International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

Original Research Article.

A Comparative Study of Vitamin D Status in Pre- and Post-Menopausal Women with and without Diabetes

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ABSTRACT

Background: Vitamin D status influences different metabolic adjustments, aside from calcium, phosphorus and bone metabolism. The pleotropic functions of Vitamin D are eminent from the presence of the Vitamin D receptors (VDR's) being present outside the skeletal system. Lower vitamin D is related to poorer glucose control. In post/peri menopausal women there could deficiency of vitamin D.

Objectives: In this study it was aimed to evaluate vitamin D levels along with fasting blood glucose, follicle stimulating hormone (FSH) and estradiol in healthy pre and postmenopausal women with or without diabetes.

Materials and Methods: Total of 92 subjects including 37 non-diabetic, 15 diabetic premenopausal women and 25 diabetic and 15 non-diabetic postmenopausal women without any major medical illness, who gave consent were included for study. Fasting blood samples were collected for glucose estimation by GOD/POD method and vitamin D, follicle stimulating hormone (FSH), estradiol was estimated by ELISA method using commercial kits. Values were reported as mean + standard deviation (SD). The data were analysed by one-way ANOVA with Tukey-Kramer Post Hoc test using SPSS version 20 and p value of < 0.05 was taken as statistically significant at 95% confidence interval.

Results: Results of the study showed that vitamin D levels were significantly lower in postmenopausal women with and without diabetes compared to premenopausal women without diabetes as well as premenopausal women with diabetes.

Conclusions: The study was concluded that the observed low levels of vitamin D in postmenopausal women indicating a supplementation of vitamin D may improve quality of life in postmenopausal women.

Keywords: Menopause, Diabetes, Vitamin D.

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Article History:

Received: 11-12-2020, **Revised:** 29-12-2020, **Accepted:** 19-01-2021

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2021.7.1.003	

INTRODUCTION

Menopause and ageing are associated with changes in circulating gonadal steroid hormones, insulin insensitivity, body composition and also lifestyle and social coordinates. Vitamin D status influences different metabolic adjustments, aside from calcium, phosphorus and bone metabolism.[1-5] The pleotropic functions of Vitamin D are eminent from the presence of the Vitamin D receptors (VDR's) being present outside the skeletal system. VDR's exist on a very wide range of tissues, including endothelium, vascular smooth muscle, cardiomyocytes, kidney, liver, and beta cells of pancreas etc.

Presence of VDR's in beta cells of pancreas has given a lot of evidence in the role of Vitamin D in the secretion of insulin (6). In experimental animals the role of calcitriol in insulin secretion has been proved. Vitamin D increases the production of some anti-inflammatory cytokines and decreases the release of some proinflammatory cytokines. Deficiency of vitamin D is associated with upregulation of TLR (toll like receptors) expression and a proinflammatory state. Thus, a deficiency of vitamin D could cause insulin resistance due to increase in proinflammatory state. Vitamin D status ameliorates the glycemic index.[7-9]

Lower vitamin D is related to poorer glucose control. In post/peri menopausal women there could be deficiency of vitamin D. The reasons being, ageing has a reduced ability on function of skin & GIT, for absorption and activation of 7-dehydro cholesterol, and second reason being estrogens activate the α 1 hydroxylase in the kidney, and they have low estrogens. Animal studies have shown low levels of vitamin D increases the risk of prediabetes. In vitamin D deficiency, insulin resistance is increased. This leads to alterations in lipid metabolism, leading to an increase in triglycerides and LDL and a decrease in HDL, leading to increased adiposity, which would exaggerate the insulin resistance. Animal experiments have shown an increase in the expression of

enzymes of lipogenesis and decreased expression of genes of beta oxidation of fatty acids. This again would exacerbate the vitamin D status.

Vitamin D and estradiol are working synergistically. Lower estradiol level is one of the factors that contributes to lower vitamin D binding protein levels in older women. FSH and estradiol is estimated in the samples to establish the postmenopausal condition.

MATERIALS AND METHODS

Sample Size

The postmenopausal women selected were those with a history of natural menopause, who had cessation of menstruation for a minimum of one year, and premenopausal women who were studied were those who had regular menstruation. In the present study the total number of participants were 92. The age group of pre-menopausal group of women was between 25 – 50 and for the post-menopausal women it is between 45 – 75. The first group consisted of 37 premenopausal women without diabetes, and second group consisted of 15 premenopausal women with diabetes, third group had 15 postmenopausal women without diabetes and fourth group consisted of 25 postmenopausal women with diabetes.

Inclusion and Exclusion Criterion

Diabetic and non-diabetic women in the study were selected depending on the exclusion criterion. Women with any type of hormonal abnormality, cardiac problems, pregnancy, hormonal therapy, heavy exercise, and familial hypertriglyceridemia were excluded.

Sample Collection

After an overnight fasting for 12 -14 hours, sample was collected from the subjects. About 5 ml of venous blood was drawn under aseptic precaution in a sterile plain vacutainer from selected subjects. Sample for glucose estimation was separately taken in fluoride, oxalate vial and remaining sample is collected into a plane voile. Glucose is estimated in plasma and lipid profile is estimated in serum. As soon as the sample is collected, serum is separated, and estimations were done on the same day.

Assay Method

Assay of samples for glucose estimations was done using Erba-chem-5 plus2 semi-automated analyser. The quality control was checked using control sera of two levels. Glucose was estimated by GOD/PAP method.[10,11] Vitamin D[12], Estradiol[13,14] and FSH[15] were estimated by ELISA method.

Results were reported as mean + standard deviation (SD). The data were analysed by one-way ANOVA with Tukey-Kramer Post Hoc test using SPSS version 20 and p value of < 0.05 was taken as statistically significant at 95% confidence interval.

Ethical Considerations

Sample was collected after taking written/oral consent from the subjects. This project has been approved by the ethical committee of Shadan Institute of Medical Sciences.

Table 1: Number and age of subjects in study groups

Study groups	No of Subjects	Age range (Mean ± SD)
Premenopausal women without diabetes	37	29 – 54 (39.2 ± 6.6)
Premenopausal women with diabetes	15	32 - 49 (39.5 ± 5.7)
Postmenopausal women without diabetes	15	45 - 62 (52.4 ± 5.8)
Postmenopausal women with diabetes	25	50 - 75 (58.8 ± 7.9)
Total number of subjects	92	29 – 75*

*Minimum and Maximum years of age

Table 2: Fasting Blood Glucose and Vitamin D, FSH and Estradiol in the study groups

Study groups	Fasting Blood Glucose	Vitamin D	FSH	Estradiol
Premenopausal women without diabetes	95.2 ± 14.1	38.82 ± 10.44	7.71 ± 6.11	44.76 ± 8.96
Premenopausal women with diabetes	151.7 ± 32.9*	36.78 ± 8.02	8.12 ± 6.84	42.47 ± 9.14
Postmenopausal women without diabetes	92.3 ± 12.4@	28.09 ± 5.64*@	28.31 ± 9.7*@	7.6 ± 6.68*@
Postmenopausal women with diabetes	154.9 ± 61.4*#	27.4 ± 5.59*@	29.99 ± 11.53*@	8.18 + 7.02*@

Statistical analysis done by one-way ANOVA with Tukey-Kramer Post Hoc test

Values are Mean ± SD; Statistically significant = $p< 0.05$

*Statistically significant when compared to premenopausal women without diabetes; @Statistically significant when compared to premenopausal women with diabetes; #Statistically significant when compared to postmenopausal women without diabetes.

RESULTS

Table 1 gives the number and age of subjects in study groups. Premenopausal women without diabetes group were with 37 number of subjects having 39.2 ± 6.6 mean ± standard deviation years of age and premenopausal women with diabetes group was with 15 subjects having 39.5 ± 5.7, Postmenopausal women without diabetes group was 15 number of subjects having 51.0 ± 7.7 mean ± standard deviation years of age and postmenopausal women with diabetes group was 58.8 ± 7.9. Overall, the subjects were from 29 to 75 years of age.

Fasting Blood Glucose, Vitamin D, FSH and Estradiol in the study groups were shown in Table 2. The analysis of results by ANOVA

indicated the statistically significant mean values ($p<0.05$) for all the parameters. Fasting blood glucose levels were clearly showed an increased level in pre- and post-menopausal women with diabetes. Vitamin D levels were significantly lower in postmenopausal women with and without diabetes compared to premenopausal women without diabetes as well as premenopausal women with diabetes. FSH and Estradiol were clearly different for premenopausal women compared to Postmenopausal women.

DISCUSSION

The incidence of type 2 diabetes is increasing day by day globally. A lot of pharmacotherapies have emerged. A lot of innovative approaches are needed to prevent it's development. Recently, vitamin D has been discovered as a potential diabetes risk modifier. Based on pre-clinical studies, vitamin D seems to play a regulatory role in insulin secretion, beta-cell survival, and calcium flux within beta-cells. A series of studies have shown that vitamin D deficiency impairs glucose-mediated insulin secretion in rat pancreatic beta cells.[16-20] Vitamin D may also have a direct effect on beta-cell function, which seems to be exerted by binding of its circulating active form to the vitamin D receptor (VDR) that is expressed in pancreatic beta-cells.[21]

In the present study we have tried to evaluate levels of vitamin D in pre and postmenopausal women with and without diabetes. The serum levels of FSH and estradiol were analyzed to demarcate pre and postmenopausal women. A clear-cut difference was seen in both the hormones in pre and postmenopausal women. In the present study it has been observed that the vitamin D levels were low in postmenopausal women with and without diabetes compared to premenopausal women. Increasing age, increased body mass index (BMI), and abnormal lipid profiles contribute to an increased risk of vitamin D deficiency. Women who have a perimenopausal and postmenopausal reduction in estrogen levels are a high-risk group for vitamin D deficiency. Type 2 Diabetes Mellitus (T2DM) and menopause are associated with vitamin D status. Estrogen decline during menopausal stages promotes hypovitaminosis D. There are studies which showed vitamin D deficiency in pre and postmenopausal women with diabetes compared with non-diabetic women.[22,23]

Low vitamin D levels are also associated with lipid profile abnormalities. Studies have shown that women with high levels of cholesterol and VLDL are shown to have low vitamin D levels. Obesity increases the risk for hypovitaminosis D due to deposition of vitamin D precursors in body fat stores, reducing its bioavailability to the skin.

In a cross-sectional study in Japan, Mori and colleagues indicated that 91.8% of postmenopausal diabetic women are deficient of vitamin D.[24] In another cross-sectional study in India, Kanwar and coworkers reported a higher prevalence of vitamin D deficiency among postmenopausal T2DM women compared to premenopausal T2DM women (80% versus 60%).[25] Another cross-sectional study in Indonesia by Hidayat et al. observed a prevalence of 78.2% vitamin D deficiency among elderly T2DM women.[26] Likewise, studies by Sarmidi et al.[27] and Setiati and Sutrisna[28] observed a prevalence of 61.9% and 35.1%, respectively

The finding of a higher vitamin D deficiency in the postmenopausal women may be related to advanced age. Aging is directly related to decreasing vitamin D levels. The diminishing levels of 25(OH) D with age is due to impaired intestinal absorption of vitamin D[29] as well as a decline in the concentration of vitamin D precursors normally stored in the skin coupled with reduced capacity to synthesize vitamin D in the skin when exposed to UV radiation.[30] Additionally, decline in oestrogen associated with postmenopausal women decreases the activity of 1-alpha hydroxylase vitamin D responsible for activating vitamin D and its receptors.

Need and colleagues as well as Ford et al.'s study[31] reported an inverse relationship between FBG and serum 25(OH) D levels. Few more studies also reported higher HbA1c levels in patients with severe vitamin D deficiency compared to subjects with mild to moderate deficiency.[32-35]

The observed association between vitamin D, FBG, and HBA1c is suggestive of the fact that good control of blood sugar is essential for optimal vitamin D levels among diabetic women. The finding of a significant negative association between vitamin D sufficiency and FBG and HBA1c in both pre- and postmenopausal women further corroborate this assertion.

Moreover, a greater number of the vitamin D deficient study participants presented with poorer glycemic control and a higher blood glucose level. In a population-based study in Australia have reported on a protective effect of higher 25(OH) vitamin D on FPG and HbA1c.[36]

Hence it was concluded that the observed low levels of vitamin D in postmenopausal women indicating a supplementation of vitamin D may improve quality of life in postmenopausal women.

ACKNOWLEDGEMENTS

The authors are grateful to Managing Director and Dean for providing the facilities and constant encouragement for the study.

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Source of Support: Nil. **Conflict of Interest:** None Declared.

Cite this article as: Ameetha Rani V, Mohammed Siddique Ahmed Khan, Swamy M, Jagannatham S. A Comparative Study of Vitamin D Status in Pre- and Post-Menopausal Women with and without Diabetes. Int J Med Res Prof. 2021 Jan; 7(1): 8-11. DOI:10.21276/ijmrp.2021.7.1.003