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Association between Vitamin-D Status and Cardiovascular Risk among Postmenopausal Women in Kerala Population

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Abstract

Introduction: cardiovascular diseases (CVD) are the leading cause of morbidity and mortality across the world. Postmenopausal women may have an increased risk of CVD. Vitamin-D (Vit-D) is believed to have an important role in the progression of CVD. Hence the study was undertaken to assess the link between Vit-D and CVD among postmenopausal Kerala population. *Materials and Methods:* A cross-sectional study was undertaken in 149 postmenopausal women. Demographic parameters were collected by using a questionnaire. Blood samples were collected and Vit-D status of all volunteers was estimated. The sample population was further grouped into three based on the Vit-D status as Vit-D deficient, insufficient and normal groups. Other parameters such as blood glucose, blood pressure, TC, TG, HDL, and LDL were measured and recorded. The result was analyzed by using appropriate statistics. *Result:* There was a significant difference in the biomarkers of CVD between the test groups. The one way ANOVA between the groups showed a significant difference ($p \leq 0.05$) in body weight, FBS, HDL, and TG. The Person correlation test indicated a negative correlation between Vit-D with SBP, LDL, Apo-B, hsCRP and Lp-PLA2. Whereas a positive correlation was noted with Apo-A1 levels. *Conclusion:* The result of the present study revealed that there is a significant association between Vit-D status and risk for CVD in the postmenopausal women of Kerala population. The study could reveal the elevated levels of conventional and specific biomarkers for cardiovascular risk.

Keywords: Postmenopausal Women; Vitamin D Status; Cardiovascular Risk; Kerala Population.

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Introduction

Cardiovascular diseases (CVD) are considered as one of the leading causes of mortality among postmenopausal women. It is calculated that nearly 95% of woman in urban locations experience the postmenopausal life for more than 30% of their lifespan [1]. Menopause increases the risk for CVD, hence it should be considered as one of the major concern faced by women [2]. It is important that when a woman experience menopause, along with the pre-existing risk factors for CVD, they should also consider their overall health to prevent the development of CVD.

Vitamin D (Vit-D) has several functions in our body, such as intestinal calcium absorption and bone mineralization. Studies have reported that Vit-D may play several roles in CVD by altering the pathophysiology of ischemic heart disease, hypertension and heart failure [3]. The exact mechanism for the influence of Vit-D in CVD is not clear; however, it is believed that the down-regulation of the renin-angiotensin-aldosterone system in Vitamin D deficiency may lead to the CVD [3]. Moreover, it has been reported that the prevalence of CVD is very high in Kerala population and some

epidemiological studies conducted among the Kerala population have noted a higher incidence of Vit-D deficiency [4,5]. The incidence of CVD is known to increase after menopause; however, studies assessing the relationship between CVD and its relationship with Vit- D levels in the postmenopausal women are lacking. Therefore, addressing this relationship among postmenopausal women in Kerala population is vital for improving health in this population.

Biomarkers are considered as an effective tool for early diagnosis of diseases and it helps to manage the condition accordingly. Conventionally, total cholesterol, LDL cholesterol, HDL cholesterol, Lipoprotein (a), Triglycerides etc, are the commonly used biomarkers to assess the cardiovascular risk [6]. The use of new biomarkers to predict cardiovascular risk has attracted substantial attention in the past decade. Evidence has gathered that inflammation plays a crucial role in the triggering and progression of atherosclerosis, proposing that biomarkers of inflammation may help in predicting an individual's risk for CVD events. High-sensitivity C-reactive protein (hs-CRP), and Lipoprotein-associated phospholipase-A2 (Lp-PLA2) has been well documented as a useful inflammatory marker in predicting future CVD [7]. Lp-PLA2 has been shown to be a cardiovascular risk marker independent and additive to traditional risk factors [8]. Therefore, the current study was undertaken to evaluate the relationship between Vit-D status and risk of CVD in postmenopausal women from Kerala by using specific biomarkers.

Materials and Methods

Study Population

A cross-sectional study was carried out; the study participants were selected from the outpatient pool of M.E.S Medical College, Perinthalmanna, a postgraduate institute. The sample collections were done by four medical camps between 2015 December – 2016 March. The ethical clearance (IEC/MES/42/2014) was obtained from the MES Medical College Institutional Ethics committee. The study details were explained and written informed consent was obtained from all the participants.

Inclusion and Exclusion Criteria

We selected the females with amenorrhea for the last12 months following the final menstrual period. We excluded male participants, females with surgical menopause, pregnant woman and patients with chronic liver or renal disease. In addition, participants were excluded if they had not provided blood samples for biochemical analysis and had not completed the questionnaire regarding the demographic and anthropometric variables such as height, weight, waist circumference (WC) and blood pressure (BP).

Variable Measurements

Anthropometric measurements such as height and weight were measured. Blood pressure was measured in the sitting position prior to blood collection to avoid BP fluctuations due to apprehension during the venipuncture. Total of 5 ml of fasting blood samples was collected. Serum was separated as per the standard protocol. Vit-D levels were estimated by Chemiluminescence Immunoassays (CLIA). Based on the Vit-D status, the test population was further grouped into three [9].

- Group 1: Vit-D deficient group (< 20 ng/mL)
- Group 2: Vit-D insufficient group (20–29 ng/mL)
- Group 3: Vit-D normal group (≥ 30 ng/mL).

A fully automated analyzer (Mindray BS-200) was used to analyze the cardiovascular biomarkers such as blood glucose, lipid profiles (TC, TG, HDL, and LDL), Apo-A1, Apo-B, hsCRP and LpPLA2.

Statistical Analysis

The demographic data like age, height, body weight were analyzed by descriptive statistics. The Pearson correlation test was used to identify the correlation between Vit-D and cardiovascular risk factors. One way ANOVA was used to identify the significant difference in cardiovascular risk between group1, 2 and 3. The statistical analysis was performed by using SPSS software (version 21.0).

Result

The present study was conducted to evaluate the role of Vit-D status in the increased risk of cardiovascular diseases among the post-menopausal Kerala population. A total of 149 (n=149) postmenopausal women were enrolled in the study. Vit-D levels were assessed and the population was grouped into group1, 2 and 3 according to the Vit-D status. The mean Vit-D levels in group1, 2 and 3 were found to be 32.64, 24.37, and 14.46 respectively. The average age of the participants was 54.29, 54.13 and 53.87 for the group1, 2, and 3 respectively (Table 1). The height of the patients doesn't show any significant difference in the study population, but

body weight was significantly different in all groups. The one way ANOVA between the groups showed a significant difference ($p \leq 0.05$) for the risk factors like FBS, HDL-C and TG (Table 2). This showed the difference in the risk factors between the test groups. Further, the statistically significant Vit- D deficient populations (Table 3). A decreased level of Apo-A1 and increased level of Apo-B clearly showed the increased risk of CVD in the group II and group III. The one way ANOVA between three groups shows a statistically significant difference in the LpPLA2, APOA, APOB and hsCRP levels. All these observations are indicated an increased vascular inflammation in group II and group III populations.

The Pearson correlation between Vit-D and cardiac risk markers (Table 4) showed a negative correlation between Vit-D and BMI, SBP, DBP, LDL, Lp-PLA2, hsCRP, Apo-B. There was also a positive correlation observed between Vit-D with HDL and Apo-A1. The significant difference in the cardiac markers between the groups indicates that Vit-D plays a role in the development of CVDs.

Table 1: Comparison of Vitamin-D status between test groups

Group		Vit D levels	F value	P value
Group I	Normal (n=48)	32.64± 2.316	845.2	0.0001***
Group II	Insufficient (n=30)	24.37±2.285		
Group III	Deficient(n=71)	14.46± 2.347		

The statistical test used: One-way ANOVA. ** p<0.01 Highly significant, *P<0.05 Significant

Table 2: Comparison of Parameters between test groups

Parameter	Group I	Group II	Group III	F value	P vale
Age	54.29±8.842	54.13± 7.333	53.87± 4.240	17.14	0.063
Body weight	70.02±6.997	74.03± 9.988	78.00± 11.46	16.49	0.0001***
Height	1.592±0.0614	1.589± 0.04381	1.588± 0.043	4.73	0.062
BMI	25.35± 1.267	27.73± 3.748	27.81± 4.475	13.82	0.075
FBS	109.1± 31.03	119.6± 33.06	131.4± 37.22	11.86	0.001***
Systolic BP	121.6±12.24	1263.7± 24.56	127.9 ± 16.89	2.07	0.129
Diastolic BP	93.54± 7.904	92.17± 10.56	92.56 ± 7.837	3.2	0.053
Total Cholesterol	250.5±28.22	247.5± 40.20	252.5± 38.72	2.529	0.083
LDL	150.5± 21.27	158.5± 22.23	154.2± 21.93	2.948	0.563
HDL	43.46± 5.403	40.57 ± 5.728	38.81± 4.512	11.18	0.031*
TG	135.8± 29.96	148.8± 46.99	155.0± 30.32	15.54	0.024*

The statistical test used: One-way ANOVA. ** p<0.01 Highly significant, *P<0.05 Significant

Table 3: Comparison of specific markers of CVD between test groups

Parameter	Group I	Group II	Group III	F value	P value
LPPLA2	529.4± 55.15	554.5± 23.36	580.6± 30.76	23.76	0.0001***
APOA	1.442± 0.289	1.256± 0.180	1.285± 0.357	5.968	0.003***
APOB	1.329± 01772	1.483± 0.3035	1.532± 0.2325	9.49	0.0001***
Hs CRP	0.9331± 0.4950	1.238 ± 0.4964	1.946± 0.05615	56.55	0.0001***

The statistical test used: One-way ANOVA. ** p<0.01 Highly significant, *P<0.05 Significant

Table 4: Pearson correlation of the cardiac risk markers and Vit-D level

Parameters	Correlation with Vit D (ng,/mL)
BMI (Kg/m2)	-0.430 (<0.08)
BP Systolic	-0.173** (<0.01)
BP Diastolic	-0.043 (0.486)
LDL (mg/dL)	-0.347* (<0.05)
HDL (mg/dL)	0.199 (<0.15)
TG (mg/dL)	0.019 (0.668)
LpPLA2 (U/L)	-0.541** (<0.01)
APO A1 (g/L)	0.353** (<0.01)
APO B (g/L)	-0.357** (<0.01)
hsCRP (mg/L)	-0.467** (<0.01)

The statistical test used: Person correlation ** p<0.01 highly significant, *P<0.05 Significant

Discussion

Several studies have undertaken to identify the effects of menopause on CVDs, showing variation in age for peak prevalence in different ethnicities. In one of our previous study, we observed the high prevalence of metabolic syndrome among the women aged above 50 years, as compared with men in Kerala population [9]. Moreover, this study also pointed out that Vit-D levels have some relationship with the prevalence of metabolic syndrome [9]. In the current cross-sectional study, we investigated whether serum Vit-D levels have any role in the development of CVD among postmenopausal woman. The test population was further divided into 3 groups based on the Vit-D status (Table 1). The comparison of parameters between the test groups (Table 2) showed a statistically significant difference in body weight, FB, HDL and TG levels. The comparison also revealed that the Apo-A1 levels where lower among Vit-D deficient population and The Apo-B levels were vice versa. The observations from the current study are in accordance with the findings of Mirshad PV, et al. and Staessen JA, et al [10,11]. Their research outcomes denote that the people with increased, FBS, TG, Apo-B, and decreased HDL and Apo-A1 levels may have an increased tendency to develop CVDs in future. The elevated levels of hs-CRP and Lp-PLA2 in the Vit-D deficient population denote that the people with Vit-D deficiency may have a tendency to increased inflammation and these observations are at par with the observation of Mirshd P.V, et al, Hatoum IJ, et al, and Kardys I, et al.[12,13,14].

A higher incidence of CVD has been reported in women, especially after the menopause, as compared with men in Indian population. [15]. Another study conducted among Indian population showed that the prevalence of CVD increased after menopause [16]. However, to the best of our knowledge, this is the first study to reveal the effect of serum levels of Vit-D on CVD among postmenopausal Kerala women.

In a recent study conducted by Mirshad PV, et al in among general population of Kerala observed an association between Vit-D status and the prevalence of metabolic syndrome and risk for CVD [12]. Some of the major points observed in the current study are the significantly low levels of HDL and higher levels of triglyceride among Vit-D deficient group. In several studies, it is found that triglycerides levels are generally known to be elevated in the postmenopausal age group when compared with that of premenopausal age group. The cardioprotective factors in women are known to be lost after attaining menopause with a significant decrease in HDL-C [17]. hsCRP is an acute-phase reactant and marker of inflammation. As we know that inflammation plays a significant role in the development of CVDs. Evaluation of hsCRP level is often carried out to assess the risk of future CVD. In our study, the levels of hsCRP in the Vit-D deficient population were significantly higher when compared to that of Vit-D normal population. The elevated hsCRP level in the group-3 indicates an increased inflammatory status and risk of CVD in menopausal women with Vit-D deficiency. Our findings are in accordance with the findings of Dallmeier D, et al. and Goff Jr DC, et al. [18,19]. It has also been recommended that hsCRP can be used as a biomarker to tailor risk modification to prevent future CVD [18]. The identification of the relationship between atherosclerosis and the inflammatory process has generated remarkable interest in the measurement of Lp-PLA2 as part of cardiovascular risk assessment. In the current study, we found that levels of Lp-PLA2 are significantly higher in Vit-D deficient population when compared to that of Vit-D normal and insufficient population. Different researchers have proven that the LpPLA2 levels found to be increased among the population with cardiovascular risk [13,14]. The observations are at par with the findings of the study conducted by Dallmeier D, et al, Hatoum IJ, et al, Kardys I, et al. and Mirshad P. V et al. [12,13,14,20]. The studies point out that higher plasma levels of Lp-PLA2 may increase the risk for CVD regardless of the other risk markers' status. The increased level of Lp-PLA2 along with the other markers like Apo-B, hs-CRP, triglycerides and decreased levels of HDL and Apo-A1 in Vit-D deficient population and its correlation with Vit-D status in the current study indicates that there is a significant relationship between Vit-D level and risk for CVD in the postmenopausal women.

Conclusion

The result of the present study revealed that there is a significant association between Vit-D status and risk for CVD in the postmenopausal women of Kerala population. The study could demonstrate the elevated levels of specific biomarkers for cardiovascular risk. Further, to establish the relationship between Vit-D status and cardiovascular risk in postmenopausal women, a prospective, follow up study need to be conducted in future. The principal limitation of our

study was its cross-sectional design, and thus the causative nature of the association couldn't b established.

Conflict of Interest

None.

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