

## Association between vitamin D status and risk of metabolic syndrome among postmenopausal women in Kerala population

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### Abstract

**Introduction:** Metabolic syndrome (MS) is a group of metabolic risk factors for cardiovascular diseases (CVD). Postmenopausal women may have an increased risk of MS and CVD. Vitamin-D (Vit-D) is believed to have an important role in the progression of CVD. Hence the study was conducted to assess the link between Vit-D and MS among postmenopausal Kerala population.

**Materials and Methods:** A cross-sectional study was carried out in 298 postmenopausal women. Anthropometric measurements were measured using the standard procedure. Blood samples were collected and Vit-D levels of all participants were estimated. The study population was further grouped into three based on the Vit-D status as Vit-D deficient, Vit-D insufficient Vit-D normal group. Other parameters such as blood glucose, TC, TG, HDL, and LDL were measured and metabolic syndrome was identified.

**Result:** There was a significant difference in the prevalence of MS between the groups. The one way ANOVA between the groups showed a significant difference ( $p \leq 0.05$ ) for the components of MS such as waist circumference, BP, FBS, HDL-C. The Triglycerides levels did not show a significant difference between the groups. The Person correlation test indicated a negative correlation between Vit-D and the components of MS except for HDL-C.

**Conclusion:** Vitamin-D deficiency was highly prevalent in Kerala menopausal women and serum Vit- D levels were significantly correlated with the prevalence of MS in postmenopausal women; this finding indicates that Vit-D could be an important factor for the development of MS and further CVD in Kerala postmenopausal woman.

**Keywords:** Metabolic syndrome, Vitamin D, menopause, Cardiovascular risk, Kerala population.

### Introduction

Metabolic syndrome (MS) is a group of disorders characterized by the presence of abdominal obesity, hypertension, dyslipidemia and hyperglycemia.<sup>1</sup> Metabolic syndrome is well-identified risk factors for CVD and type-2 diabetes mellitus (DM).<sup>2</sup> Recent studies have suggested that the number of people with MS is increasing in the developing countries like India due to the increased intake of a westernized diet with a sedentary lifestyle.<sup>3</sup> The increased incidence of MS may directly contribute to the increased cardiovascular morbidity and mortality.

Postmenopausal women may have the high incidence of cardiovascular disease (CVD) due to the hormonal changes after the menopause. Identifying the risk for CVD is significant because more than 90% of the women experience menopause for more than one-third of their total lifespan.<sup>4</sup> Since menopause is a risk factor for CVD; it should be addressed as one of the most important issues faced by modern women. When women attain menopause, they should closely observe their overall health to prevent CVD. The hormonal changes after menopause are also believed to be a contributing factor for the development of MS at menopausal transition.<sup>5</sup> This may increase the risk for CVD among postmenopausal women.

Evidence from various studies has proven that suboptimal levels of Vitamin-D (Vit-D) are thought to influence risk for CVD by altering risk factors such as hypertension, dyslipidemia and other components of MS.<sup>6,7</sup> The incidence of MS is known to increase after menopause; however, studies assessing the relationship between MS with serum levels of Vit- D in postmenopausal women are lacking. Moreover, it has been reported that the prevalence of MS and 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.<sup>8</sup> Therefore, the aim of this study was to evaluate the prevalence of Vit-D deficiency and MS in postmenopausal women from Kerala

### Materials and Methods

A cross-sectional study was carried out; the study participants were selected from the outpatient pool of M.E.S Medical College, Perinthalmanna, a tertiary care teaching hospital in Kerala, India. 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 recruited the females with amenorrhea for 12 months following the final menstrual period (9). 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) (systolic & diastolic blood pressure).

**Variable Measurements:** Anthropometric measurements such as height weight and waist circumference were measured using the standard procedure. Blood pressure was measured in the sitting position prior to blood collection to avoid BP fluctuations due to apprehension during the vein puncture. Total of 5 ml blood sample was collected after overnight fasting, serum was separated as per the standard protocol. Vit-D levels were estimated by Chemiluminescence Immunoassays (CLIA) and test population was further grouped into three based on the Vit-D status.<sup>10</sup>

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

A fully automated analyzer (Mindray BS200) was used to analyze the cardiovascular biomarkers such as blood glucose, lipid profiles (TC, TG, HDL, and LDL). Metabolic syndrome was identified as per the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III).<sup>11</sup>

### Statistical Analysis

The demographic data like age, height, body weight were analyzed by descriptive statistics. Chi-square test was used to differentiate the presence of MS between the groups. One way ANOVA was used to identify the difference in parameters like BMI, SBP, DBP, Total Cholesterol, HDL, LD, Triglycerides between the groups. The statistical analysis was conducted by using SPSS software (version 21.0).

### Result

The study was conducted to assess the prevalence of MS among the post-menopausal population of Kerala. A total of 298 postmenopausal women were enrolled in the study and 289 participants filled the consent form and allowed to participate 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 average age of the participants was 55.45, 57.50 and 59.63 for the group1, 2, and 3 respectively. This shows a comparable age difference of the subjects in three groups.

The Chi-square test between the groups indicated that there is a significant difference in the prevalence of MS between the groups. Group-1 had a higher prevalence of MS compare to group-2 and 3 (**Fig. 1**). The one way ANOVA between the groups showed a significant difference ( $p \leq 0.05$ ) for the components of MS such as waist circumference, BP, FBS, HDL-C. The Triglycerides levels did not show a significant difference between the groups (**Table 1**). The Person correlation test of Vit-D with components of MS such as waist circumference, FBS, BP, and TG is showing a negative correlation. Vit-D levels showed a positive correlation with HDL levels. This indicates that Vit-D plays an important role in the development Of MS (**Table 2**).

**Table 1: Comparison of the components of MS between three groups**

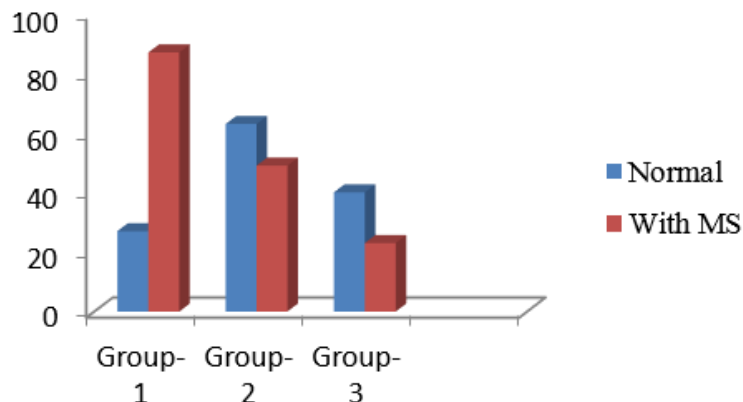
Components of MS		Sum of Squares	df	Mean Square	F	Sig.
<b>WAIST</b>	Between Groups	76.476	2	38.238	4.647	.010*
	Within Groups	2353.198	286	8.228		
	Total	2429.674	288			
<b>BMI</b>	Between Groups	48.933	2	24.466	1.512	.02*
	Within Groups	4627.056	286	16.179		
	Total	4675.989	288			
<b>BP SYS</b>	Between Groups	1976.279	2	988.140	3.951	.020*
	Within Groups	71520.960	286	250.073		

	Total	73497.239	288			
<b>BP DIA</b>	Between Groups	594.713	2	297.357	3.027	.050*
	Within Groups	28096.000	286	98.238		
	Total	28690.713	288			
<b>FBS</b>	Between Groups	79674.961	2	39837.481	33.850	.000* *
	Within Groups	336587.849	286	1176.881		
	Total	416262.810	288			
<b>HDL</b>	Between Groups	1972.862	2	986.431	29.533	.000* *
	Within Groups	9552.730	286	33.401		
	Total	11525.592	288			
<b>LDL</b>	Between Groups	4177.338	2	2088.669	3.007	.035*
	Within Groups	198627.597	286	694.502		
	Total	202804.934	288			
<b>TG</b>	Between Groups	1812.253	2	906.126	.634	.531
	Within Groups	408531.075	286	1428.430		
	Total	410343.328	288			

Statistical test used: One Way Anova F test, \*\* p<0.01 Highly significant, \*P<0.05 Significant

**Table 2: Pearson correlation of the components of MS with Vit-D levels**

Parameters	Vit D (ng./mL)
WC (Inches)	-0.414** (<0.01)
BMI (Kg/m <sup>2</sup> )	-0.314** (<0.01)
TC (mg/dL)	-0.124** (<0.01)
LDL (mg/dL)	-0.164** (<0.01)
HDL (mg/dL)	0.351** (<0.01)
TG (mg/dL)	-0.402** (<0.01)
SBP (mm/Kg)	0.421** (<0.01)
DBP (mm/hg)	0.331** (<0.01)
FBS (mg/dl)	0.351** (<0.01)



**Fig. 1: Prevalence of MS in different groups**

## Discussion

In this study, we investigated whether serum levels of Vit-D have associations with the prevalence of MS in postmenopausal Kerala population. In this cross-sectional study, the prevalence of MS in postmenopausal women tended to decrease as serum levels of Vit-D increased, this association was statistically significant.

A higher prevalence of MS has been reported in women, especially those aged more than 50 years, as compared with men.<sup>12</sup> Another Indian study reported that the prevalence of MS increased after menopause.<sup>13</sup> A study in the U.S. conducted by Park YW et al, demonstrated an increased risk of MS up to more than 20% among postmenopausal women.<sup>14</sup> Moreover, a study that examined the prevalence of MS and its association with hyperinsulinemia in the urban Korean population concluded by Oh JY et al found that the prevalence of MS increased with increasing incidence of insulin resistance.<sup>15</sup> However, to the best of our knowledge, this is the first study to reveal the effect of serum levels of Vit-D on MS among postmenopausal Kerala women

Several reports have demonstrated a significant inverse association between serum Vit-D levels and the prevalence of MS.<sup>16-18</sup> Other studies, similar to ours, have observed an association between serum levels of Vit-D and MS and the results were at par with our findings. In a study conducted among general population of Kerala by Mirshad et al, observed an association between Vit-D deficiency and the prevalence of MS and risk for CVD.<sup>19</sup> Several studies have conducted across the world and observed that Vit-D status can influence the progression of MS. In a study conducted by Botella-Carretero JI et al, found that Vit-D status is associated with MS among the obese population in U.S.<sup>20</sup>

Some of the major factors observed in our study are the considerable abnormalities in lipid profiles. In our study, the Vit-D deficient group had high LDL-C and reduced the HDL-C level. In several studies, it has found that the levels of LDL-C and TGs levels generally known to be increased in the postmenopausal stage as compared with premenopausal stage, and the cardio protective effects in females are known to be lost after menopause with a considerable fall in HDL-C levels.<sup>21</sup> Even though the relationship between Vit-D and dyslipidemia are not well clear, one pre-clinical study reported that the serum Vit-D concentration was positively associated with HDL-C point out that that low Vit-D would be related with a more atherogenic lipid profile, which is an important risk factor for progression towards ms and CVD.<sup>22</sup>

Our study pointed that elevated BP (both systolic and diastolic) and fasting blood sugar levels were significantly elevated and associated with Vit-D levels

in postmenopausal Kerala population, these findings are at par with several other studies.<sup>23,24</sup> This could be due to the effect of Vit-D on renin gene expression and proliferation of vascular endothelium. Deficiency of Vit-D may lead to up-regulation of the renin-angiotensin system (RAS), ultimately leading to increased BP and ventricular remodeling.<sup>25</sup> It is known that menopause may increase central adiposity and abdominal obesity; a similar research reported that serum Vit-D levels were negatively associated with waist circumferences (WC).<sup>26</sup> In our study, WC, the occurrence of abdominal obesity, increased among Group-1. This could possibly be explained by a cultural tendency in Kerala woman who is not much bothered about their appearance and does not make the effort to maintain their physical appearance after the menopause. Further and elevated FBS was found to be related to serum Vit-D levels and the finding was at par with similar studies conducted at various places.<sup>27</sup> The current study could reveal a high prevalence of Vit-D deficiency in Kerala postmenopausal population, which may be defended by lack of outdoor activities and the use of sunscreen lotion. Moreover, the studies have proven that endogenous Vit-D synthesis among elderly people is known to diminish and the levels of Vit-D could be less among old women.<sup>28</sup> Since it is a cross-sectional study, the direct relationship between the variables of interest could not be determined and we could not consider parameters such as intensity of sunlight exposure, calcium supplementation, and Vit-D intake which could have influenced the Vit-D levels in the blood. Further studies regarding these aspects would clarify the underlying factors and help to establish this relationship.

## Conclusion

To conclude, the Vit-D deficiency was highly prevalent in Kerala menopausal women and serum Vit-D levels were significantly correlated with the prevalence of MS in postmenopausal women; this finding indicates that Vit-D could be an important factor for the development of MS in postmenopausal population in Kerala. Based on our findings, it is recommended to have a periodical cardiovascular health monitoring for the postmenopausal population with MS. It is desirable to have Vit-D supplementation for minimizing the cardiovascular risk among these populations.

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