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ASSESSMENT OF VITAMIN D STATUS IN PREGNANT WOMEN, A PROSPECTIVE OBSERVATIONAL STUDY FROM KASHMIR VALLEY

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ABSTRACT

Back ground: Vitamin D deficiency during pregnancy has important health implications for the mother and infant, including fetal hypovitaminosis D, neonatal rickets and tetany, infantile rickets. Recent studies, in many countries, have shown that low maternal vitamin D status is common during pregnancy, the magnitude of which warrants public health intervention.
Aims: To prospectively assess the vitamin D nutritive status in pregnant women in Kashmir Valley and to study the prevalence of suboptimal vitamin D status in apparently healthy pregnant Kashmiri women. Study Design: One hundred and ninety three consenting pregnant women attending the antenatal clinic of the Gynecology & Obstetrics Department of SKIMS over the study period of 18months were enrolled.
Materials: The subjects found eligible underwent a detailed history and physical examination as per a pre-formed proforma. History was focused on occupation, dietary history including diet taken in last 24 hours, exposure to sunlight, drug intake, menstrual history and history of any systemic illness. A particular record was made of the women's dressing habits. Of the 193 subjects recruited, only 165 subjects (in whom Vitamin D levels could be estimated) were further analyzed for the study. Serum levels of [25 (OH) D] were estimated by DiaSorin 25-OH-D assay, an RIA based procedure.
Results: In the present study, vitamin D insufficiency (defined as serum 25[OH] D levels <30 ng/ml) was observed in about 82% of pregnant Kashmiri women while as vitamin D deficiency (serum 25[OH] D <20 ng/ml)2 was observed in 68.5%. In only about 18% subjects vitamin D sufficiency (serum 25[OH] D >30 ng/ml) was observed.
Conclusion: From our study we conclude that vitamin D deficiency is quite prevalent in normal pregnant women in Kashmir valley. Taking a cut off value of 25 (OH) D of less than 20 ng/ml as vitamin D deficiency, overall 68.5% of pregnant women were found to be vitamin D deficient.

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INTRODUCTION

Vitamin D and its metabolites are hormones and hormone-precursors rather than vitamins, since in the proper biological setting, they can be synthesized endogenously. (Bringhurst *et al*., 2005) Vitamin D plays an important role in calcium homeostasis and also has numerous extra-osseous effects.

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While overt vitamin D deficiency manifests as rickets and fractures in children and osteomalacia in adults, less severe deficiency has also been associated with detrimental skeletal consequences including secondary hyperparathyroidism, increased bone turnover, enhanced bone loss and fracture risk. (Adams and Hollis, 2002; Webb *et al*., 1988) Vitamin D deficiency during pregnancy has important health implications for the mother and infant, including fetal hypovitaminosis D, neonatal rickets and tetany, infantile rickets. (Balasubramanian *et al*., 2003; Thacher *et al*., 1999; Purvis *et al*., 1973).

Rickets during infancy has been associated with higher prevalence of lower respiratory tract infections (Muhe *et al*., 1997), the largest cause of infant mortality in India. Despite data from other countries indicating low maternal vitamin D status is common during pregnancy, there is a dearth of information about vitamin D status during pregnancy in India in general and in Kashmiri female population in particular. This fact and the plethora of established and speculated influences of vitamin D on the health of the mother and the developing fetus prompted us to prospectively assess the vitamin D nutritive status and the prevalence of suboptimal vitamin D status in apparently healthy pregnant Kashmiri women.

Aims & Objectives

The main objective of this study was to prospectively assess the vitamin D nutritive status in pregnant women in Kashmir Valley and to study the prevalence of suboptimal vitamin D status in apparently healthy pregnant Kashmiri women.

Study Design

This study was conducted at the Departments of Endocrinology and Immunology of Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura, Srinagar, a tertiary care hospital in the valley of Kashmir. One hundred and ninety three consenting pregnant women attending the antenatal clinic of the Gynecology & Obstetrics Department of SKIMS over the study period of 18 months were enrolled. Subjects were preferably enrolled at the booking visit and particular attention was given that chosen subjects were representing pregnant women with different occupations like house wives, teachers, professionals, and other working women. Women from both rural and urban areas were included in the study. Inclusion and exclusion criteria: The selected pregnant subjects had to be: Apparently healthy,18 to 40 years old, residing in the valley for at least five years, carrying a singleton pregnancy. Females with the presence of renal, hepatobiliary, or any other disease known to influence vitamin D metabolism, lactating females, history of having received therapeutic doses of vitamin D within the previous 6 months, prior diagnosis of osteomalacia, tuberculosis and sarcoidosis, history of intake of drugs known to affect mineral homeostasis, age less than 18 or more than 40 and females with twin pregnancy were excluded from the study.

Clinical Assessment

Of the 193 subjects recruited, only 165 subjects (in whom Vitamin D levels could be estimated) were further analyzed for the study. The subjects found eligible underwent a detailed history and physical examination as per a pre-formed proforma. History was focused on occupation, dietary history including diet taken in last 24 hours, exposure to sunlight, drug intake, menstrual history and history of any systemic illness. A particular record was made of the women's dressing habits. Clinical examination was performed of various systems to rule out any systemic illness. Direct sunlight exposure was assessed by average daily duration of exposure and percentage of body surface area exposed. (Mike Tyler, 2004) During the study period the average duration of cloud free sunshine was 4.4 hours/day in winter months (October to March) and 6.5 hours/day in summer months (April to September) in Kashmir valley which is situated at an altitude of 1574 feet to 5425 feet above the sea level. Kashmir valley is situated at latitudes 32" 20'-34" 50'N and longitude 73" 45'-75" 35'E as per data provided by Meterology department, Kashmir. On the basis of sunlight exposure subjects were divided into three categories; those having good exposure (20-30 hours/week), moderate exposure (10-19 hours/week) and poor exposure (less than 10 hours per week). The study subjects were visually characterized as dark and fair on the basis of skin pigmentation. Kashmiris as a race are fair and very few study subjects were dark. Nutritional status was assessed by interviewing subjects about their food habits and estimating the composition of daily diet in terms of energy, carbohydrate, protein, fat and calcium intake by using a semi quantitative food frequency questionnaire and published data on the relevant composition of Indian foods (Willet *et al*., 1985; Gopalan and Balasubramaniam, 1996) .On the basis of diet subjects were classified as having good, satisfactory and poor dietary status. The laboratory evaluation comprised the estimation of serum calcium, phosphorus, ALP and 25–hydroxyl vitamin D_3 [25 (OH) D] levels. The samples were taken for estimation throughout the study period in both summer and winter months. In addition, detailed hemogram, liver and kidney function tests and lipid levels were estimated in all subjects. Serum levels of [25 (OH) D] were estimated by DiaSorin 25-OH-D assay which is a two-step procedure. The first step involves a rapid extraction of 25-OH-D and other hydroxylated metabolites from serum or plasma with acetonitrile. Following extraction, the treated sample was then assayed using an equilibrium RIA procedure. Vitamin D levels in the studied subjects were graded as**,** Deficiency < 20 ng/mL (0-50 nmol/L), Insufficiency 20-30 ng/mL (50-75 nmol/L), Sufficiency 30-100 ng/mL (75-250 nmol/L) and Toxicity > 100 ng /mL (>250nmol/L). (Holick, 2007)

Statistical Analysis

Statistical Package for Social Sciences (SPSS) version 11.5 was used for statistical analysis of the data. Pearson's Chi-square method was used for comparing proportions and rates; a Fisher exact test was used wherever required. Student's t-test and ANOVA were used for comparison of continuous variables. Where the data was not normally distributed, a non-parametric test like Mann-Whitney U test for two-independent samples or Kruskal-Wallis-H test for several independent samples was used. Logistic regression analysis was performed to study the factors affecting the prevalence of vitamin D deficiency. A two-tailed p value was used for calculating statistical significance; a value of P <0.05 was taken as significant.

Ethical Consideration

A written informed consent was obtained from all the patients involved in the study protocol. The study was taken only after clearance by institutional ethical committee.

RESULTS

One hundred and ninety three, apparently normal, pregnant, Kashmiri women were recruited for the study. The mean age of the study subjects was 26.72 ± 3.82 years. On the basis of sunlight exposure the subjects were classified into those with good exposure, moderate exposure and poor exposure; 15.3% of our subjects had poor exposure (<10 hours/week), 67.2% had moderate exposure (10 to 20 hours/week) and 17.5% were

having good exposure (>20 hours/week). Of the 193 subjects recruited, only 165 subjects (in whom Vitamin D levels could be estimated) were further analyzed for the study; 94 (57%) of these subjects were from rural habitat. Based on duration of pregnancy at the time of sample collection, 44 (27%) were in the first, 54 (33%) in the second and 67 (40%) were in third trimester. Estimation of 25-hydroxy vitamin D levels (25[OH]D) revealed that 25[OH]D ranged from undetectable levels (<0.001 to 400 ng/ml) with a median level of 11.4 ng/ml. About 28% of the studied 165 pregnant women had 25[OH]D levels less than 5ng/ml whereas, two patients (1%) had 25[OH]D levels more than 100 ng/ml (Table 1).

Table 1. Circulating 25[OH]D levels in the study subjects

25[OH]D, (ng/ml)	N	Percent
• <5	46	27.9%
• 5-9	33	20.0%
• 10-14	22	13.3%
• 15-19	12	7.3%
• 20-24	12	7.3%
• 25-30	10	6.1%
• 30-100	28	17.0%
• >100	02	1.2%

To know the vitamin D status of our study population, we categorized our subjects into four groups, i.e., Deficiency, Insufficiency, Sufficiency and Toxicity group (Table 2).

Table 2. Vitamin D status of the study population (n= 165)

Vitamin D status	N	Percent
Deficiency (<20 ng/ml)	113	68.5%
Insufficiency (20-30)	22	13.3%
Sufficiency (30-100)	28	17.0%
Toxicity > (100)	2	1.2%

Taking 25[OH]D < 20 ng/ml as vitamin D deficiency we observed that 113 (68.5%) were having vitamin D deficiency, 22 (13.3%) subjects were having insufficient 20-30 ng/ml and 28 (17%) subjects had sufficient (30-100 ng/ml) vitamin D levels. Only 2 (1.2%) of our subjects were found to have vitamin D levels in the toxic range (>100ng/ml) Overall, only 18% of pregnant Kashmiri women had sufficient vitamin D levels of 30ng/ml or more and 82% were vitamin D defficient. Vitamin D deficiency was directly related to duration of pregnancy; a level of <5 ng/ml was seen in 29.5% subjects in the first trimester as compared to 37.9% in third trimester. There was no correlation of Vitamin D deficiency with skin pigmentation; only 7 cases had pigmentation, rest of the subjects had fair complexion as expected in our Kashmiri race. Five out of 7 subjects (71%) with pigmentation were vitamin D deficient (<20 ng/ml) as against 68% in the non pigmented subjects.

DISCUSSION

Some recent studies have expressed concern about the prevalence of low vitamin D status amongst pregnant women (Hollis and Wagner, 2006) and have even suggested that vitamin D deficiency during pregnancy may be at epidemic levels. (Hollis and Wagner, 2004)In the present study, vitamin D insufficiency (defined as serum 25[OH] D levels <30 ng/ml) (Holick, 2007) was observed in about 82% of pregnant Kashmiri women while as vitamin D deficiency (serum 25[OH] D <20 ng/ml) was observed in 68.5%. In only about 18% subjects vitamin D sufficiency (serum 25[OH]D >30 ng/ml) was observed.

In majority of women vitamin D insufficiency was observed in all seasons as well as all trimesters; even during the light season (March to November, during which one would expect vitamin D status to be much improved upon winter values), only 17% of women had sufficient vitamin D status. This is the first study, to report vitamin D status data for Kashmiri pregnant women. However, the findings are in line with those from other studies of pregnant women in countries elsewhere .(Johnson *et al*., 2010)' (Nicolaidou *et al*., 2006; Ainy *et al*., 2006; van der Meer *et al*., 2006; Morley *et al*., 2006; Javaid *et al*., 2006; Holmes *et al*., 2009; O'Riordan *et al*., 2008; Harris *et al*., 2010) Of even more concern are the extremely low values of 25-hydroxy vitamin D observed in some of Kashmiri pregnant women.

The reasons for the very high prevalence of low vitamin D status in our subjects, though disturbing can be only speculative. First, one needs to understand the factors that influence vitamin D status of any population. These factors include unfavourable latitude and Zenith angle at the places studied, cloudy weather and season, time and duration of exposure to sunlight, skin type, colour and texture, use of sunscreens, socioeconomic status and diet. (Webb *et al.,* 1988; Clemens *et al.,* 1982; Need *et al.,* 1993; Pfeifer *et al.,* 2000) Mean age of our study subjects was 27.0±4.2 years. Majority (84 out of 165) of these were in the age group of 25-29 years with a median vitamin D level of 9.2ng/ml. Taking <20ng/ml of vitamin D level as deficiency (Holick, 2007), we reported a high prevalence (68%) of vitamin D deficiency in our study. O'Riordan MN et al in 2008 reported that 14.3-23.7% of Irish women had vitamin D deficiency (serum 25 (OH) D <25 nmol/l or < 10ng/ml) during pregnancy which was quite low to what we observed in our respective population. (O'Riordan *et al*., 2008) We found that only 18% of our study population was having sufficient (>30ng/ml) vitamin D levels. We observed a median level of 25(OH)D of about11.4 ng/ml in Kashmiri pregnant women. A recent study by Johnson and colleagues, revealed that the mean 25 (OH) D levels in African-American, Hispanic, and Caucasian pregnant women were 15.5±7.2 (standard deviation), 24.1±8.7 and 29.0±8.5 ng/mL, respectively. Ninety-seven percent of African-Americans, 81% of Hispanics, and 67% of Caucasians were deficient (25 (OH) D levels <20 ng/mL) or insufficient (<32 ng/mL). Of these pregnant women, 82% had vitamin D levels <32 ng/mL.[27] Our results were consistent with their study as we also found that 82% of the study subjects were having insufficient vitamin D levels (<30ng/ml). In summary, we report a high prevalence of both vitamin D deficiency (68%) or insufficiency (82%) in pregnant Kashmiri women living at 32–34 N. Women reporting multivitamin supplement usage during pregnancy did have higher vitamin D status, but many remained vitamin D insufficient. Suboptimal vitamin D status has significant consequences for maternal and neonatal health and, therefore, further research is needed to determine the dietary vitamin D intake required to maintain vitamin D sufficiency during pregnancy, and to underpin guidelines for supplement use during pregnancy.

Conclusion

Despite abundant sunlight, majority of normal pregnant women of Kashmir valley are Vitamin D deficient. From our study we conclude that vitamin D deficiency is quite prevalent in normal pregnant women in Kashmir valley. Taking a cut off value of 25 (OH) D of less than 20 ng/ml as vitamin D deficiency, overall 68.5% of pregnant women were found to be

vitamin D deficient. Only 18% of subjects are having a vitamin D sufficient status (serum 25[OH]D of 30ng/ml or more)

Conflict of interest

The authors have no conflict of interest to declare.

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