Materials and Methods:

- **Study area:** The study was done in the Department of Biocemistry, Nil Ratan Sircar Medical College And HOSPITAL, Kolkata, West Bengal, India.
- **Study type:** Cross sectional, observational study.
- **Study period:** The study was conducted from 13th June-17th July, 2018.
- **Sample selection:** Total 68 participants, all coming to the Biochemistry Laboratory for Vitamin D measurement were included in the study.
- **Inclusion Criteria:** Individuals, visiting the Biochemistry Laboratory of with advice of serum Vitamin D measurement.
- **Exclusion Criteria:** Individuals having prior history of Cardiovascular Disorders or Diabetes Mellitus
- **Collection of Sample:** Blood samples were taken from the participants after overnight fasting in Clotted and Fluoride vials. The samples were allowed to stand for 1hr and then centrifuged and serum and Plasma were separated and the tests done on the same day. The serum was collected for vitamin D, cholesterol, and insulin measurement and Plasma from Fluoride vial for Blood Glucose estimation.
- **Parameters to Be Studied:** Vitamin D, Cholesterol and Insulin were tested from the serum and Fasting Plasma Glucose was measured in the Plasma from the Fluoride vial. Blood Pressure were also measured in each of the participants before phlebotomy was done.
- **Measurement Methodology:**
  25 Hydroxy Vitamin D: Measured by standardized commercial ELISA kit
  Insulin: Measured by standardized commercial ELISA kit
  Cholesterol: Measured in Chemistry Autoanalyser by Cholesterol Oxidase - Peroxidase method, using standardized commercial kit.
  Fasting Blood Glucose: Measured in Chemistry Autoanalyser by Glucose Oxidase - Peroxidase method, using standardized commercial kit.
- **Statistical Analysis:** Statistical analysis of the data was done using SPSS (version 17) software. study subjects were divided into 3 groups, according to their Vitamin D levels. i. Vitamin D sufficient (>30)ii. Vitamin D insufficient (20-30)iii. Vitamin D deficient (<20); Different parameters were compared between these three groups by ANOVA test. Different parameters were also studied for any correlation with the Vitamin D levels, among all the participants, by Pearson Correlation test. Statistical significance were considered at a P value of <0.05.

III. Result:

The study subjects were divided into 3 groups, according to their Vitamin D levels.
i. Vitamin D sufficient (>30ng/mL))ii. Vitamin D insufficient (20-30ng/mL) iii. Vitamin D deficient (<20ng/mL);
Different parameters were compared between these three groups.

Table1: Showing comparison of means (by ANOVA) between three groups of study subjects

Parameter	Vitamin D Sufficient group (Mean ±SD)	Vitamin D Insufficient group (Mean ±SD)	Vitamin D deficient group (Mean ±SD)	Significance
Systolic BP (mm of Hg)	119.6±11.4	129.6±10.8	149.4±12.2	<0.001*
Cholesterol (mg/dL)	145.1±26.8	207±32.8	295.3±43.4	<0.001*
Insulin (mIU/L)	8.1±2.7	16.7±6.3	28.1±5.4	<0.001*
FBG (mg/dL)	95.6±13.4	97.1±33.5	92.3±13	0.583

*. Statistical Significance at P< 0.05

Fig 1: Comparison of Means of Different Parameters Between Three Groups

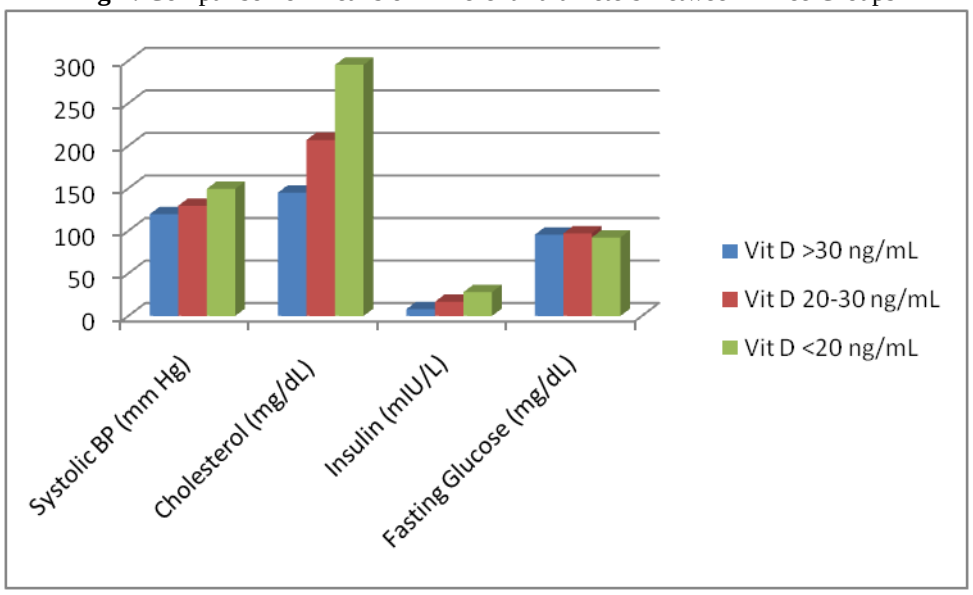


Table2: Showing Correlation of Vitamin D with various parameters

Parameter	Pearson Correlation co-efficient (R)	Significance (P)
Systolic BP	-0.591	<0.001*
Cholesterol	-0.761	<0.001*
Insulin	-0.712	<0.001*
Fasting Blood Glucose (FBG)	-0.067	0.815

*. Correlation is significant at P< 0.05

Fig2: Showing Correlation between Vitamin D And Systolic BP

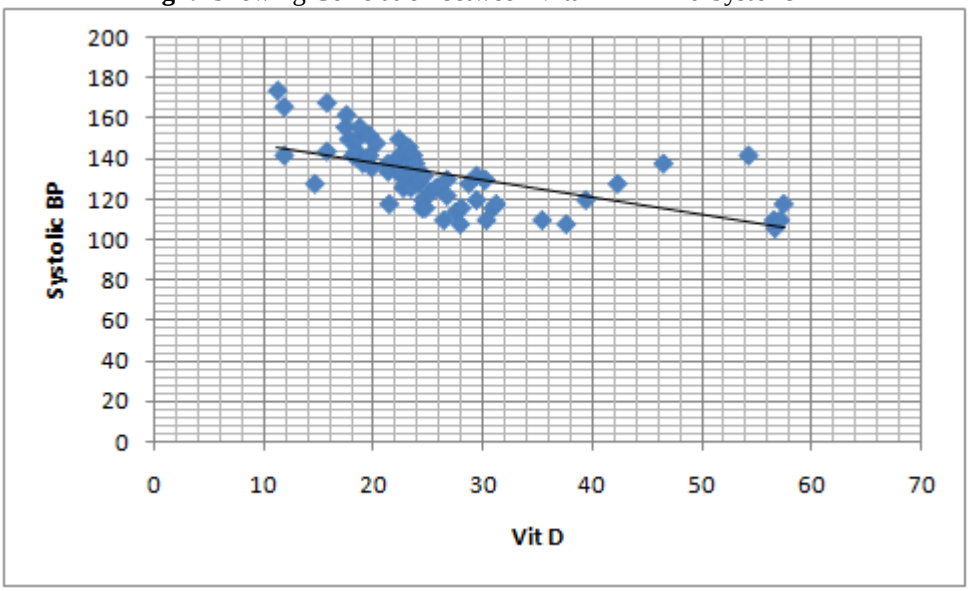


Fig 3: Showing Correlation between Vitamin D and Cholesterol

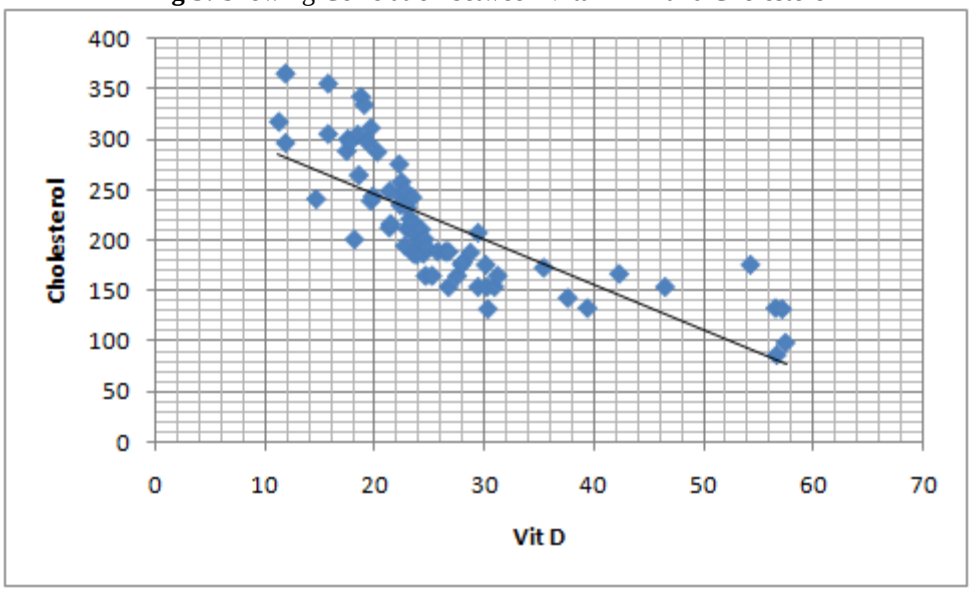
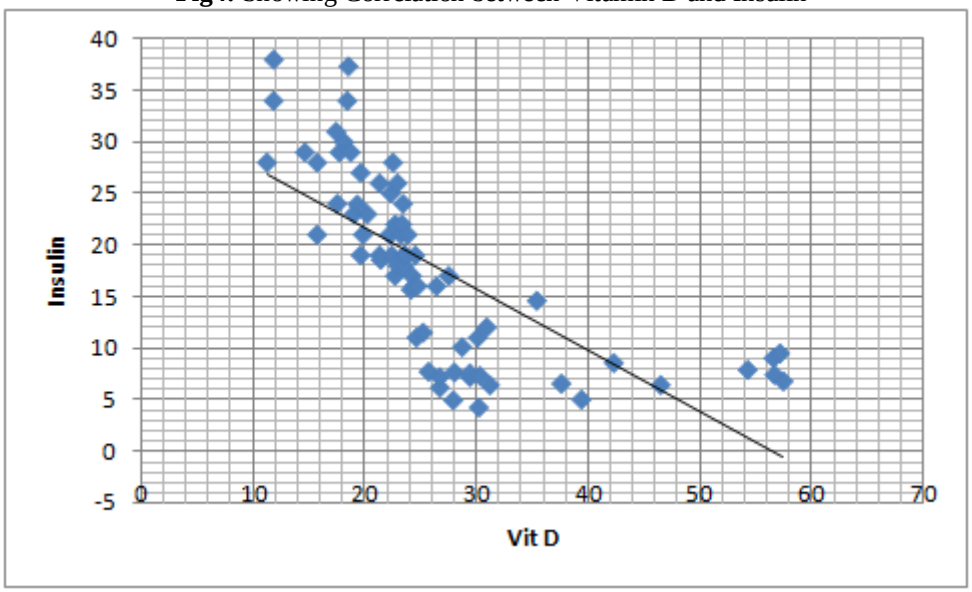


Fig4: Showing Correlation between Vitamin D and Insulin



IV. Discussion

In our study, we found systolic BP, insulin, cholesterol to be significantly higher in the vitamin D deficient and insufficient subjects in comparison to the subjects with sufficient levels of vitamin D($p<0.001$) [Table 1]. When we calculated the correlation of vitamin D with various parameters, we found that systolic BP ($R= -0.591$, $p= <0.001$), insulin ($R= -0.712$, $p= <0.001$), and cholesterol ($R= -0.761$, $p = <0.001$) showed significant negative correlation[Table 2].

However, we did not find any significant correlation of Vitamin D with FBG levels [Table 2]. We also did not find any significant difference in FBG levels between vitamin D deficient & sufficient groups [Table 1].

Vitamin D has effects on cholesterol metabolism & transport. Low levels of 25-OH Vit D is found to be associated with lower total cholesterol, lower LDL cholesterol, and higher high-density lipoprotein (HDL) cholesterol by different studies[7]. In the presence of sunlight, squalene in exposed skin is converted into 7-dehydrocholesterol & vitamin D, in the absence of effective sun-light, its metabolic pathway is diverted into the formation of cholesterol[8].

Vitamin D deficiency is detrimental to insulin synthesis& secretion. In human, vitamin D is positively correlated with insulin sensitivity & its role is mediated both by direct mechanism through the availability of vitamin D receptors in several tissues & indirectly through the changes in calcium levels. The activated form of vitamin D, Calcitriol, enhances the efficiency of intestinal calcium absorption[9]. A positive role for vitamin D in

the modification of the function of β cells of pancreas was found[10]. This role is mediated through several pathways, including direct stimulation of insulin secretion by vitamin D through the presence of VDR in β cells of the pancreas[10] and their expression of 1-ά- hydroxylase enzyme[11]. Also 1, 25-(OH) Vit D is able to activate transcription of the gene of human insulin & thus play an essential role in insulin secretion[12]. In a study of adults from North America, insulin resistance was noted to be associated with deficiency of serum 25(OH) Vit D[13].

There are also other mechanisms involved in the relationship between blood pressure (BP) and vitamin D. Vitamin D helps to lower blood pressure, by acting on smooth muscle cells of blood vessel wall. It also has role through "rennin-Angiotensin system". One large study found that people with higher levels of vitamin D had lower blood pressure and a lower risk of developing hypertension[14,15].

A study found that lower vitamin D levels are associated with higher FBG levels and pre-diabetes in Asian Indian women living in North India[16]. Many studies have shown an association between vitamin D deficiency and chronic diseases including cardiovascular disease and its risk factor including dyslipidemia[17].

Vitamin D status and CVD risk were paralleled by experimental studies elucidating mechanisms by which vitamin D deficiency may confer increased CVD risk. For example, VDR knockout results in increased ventricular mass and atrial natriuretic peptide levels and dys-homeostasis of cardiac metalloproteinase and fibroblasts, thereby promoting formation of a fibrotic extracellular matrix and leading to ventricular dilation and impaired electromechanical coupling[18,19].

Overall, our study results further confirm the concept of Vitamin D deficiency being associated with the increase in risk for cardiovascular diseases, especially confirming the same in the eastern Indian population.

V. Conclusion:

The present study clearly shows the strong association of Vitamin D deficiency with multiple clinico-pathological abnormalities that can be considered as risk factors for Cardio Vascular Disease. Vitamin D deficiency, which is quite common in our population, and often remains un-noticed, thus can be considered to be silently increasing the cardio vascular risk in the deficient individuals. Under the light of these evidences, more extensive, prospective studies on the presence of Vitamin D deficiency and its long term effect on cardiovascular risk factors are urgently warranted. Whether the Vitamin D supplementation has any long term beneficial effect on cardio vascular risk improvement is also needed to be studied.

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