ABSTRACT

Introduction: Vitamin D, popularly known as sunshine vitamin is both vital and indispensable for human beings. Ecological studies have reported higher rates of coronary artery disease (CAD) and hypertension attributed to the higher prevalence of vitamin D deficiency in regions with less exposure to sunlight. However, evidence concerning the relationship between vitamin D intake and CAD is still inconclusive with scientist recommending more studies and clinical trials. Aims & Objectives: To assess the lipid profile, plasma glucose and vitamin D levels in postmenopausal women with coronary artery disease and compare them with postmenopausal women without coronary artery disease. Materials & Methods: This cross sectional study was conducted on 82 postmenopausal women with 42 having angiographically proven CAD and 40 without CAD. Fasting blood sugar, lipid profile and Vitamin D3 levels were measured. Serum 25(OH) vitamin D was estimated by ELISA. Results: 54% of the postmenopausal women with CAD were diabetic and 17% of them were hyperlipidemic. About 72% of postmenopausal women were suffering from either vitamin D deficiency or inadequacy. Vitamin D levels were significantly decreased in patients with CAD than patients without CAD (19.2 ± 13.6 ng/dl vs 26.4 ± 13.01 ng/dl, p-value<0.022). A significant relationship was found between incidence of CAD and low levels of Vitamin D (p-value< 0.001). Conclusion: The establishment of association between vitamin D levels and CAD could be a milestone in the prevention of CAD among postmenopausal women. Exposure to sunlight and adherence to healthy life styles can help the postmenopausal women to achieve optimum vitamin D levels and further prevent the risk of CAD.

KEYWORDS: Vitamin D deficiency, Menopause, CAD.

INTRODUCTION

Vitamin D [1, 25(OH)2D], a fat-soluble steroid hormone plays an important role in calcium homeostasis and skeletal development. Vitamin D influences many physiological processes besides calcium/ phosphate homeostasis. Around 80% the Indian population have vitamin D levels less than normal. Vitamin D, popularly known as sunshine vitamin is both vital and indispensable for human beings. Ecological studies have reported higher rates of coronary heart disease and hypertension with increasing distance from the equator, a phenomenon that has been attributed to the higher prevalence of vitamin D deficiency in regions with less exposure to sunlight. However, evidence concerning the relationship between vitamin D intake and CHD is still inconclusive with scientist recommending more studies and clinical trials. Measurement of 25(OH) D in the circulation is the best diagnostic test to determine the vitamin D status of a person. Indian studies have reported that the vitamin D levels are considered normal when it is >30ngms/ml and it is insufficient when the level is between 20 – 30 ngms/ml and deficit when it is less than 20ngms/ml.[7]

Several studies have shown that cardiac myocytes express a functional VDR, which is primarily located in the nucleus and within, or adjacent to the t-tubules Cardiac fibroblasts also express the VDR. Considering that the conversion of 25(OH)D to 1,25(OH)2D by 1-alpha-hydroxylase in extra renal tissues is mainly dependent on substrate availability, this latter finding suggests that, apart from 1,25(OH)2D plasma levels, the concentrations of circulating 25(OH)D levels might be a significant determinant of vitamin D effects in the myocardium.

Coming to importance of Vitamin D in postmenopausal women a recent systematic review by Michael F Holic et al[8] concluded that the prevalence of inadequate 25 (OH)
D levels appears to be high in postmenopausal women and especially those with osteoporosis and a history of fracture.

In recent years, there has been an increase in interest to evaluate other potential functions of vitamin D and particularly with its relation to CHDs. Few studies have demonstrated an increased risk for CHD death in individuals with vitamin D deficiency. Some experimental studies have suggested several CHD protective mechanisms such as anti-atherosclerotic, anti-inflammatory and direct cardio protective actions.

Currently there are ongoing investigations as to whether there exists a relation between serum vitamin D level and CHD mortality in patients with heart conditions. However, a little evidence demonstrating the association is available. Accumulating evidence from several non-randomized studies also indicate that deficient 25(OH)D concentrations are associated with excess CHD mortality in the general population.

Randomized controlled trials with vitamin D supplementation have found some effect on CHD risk reduction. Forman JP et al performed a detailed investigation in United States among 283 African American subjects by giving Vitamin D for a period of 3 months in dosage of 2000/4000IU and followed them for the period of 6 months. Their results showed that there was a significant reduction in systolic blood pressure along with reduction in the incidence of coronary artery disease. This was also seen in a study done by Lind et al. Similarly, significant improvement in the cardiovascular risk markers was found by Zitterman et al in Germany.

Based on this background, the present study was designed to estimate the vitamin D levels in postmenopausal women with and without coronary artery disease. The study also evaluated the association of vitamin D levels with lipid profile in postmenopausal women and to correlate them with presence of CAD.

MATERIALS AND METHODOLOGY
The present cross sectional study was undertaken in 42 postmenopausal women with angiographically proven coronary artery disease and 40 postmenopausal women without coronary artery disease were recruited for this study. Study subjects were selected from the patients attending the cardiology and Gynecology departments. The study protocol and all the study methods were approved by the Institutional ethical committee. Informed consent from patients was obtained after explaining the nature of the study. During selection of study subjects, the inclusion and exclusion criteria were taken care of. Postmenopausal women who have had at least 12 consecutive months of amenorrhea, with angiographically proven coronary artery disease were included in the study. Patients who had surgical menopause, patients with chronic diseases were excluded. With the use of a standard questionnaire, a detailed medical history of patients were taken and general examination was done and carefully recorded in a structured protocol format. Blood samples were drawn by (venipuncture) from anterior-cubital vein after a 12 hrs overnight fast. Fasting blood sugar, lipid profile and Vitamin D3 levels were measured. Serum 25(OH) vitamin D was estimated using DIAsource 25(OH) Vitamin D total ELISA Kit (DIASource ImmunoAssays S.A., Rue du Bosquet, 2 B-1348 Louvain-la Neuve-Belgium).

STATISTICAL ANALYSIS
Statistical analysis was done by using the SPSS software. Results of the study were given as mean ± standard deviation. Comparison of parameters among postmenopausal women with and without coronary artery disease was done by applying the unpaired t test. Comparison of parameters based on Vitamin D levels was done using ANOVA. Correlation of presence or absence of CAD with Vitamin D levels was analyzed by using the Kruskal wallis test. A p-value of less than 0.05 was considered as the cut off level for significance.

RESULTS
Among 82 patients in our study population, 42 patients were with CAD among which majority were in the age group of 50-65 years. The mean age was 54.5 years. Among 40 patients without CAD. Majority of them were in the age group of 45 – 55 years. The mean age among them was 52.7 years and it is almost similar to that of the patients with CAD.

We also analysed the mean value and standard deviation of various parameters like Vitamin D level, Blood Sugar and lipid profile and compared the values between patients with and without CAD using unpaired ‘t’ test(Table 1).

Table 1: Comparison of various parameters in patients with CAD and without CAD.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>WITH CAD(42)</th>
<th>WITHOUT CAD(40)</th>
<th>T TEST</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLOOD SUGAR</td>
<td>161.07±78.49</td>
<td>136.85±49.92</td>
<td>0.101</td>
<td></td>
</tr>
<tr>
<td>TOTAL CHOL</td>
<td>169.72±34.30</td>
<td>152.42±43.46</td>
<td>0.050</td>
<td></td>
</tr>
<tr>
<td>TGL</td>
<td>157.92±95.70</td>
<td>180.47±99.75</td>
<td>0.299</td>
<td></td>
</tr>
<tr>
<td>HDL</td>
<td>36.52±6.99</td>
<td>43.72±8.03</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>110.65±26.75</td>
<td>97.38±32.44</td>
<td>0.047</td>
<td></td>
</tr>
<tr>
<td>VLDL</td>
<td>31.40±19.09</td>
<td>35.92±19.96</td>
<td>0.298</td>
<td></td>
</tr>
<tr>
<td>LDL:HDL</td>
<td>2.69±0.90</td>
<td>2.58±0.70</td>
<td>0.523</td>
<td></td>
</tr>
<tr>
<td>CHOL:HDL</td>
<td>4.19±1.15</td>
<td>3.94±0.97</td>
<td>0.284</td>
<td></td>
</tr>
</tbody>
</table>
We also divided all the 82 patients into 3 groups based on their serum Vitamin D levels into deficient, insufficient and sufficient and analyzed the difference in all parameters between these three groups (Table 2), which was not significant for any variable.

### Table 2: Comparison of various parameters based on Vitamin D level.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>MEAN ± SD</th>
<th>ANOVA P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLOOD SUGAR</td>
<td>149.79±55.64</td>
<td></td>
</tr>
<tr>
<td>TOTAL CHOL</td>
<td>155.34±42.31</td>
<td>0.487</td>
</tr>
<tr>
<td>TGL</td>
<td>153.27±88.38</td>
<td>0.116</td>
</tr>
<tr>
<td>HDL</td>
<td>38.69±8.01</td>
<td>0.247</td>
</tr>
<tr>
<td>LDL</td>
<td>97.81±30.94</td>
<td>0.166</td>
</tr>
<tr>
<td>VLDL</td>
<td>30.48±17.63</td>
<td>0.117</td>
</tr>
<tr>
<td>LDL: HDL</td>
<td>2.55±0.71</td>
<td>0.591</td>
</tr>
<tr>
<td>CHOL: HDL</td>
<td>4.03±1.00</td>
<td>0.958</td>
</tr>
</tbody>
</table>

Finally we analyzed the correlation between levels of Vitamin D by separating them into two groups based on their values and relating it with the presence of CAD (Table 3). There was significant relationship between Vitamin D levels and presence of CAD with P value of 0.001.

### Table 3: Correlation between presence of CAD and Vitamin D levels.

<table>
<thead>
<tr>
<th>VITAMIN D</th>
<th>WITH CAD</th>
<th>WITHOUT CAD</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEFICIENT</td>
<td>29</td>
<td>14</td>
<td>43</td>
</tr>
<tr>
<td>INSUFFICIENT</td>
<td>2</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>SUFFICIENT</td>
<td>11</td>
<td>13</td>
<td>24</td>
</tr>
<tr>
<td>TOTAL</td>
<td>42</td>
<td>40</td>
<td>82</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Menopause not only marks an end of a woman’s reproductive life but also embraces various other changes like increased risk of cardiovascular diseases. Postmenopausal period is associated with an increased risk of obesity and a shift to an abdominal fat distribution with associated increase in health risks. Ageing affects multiple steps of vitamin D metabolism as ageing skin has reduced efficiency to absorb sunlight and synthesize the required amount of vitamin D. So, postmenopausal women are more vulnerable to vitamin D deficiency, owing to their inevitable ageing process coupled with obesity.

This study was conducted on 82 postmenopausal women with 42 having CAD and 40 without CAD. The mean age of postmenopausal women with CAD was 54.5 ± 9.3 years and without CAD also 52.7 ±11.5 years. In our study, 54% of the postmenopausal women with CAD were diabetic and 17% of them were hyperlipedimic. Mean blood sugar levels of women with CAD were 161mg/dl and without CAD are 137mg/dl(table). Although the blood glucose values of women with CAD were more than women without CAD, we did not find any statistical significance between them.

About 72% of postmenopausal women were suffering from either vitamin D deficiency or inadequacy. A similar trend of vitamin D deficiency was observed in few other Indian studies like Harshdeep Joshi et al,[9] where they have observed that 80% of the postmenopausal women were suffering from vitamin D deficiency. Our results were in accordance with another south Indian study where they had observed 70% of postmenopausal women were vitamin D deficient.[18] These findings clearly depict that more postmenopausal women suffer from vitamin D deficiency owing to the reduced capacity of ageing skin to effectively synthesize vitamin D. The overall prevalence was 72%, whereas 69% of postmenopausal women with CAD and 35% of women without CAD were found to be having less than normal Vitamin D levels. The mean value of vitamin D levels in patients with CAD were 19.2 ± 13.6 ng/dl and without CAD were 26.4 ±13.01ng/dl. A statistically significant difference was observed between the two groups of women (p-value<0.022).

Accumulating evidence suggests an increasing trend of cardiovascular disease among people with vitamin D deficiency irrespective of age, sex and race. During a Framingham–Offspring study on 1739 participants who were followed up within 5.4 years, Wang and colleagues revealed that vitamin D deficiency is associated with cardiovascular disease.[19] Motiwala SR et al also showed that vitamin D deficiency is associated with cardiovascular risk factors such as hypertension, hypercholesterolemia, obesity and diabetes mellitus.

In a study done by Giovannucci E et al[20], about nine hundred matched controls without cardiovascular disease...
were randomly selected from study participants and were compared with the 454 participants who experienced an event. Plasma 25(OH)D levels were significantly lower in cases compared with controls, and men with deficient levels of 25(OH)D had a significantly elevated risk for acute myocardial infarction. These observational studies have shown a strong link between vitamin D deficiency and several types of vascular diseases, including increased carotid artery intimal medial thickness, and myocardial infarction.\textsuperscript{21}

Deviation from desirable range of triglyceride and cholesterol level is suggestive of cardiovascular risk. Many studies have linked vitamin D deficiency with metabolic syndrome which includes high blood pressure, obesity, high cholesterol and insulin resistance. Similar results were found in a study conducted among Malay adults in Malaysia which documented that triglyceride level was high among vitamin D insufficient group. Also vitamin D insufficiency was linked higher metabolic risk scores (p=0.009).

In accordance with these findings, in our study, serum TG and VLDL were significantly elevated in the CAD women from that of the women without CAD. Serum 25(OH) D levels showed a negative correlation with serum TG and VLDL levels. Also serum HDL levels showed a significant decrease in the CAD group, compared to the controls. A positive correlation was found between HDL-C and vitamin D, but the correlation was not statistically significant. A decrease in HDL-C can result in endothelial damage and trigger an increase in BP. HDL also exhibits potent anti-inflammatory and antioxidant effects that inhibit the atherogenic process.\textsuperscript{22}

Finally we analyzed the correlation between the vitamin D levels and presence of CAD in all patients which clearly showed a significant relationship between incidence of CAD and low levels of Vitamin D with a P value of 0.001. This is proved by all above said mechanisms and pathogenesis. These findings suggest the positive correlation of CAD where decrease in vitamin D level is proportional to increase in incidence of CAD.

**CONCLUSION**

Vitamin D deficiency is an alarming issue among postmenopausal women in India and is related to numerous negative health outcomes. Our study has shown that 25(OH)D levels were significantly decreased in menopausal patients with CAD and have an association with lipid parameters. The establishment of association between vitamin D levels and CAD could be a milestone in the prevention of CAD among postmenopausal women. Exposure to sunlight and adherence to healthy life styles can help the postmenopausal women to achieve optimum vitamin D levels and further prevent the risk of CAD.

Vitamin D is not only responsible for safeguarding skeletal integrity but also involved in various extra skeletal functions of the body like cardiac function, mood elevation and is protective against cancers owing to anti proliferative effect on cells.

**Limitations**

The study could have been done as a prospective study and in a larger population to emphasize the association of vitamin D with CAD. Also this study could have been continued as an interventional study after supplementation of vitamin D for deficient patients.

**BIBLIOGRAPHY**


