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Original Research Article

Relation of serum 25(OH) D with variables of thyroid and lipid profile in perimenopausal women

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ABSTRACT

Background: Deficiency of vitamin D is quite prevalent among elderly population or postmenopausal women worldwide and may affect various function of the body. The status of its deficiency with their relation with other variables are not well explored in perimenopausal women.
Methods: 100 perimenopausal women from the department of obstetrics and gynaecology were selected without having known risk of thyroid disorder and cardiovascular disease. The age group criteria for these women were 40 to 50 years. Thyroid profile including TSH, T3, and T4 were estimated by using enzyme linked immunesorbent assay. Serum levels of 25(OH) D3 was estimated by using spectrophotometric method. Lipid profile including TC, TG and HDL-C were estimated CHOD-POD method, GPO-PAP method, and CHOD-POD/Phosphotungustate method. LDL-C was calculated by friedewald formula.
Results: There 58 women were presented with insufficient amount of vitamin D. They were characterised with increased BMI, elevated thyrotropin alongwith lower concentrations of T3 and T4. Increased levels of TC, TG and LDL-cholesterol alongwith lower concentration of HDL-C were also observed in women with vitamin d deficiency. Women having vitamin D deficiency were presented with overweight (OR-18.0, p-value=<0.001) and dyslipidemia (OR-12.13, p-value≤0.001). Vitamin D was negatively correlated with variable i.e. BMI, TSH, TC, TG and LDL-C. This negative association was significant (<0.001) while HDL-C and T4 were positively correlated with vitamin D levels in this study population.
Conclusions: Vitamin D deficiency frequently occurs in middle aged perimenopausal women. Negative correlation of it with BMI, TSH and lipid variables may suggest the development of cardiovascular disease and hypothyroidism in coming years. Vitamin D supplements or vitamin D containing diet and regular exposure to sun is highly recommended to perimenopausal women.

Keywords: Dyslipidemia, Overweight, Perimenopause, Vitamin D

INTRODUCTION

Vitamin D deficiency is widespread irrespective of age, gender, race both urban as well as rural population, not uncommon in India.[1] Around 70 to 90% of Indian population suffers with this deficiency.[2] vitamin D is not only a vitamin but also a hormone since human body produces it endogenously. Vitamin D3 (cholecalciferol) is most common form of vitamin. Sunlight is the best sources of vitamin D since by direct exposure to sun, 10,000 to 20,000 IU of vitamin D can be produced in 30 minutes of whole body.[3] Dietary intake are the other sources of vitamin D in the body so its production in the skin depends on the exposure to sunlight, cloth covering,

latitude, consuming nutritional diet or using of sunscreen lotions.[4] Since vitamin D plays an important role in bone metabolism, the deficiency with vitamin D is quite common in older age population or post-menopausal women having osteoporosis.[5] Vitamin D deficiency can cause various other health problems since its deficiency often associated with obesity.[6] Its deficiency may also alter insulin synthesis since glycemia is improved with replenishment of vitamin D in type 2 diabetic patients hence proving its significance in diabetes mellitus.[7] Moreover vitamin D deficiency may also be cause of atherosclerosis since vitamin D supplement have some beneficial effect on elastic properties of artery wall of post-menopausal women.[8]

Studies have suggested that postmenopausal women are more prone to D deficiency and changes in thyroid profile are frequently observed in elderly population or women with menopause but its role in perimenopausal women still not very well explored.[9] A stage prior and end with menopause is termed as perimenopause. It is the term coined by medical professional refers to those women who moves closer to menopause.[10] The variety of changes from psychological to physiological are experienced by women in this stage of life which may include depression, irritability, mood swings, anxiety, weight gain, fatigue, insomnia, etc. Perimenopausal age along with oestrogen deficiency due to lesser ovarian function are more at risk.[11] Moreover, due to sedentary life style and vegetarian diet of women its insufficiency prevails and get precipitated as general pains and aches which in later life may derange lipid levels and bone health. So, the main objective of this study was to investigate the effect of vitamin D on thyroid profile and lipid profile of perimenopausal age group women.

METHODS

This study was carried out in Venkateshwara Hospital from Venkateshwara Institute of medical sciences, Gajraula, Uttar Pradesh, India. Total 100 perimenopausal women were selected for the study from the department of obstetrics and gynaecology. They were categorised into two sections on the basis of their vitamin D status: Section-I (<30 ng/ml) and Section-II (30-100 ng/ml). The age group criteria for perimenopausal women were 40 to 50 years of age. Fasting blood sample was obtained from all the study participants. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All the women voluntarily participated in this study. The written and oral consent for this study was taken from each and every participant. This study was ethically approved by the institutional ethical committee.

Exclusion criteria

- Women having the previous history of diabetes, and hepatic disorder.
- Women having the history of cardiovascular disease or hypertension.
- Women with known risk of thyroid disease e.g. hypothyroidism or hyperthyroidism and taking thyroid medication
- Perimenopausal women with BMI>30kg/m^2
- Women with irregular menstrual cycle
- Women with hormonal replacement therapy
- Women with forced menopause i.e. hysterectomy
- Women taking vitamin D supplements or last two years history of fracture
- History of medical conditions where Vitamin D supplementation is not indicated (i.e. chronic renal insufficiency, elevated calcium, sarcoidosis or other granulomatous disease, lymphoma, or tuberculosis

Inclusion criteria

Only Perimenopausal women without any diagnosed risk or disease, 40-50 years of age group were included in the study.

Methods

All the baseline parameters were performed in the fasting state and fasting blood sample was used for performing biochemical parameters.

Body mass index

BMI is presented in kg/m^2 which is calculated by measuring their weight in kg which will be divided by square of the height of that individual in meter.[12]

Thyroid profile

TSH, T4 and T3 will be investigated by enzyme linked immunosorbent assay (ELISA) in the study population.[13]

Vitamin D

Estimation of serum 25 (OH) D levels using the spectrophotometric method. This method is based on that vitamin D forms with antimony trichloride in chloroform a pink colour that can be read at 500 nm wavelength. The reference range for vitamin D was 30-100 ng/ml. They were categorised into three groups with this reference range: Group-I (deficiency<20ng/ml), Group-II (insufficient 20-30 ng/ml) and group-III (sufficient 30-100 ng/ml).[14]

Lipid profile[15]

- Total cholesterol (TC): It will be investigated by CHOD-POD method by using spectrophotometer.

- Triglycerides (TG): It will be measured by GPO-PAP method by also using spectrophotometer
- High density lipoprotein cholesterol (HDL-C): HDL-Cholesterol will be measured by CHOD-POD/ Phosphotungstate method by spectrophotometer
- Low density lipoprotein cholesterol (LDL-C): LDL-cholesterol will be calculated by friedewald formula.

$$\text{LDL} = \text{TC} - \text{HDL} - \frac{\text{TG}}{5}$$

Statistical analysis

All baseline parameters (Age, BMI, TSH, T3, T4, Vitamin D, TC, TG, HDL-C and LDL-C) were expressed in Mean±SD. An unpaired student's t test was used for differentiating of various parameters between two groups. An ANOVA was used for the difference of various parameters based on vitamin D concentration. For the association between various parameters, Pearson correlation coefficient was used. The odd ratio was also calculated. All the statistical analysis was used by using statistical software IBM-SPSS (statistical package for statistical analysis) version 23.0. A p-value <0.05 was used as statistically significant.

RESULTS

There were 58 women found with the lower concentration of vitamin D below the reference range, in which 39 with the deficient production of vitamin D and 19 women with insufficient production of vitamin D while remaining 42 women were found with the normal level of vitamin D within reference range (Figure 1) with non-significant difference in the age group between them.

In thyroid profile, there were high concentrations of TSH and T3 in women with a lower concentration of vitamin D and women with the normal level of vitamin D respectively compared to opposite group and this difference was significant. Similarly, there was a higher concentration of T4 in section-II when compared with Section-I. BMI was significantly higher in women in section-I compared to those in section-II. In the case of lipid profile, elevated concentrations of TC, TG, and LDL-C was observed in overweight women compared to normal healthy women, while there was the lower concentration of HDL-C was observed in overweight women compared to normal perimenopausal women. These differences were statistically significant (Table 1).

Table 1: Baseline parameters in different sections of peri-menopausal women.

Parameters	Section-I (58)	Section-II (42)	P value
Age	44.13±3.12	44.14±3.25	0.994
TSH	3.76±1.74	2.96±1.01	0.005
T4	8.14±1.79	8.71±1.32	0.068
T3	102.74±17.62	111.02±19.28	0.031
BMI	24.70±1.12	24.39±2.37	<0.001
Vitamin D	15.42±7.26	47.17±15.96	<0.001
TC	228.18±23.79	193.64±22.39	<0.001
TG	161.84±64.92	118.45±41.43	<0.001
HDL-C	41.09±2.87	47.56±4.65	<0.001
LDL-C	155.75±21.82	128.24±24.94	<0.001

Variables were expressed in Mean±SD. p value <0.05 is statistically significant.

Table 2a: Different parameters among different groups of vitamin D.

Parameters	Group-I (39)	Group-II (19)	Group-III (42)	P value
Age	44.51±3.05	43.36±3.21	44.14±3.25	0.437
TSH	3.81±1.81	3.64±1.63	2.96±1.01	0.032
T4	7.93±1.74	8.58±1.85	8.71±1.32	0.078
T3	100.34±18.92	107.65±13.75	111.02±19.28	0.033
BMI	26.77±1.24	26.56±0.85	24.39±2.37	<0.001
TC	233.51±22.75	217.26±22.62	193.64±22.39	<0.001
TG	169.64±68.55	145.84±54.98	118.45±41.43	<0.001
HDL-C	40.86±3.01	41.58±2.57	47.56±4.65	<0.001
LDL-C	161.44±21.91	144.06±16.74	128.24±24.94	<0.001

Variables were expressed in Mean±SD. p value <0.05 is statistically significant.

After comparing this study population on the basis of vitamin D level, an elevated body mass index was observed in Group I and Group II above the normal range. Significant (<0.01) highest concentration of TSH was observed in Group I and lowest in group III. Opposite findings of T4 and T3 was observed showing the highest level in group-III and the lowest level in group-I. Lipid fractions including TC, TG, and LDL was also significantly (<0.05) higher in group-I compared to remaining groups. The concentration of HDL-C was significantly higher in group-III compared to other groups (Table 2a and 2b). There was an inverse correlation of vitamin D with BMI and TSH and positive correlation with T3 and T4. Except for T3, this

correlation was significant in other parameters. Moreover, there was a significant negative association of vitamin D with lipid parameters including TC, TG and LDL-C and positive association with HDL-C in this study population. (Table 3) there was significant presence of overweight (OR-18.0, p-value ≤0.001) and dyslipidemia (OR-12.13, p-value ≤0.001) in this study population. (Table 4).

Table 2b: Odd ratio for different parameters in study population.

Parameters	OD (CI)	P value
Overweight	18.00 (5.50-58.89)	<0.001
Elevated TSH	12.37 (0.68-223.05)	0.088
Dyslipidemia	12.13 (3.36-43.73)	<0.001

OD-odd ratio, CI-confidence interval at 95%.

Table 3: Correlation of various parameters with vitamin D in study population.

Parameters	R value
TSH	-0.381**
T4	0.317**
T3	0.178
BMI	-0.690**
TC	-0.587**
TG	-0.378**
HDL-C	0.665**
LDL-C	-0.585**

By Pearson correlation coefficient. *<0.05 is statistical significant.

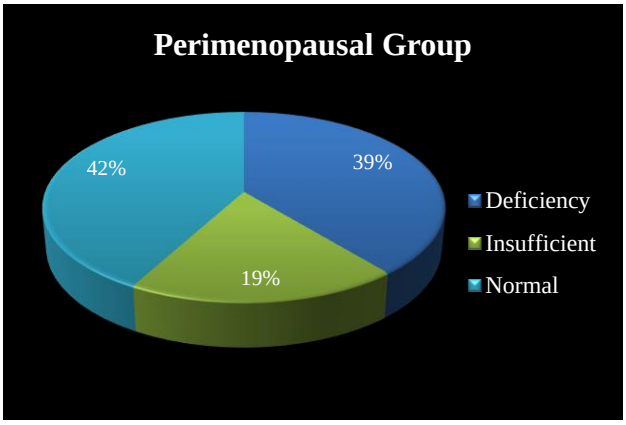

Figure 1: Percentage of women in different groups on the basis of vitamin D level.

DISCUSSION

Vitamin D also called as sunlight vitamin, is synthesised in the skin by direct sun exposure and plays a great role on women health. Vitamin D functions as endocrine hormone in calcium absorption and as autocrine in facilitation of gene expression.[16] Apart from its role in skeleton by inducing calcium metabolism, it is essentially required for muscle contraction and nerve conduction.[17] Its deficiency is highly prevalent worldwide. Perimenopausal women with higher percentage of body fat experience more hot flushes within 4-5 years. Hot flushes along with mood swings are attributed to vitamin D deficiency since vitamin D is known to protect the depletion of serotonin which is a mood elevator.[18] Similar to this, 58 out of 100 perimenopausal women were found with decreased levels of vitamin D in this study, with higher BMI, altered lipid profile and elevated TSH. Numerous changes from psychological to physiological, experienced by perimenopausal women, may be a supportive cause for the presence of vitamin D deficiency.[19] Lagunova Z et al concluded that 1 in 3 women with higher BMI is characterised by vitamin D deficiency.[20] In this study, women with vitamin D deficiency were presented with higher BMI compared to women with a normal concentration of vitamin D. The reason behind the association of vitamin D deficiency with obesity was observed due to deposition of vitamin D in body fat compartments which decreased the availability of vitamin D3 from sources including skin and diet.[21] In the adult population, there was a significant inverse weak correlation observed between serum vitamin 25(OH)D and BMI.[22] In this study, a significant negative correlation was found between serum concentration of vitamin D and BMI in perimenopausal women.

A Study based on post-menopausal women also observed the elevated concentration of TSH and increased BMI in women with vitamin D deficiency. Highest percentage of deficient levels of vitamin D was found with elevated concentration of TSH.[23] So increased level of BMI was the reason for elevation of TSH in perimenopausal women[24] may not be the conclusive evidence since Barchetta I et al stated that despite possible link between Vitamin D and fat mass, an inverse correlation between TSH and vitamin D does not depend on BMI.[25] Additionally, negative correlation between serum vitamin D and TSH in this women based study was supported by Sudha K et al study after observing a consistent increase in TSH separating the level of vitamin D in decreasing order.[26] Similar to other observations women with vitamin D deficiency were also characterised with altered lipid variables. Since studies have shown some association of vitamin D with dyslipidemia. An Indian population based study concluded this significant association with dyslipidemia after observing a positive correlation with HDL and negative correlation with remaining fractions of lipid profile.[27] Deficiency of vitamin D may initiate the elevation of lipolysis circulating free fatty acids and increase hepatic synthesis of LDL cholesterol. Furthermore, in support of these findings, a study based on premenopausal women concluded even after considering lifestyle factors serum 25(OH) D was negatively associated with TC, TG and LDL-C and positive association with HDL-C.[28]

CONCLUSION

The outcome of this study suggests that vitamin D deficiency is equally prevalent in perimenopausal women similar to an elderly population. Elevated concentration of TSH along with increased BMI may precipitate hypothyroidism in later stages. The presence of altered lipid profile in women with vitamin D deficiency predisposes the development of cardiovascular disease. Generally, people or clinicians may overlook the presence of vitamin D deficiency except bones related disorders so exposure to sun light and vitamin D rich food or supplements should be regularly taken and routine screening of vitamin D status is quite necessary. Although the sample size of this study could be small despite that findings of this study should not be neglected. Therefore, more studies should be conducted with other parameters to establish the fact.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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