Original Article

Cross-sectional Study on Vitamin D Levels in Stress Urinary Incontinence in Women in a Tertiary Referral Center in India

Jai B. Sharma, Vivek Kakkad, Sunesh Kumar, K K. Roy
Department of Obstetrics and Gynaecology, AIIMS, New Delhi, India

Abstract

Objective: To assess the levels of vitamin D in patients with Stress Urinary Incontinence (SUI) in gynecology clinic of All India Institute of Medical Sciences, New Delhi. **Materials and Methods:** This is a cross sectional study on a total of 40 women presenting to gynecology outpatient department with stress urinary incontinence diagnosed by history and examination. The women were divided with moderate, severe and very severe SUI confirmed by incontinence severity index (ISI) and pad test. Vitamin D (serum 25 OH D) levels were measured in all cases by electrochemiluminenscene Immunoassay (ECLIA) using Roche Elecsys 2010 and levels of >30 ng/ml were taken as sufficient while levels between 20-30 ng/ml as insufficient and <20 ng/ml as deficient. Statistical analysis was performed using ANOVA test with *P* value of <0.05 taken as significant. **Results:** Mean age of patients was 41.6 years. Mean parity was 2.73 and mean duration of symptoms was 4.14 years. Vitamin D levels ranged between 6-38 ng/ml with mean being 17.15±8.1 ng/ml. Levels were deficient (<20 ng/ml) in 30 (75%) women, insufficient (20-30ng/ml) in 7 (17.5%) women and sufficient (>30ng/ml) in 3 (7.57%) women. There was no significant correlation between severely of SUI and levels of vitamin D with Vit D being 19.18±5.76 ng/ml in moderate SUI, 16.96±9.03 ng/ml in severe SUI and 13.60 ± 2.09 ng/ml in very severe SUI. **Conclusion:** There was very high prevalence of vitamin D deficiency in SUI patients with 75% patients showing deficient levels and 17.5% showing insufficient levels in SUI patients. There is need to provide vitamin D supplementation in such women.

Keywords: Incontinence severity index (ISI), pad test, Stress urinary incontinence (SUI), vitamin D

Introduction

Urinary incontinence is defined by the International Continence Society as the involuntary loss of urine that represents a hygienic or social problem to the individual.[1] Stress urinary incontinence occurs during periods of increased intraabdominal pressure (e.g., sneezing, coughing, or exercise) when the intravesical pressure rises higher than the pressure that the urethral closure mechanism can withstand, and urine loss results. Stress urinary incontinence is the most common form of transurethral urinary incontinence in women, mainly seen in the reproductive age group and post-menopausal women. There is some evidence that age, pregnancy, childbirth, obesity, functional impairment, and cognitive impairment are associated with increased rates of incontinence or incontinence severity.[2] Vitamin D is a fat-soluble vitamin whose active metabolite [1, 25 (OH) D3] plays a vital role in calcium homeostasis and thus is important to overall health. Vitamin D insufficiency is very common among the population of India.[3-6] Insufficient vitamin D levels have been shown to be associated with various extra-skeletal medical conditions including cardiovascular disease, diabetes, asthma, and preeclampsia.[7-9] However, the most notable effect of insufficient vitamin D has been on musculoskeletal health. Observational and randomized studies have confirmed that lower levels of serum 25-hydroxyvitamin D [25(OH)D] are associated with decreased postural stability[10] and increased risk of falls.[11]

Recently, Vitamin D has been implicated in the causation of pelvic organ prolapse and SUI. Because vitamin D receptors are present in human muscle tissue,[12] a direct effect of vitamin D on muscle physiology is biologically plausible.[13] Thus, it is not surprising that vitamin D deficiency has long been clinically associated with impaired muscle strength and loss

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Address for correspondence: Dr. Jai B. Sharma, Department of Obstetrics and Gynaecology, AIIMS, New Delhi, India. E-mail: jbsharma2000@gmail.com

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of muscle mass[14] Vitamin D inadequacy is well known in osteoporosis patients.[15] Given that vitamin D insufficiency or deficiency is epidemic among adults, it is plausible that low vitamin D status contributes to the development of poor muscle strength and can lead to different pelvic floor disorders (PFD) such as urinary/fecal incontinence and pelvic organ prolapse (POP). The pelvic floor is composed of the levatorani and coccygeus skeletal muscles. Pelvic floor muscle weakness is clinically observed in women with PFD symptoms and thus may be affected by insufficient serum vitamin D. Crescioli *et al*.[16] hypothesized that bladder dysfunction may be related to vitamin D deficiency through effects on the detrusor muscle.

Badalian *et al*[17] had done cross-sectional study in 2010 and found that mean vitamin D levels were significantly lower for women reporting at least one PFD and for those with urinary incontinence, irrespective of age. The likelihood of urinary incontinence was significantly reduced in women 50 and older with vitamin D levels 30 ng/ml or higher.

Higher vitamin D levels are associated with a decreased risk of PFDs in women. Although vitamin D deficiency is highly prevalent in India as seen in many Indian cohorts (3-6), there are no Indian studies which looked at the prevalence of vitamin D deficiency in stress urinary incontinence as a subgroup. hence, the present study was planned.

In the present study, vitamin D levels were measured in woman with stress urinary incontinence in India to know the levels of vitamin D deficiency in stress urinary incontinence patients.

Materials and Methods

It was a prospective study on 40 women presenting with stress urinary incontinence in the outpatient department in gynecology in a tertiary referral center and who agreed to participate in the study. Women with prolapse, urge incontinence, cancer, systemic diseases, and on vitamin D supplementation in last month or on medication with vitamin D levels were excluded from the study.

Written informed consent was taken for all patients. Ethical approval was taken from the Institute Ethical committee. Detailed history was taken as per questionnaire including symptoms, menstrual history, incontinence history, and obstetrics history. Clinical examination was done in all patients including general physical examination, abdominal examination, speculum examination, vaginal examination, and Bonney's test. Incontinence severity index was used in all patients as below.

Incontinence severity index

I. How often do you experience urinary leakage? (Please tick one)

None	0
Less than once a month	1
A few times a month	2
A few times a week	3
Every day and/or night	4

II. How much urine do you lose each time? (Please tick one)

None	0
Drops	1
Small Splashes	2
More	3

ISI score = I + II

ISI category:

Slight (1–2) Moderate (3–6) Severe (8–9) Very severe (12).

In all patients, 24-h pad test using Kitchen scale with accuracy of 1 g weight of total number of pads used by patients for 24 h was done and pad weight difference (post soakage weight- pre soakage weight) was taken in all cases. Incontinence was graded as follows:

Mild incontinence: 24 h leak	1.3–19 g
Moderate incontinence: 24 h leak	20–74 g
Severe incontinence: 24 h leak	75 g or more

Vitamin D (serum 25 0H D) levels were measured by electrochemiluminescence immunoassay (ECLIA) using Roche Elecsys 2010 immunoassay analyser and in the Department of Endocrinology, AIIMS, New Delhi. Patients were divided as follows:

Vitamin D levels >30 ng/ml: Sufficient

Vitamin D levels 20–30 ng/ml: Insufficient

Vitamin D levels <20 ng/ml: Deficient

Correlation of vitamin D was made with different grade of SUI as per ISI grading and pad test.

Statistical analysis

Data analysis was carried out using statistical package SPSS IBM Version 21.0.

Descriptive statistics such as mean, standard deviation, and range values were computed for continuous variable. Normality of data was tested using appropriate statistical tests. For the variables which showed approximate to normal distribution, student's t independent test was used to compare mean values of two groups. For the same group, pre and post values were compared by paired t-test. Frequency distribution by categories was compared using Chi-square or Fisher's exact test as appropriate. To find out the correlation between variable parameters, Pearson's Correlation coefficient was computed. Comparison among subgroup was done by ANOVA test. For all statistical tests, P value < 0.05 was considered statistically significant.

All patients with vitamin D deficiency were given 2 satches (1, 20, 000 {60, 000 each}) of vitamin D per month for 6 months. All patients of SUI were also treated as per the standard protocol of SUI in the hospital using Kegel's exercises, duloxetine therapy, or surgical treatment (tension-free vaginal tape or Burch's Colposuspension) as per clinical protocol of hospital depending upon severity of SUI on individualized basis.

Sample size calculation

An earlier study by Chai *et al*. (2016)[18] had shown that mean value of total vitamin D was 33.5 (standard deviation 14.4). Based on this information by assuming an effect size of 0.5 with 10% attrition rate, the required sample size hat will have 80% power at 5% level of significance was 40**.**

Statistical analysis

Data was computerized using EXCEL spreadsheet. Data analysis was carried out using statistical package SPSS IBM Version 21.0. Descriptive statistics such as Mean, Standard Deviation and range values were computed for continuous variable. Normality of data was tested using appropriate statistical tests. For the variables which showed approximate to normal distribution student's t independent Test was used to compare mean values of two groups. For same group pre & post values compared by paire t Test. Frequency distribution by categories were compared using Chi square or Fisher's exact test as appropriate. To find out the correlation between to variable parameter, Pearson's Correlation Cofficient was computed. Comparision among subgroup done by ANOVA test. For all statistical tests p value < 0.05 was considered statistically significant.

Results

A total of 40 women presenting to AIIMS gynecology OPD with stress urinary incontinence diagnosed on history taking, clinical examination, and incontinence severity index (ISI) were enrolled in this prospective study. The characteristics of women are shown in Table 1. Thus, age ranged from 31–61 years with mean being 41.6 years while parity ranged from 1 to 6 with mean being 2.73. Duration of symptoms ranged from 6 months to 14 years with mean being 4.14 years. The mode of delivery is also shown in Table 1. The majority (85%) had normal vaginal deliveries, while 5 (12.5%) had both vaginal delivery and one cesarean section, and only 1 (2.55%) patient had only cesarean sections.

Vitamin D levels in SUI patients are shown in Table 2. Vitamin levels ranged from 6–38 ng/ml with men being 17.15 ± 8.1 ng/ml. Vitamin D levels were deficient (<20 ng/ml) in 30 (75%) patients, while they were insufficient (20–30 ng/ml) in 7 (17.5%) patients and only 3 (7.5%) women had sufficient vitamin D (>30 ng/ml) levels.

Patients of SUI were divided into moderate, severe, and very severe SUI as per incontinence severity index (ISI) as shown in Table 3. Thus, a total of 11 (27.5%) patients had moderate SUI as per ISI (ISI 3–6), 24 (60%) patients had severe SUI (ISI 8–9), while 5 (12.5%) patients had very severe SUI (ISI 12).

Vitamin D levels as per ISI index are shown in Table 4. Thus, mean vitamin D levels were 19.18 ± 6.78 ng/ml in moderate SUI (ISI 3–6), 16.96 ± 9.03 ng/ml in severe SUI (ISI 8–9), and were 13.60 ± 2.09 in very severe SUI (ISI 12).

Overall levels of vitamin D were 17.15 ± 8.12 ng/ml. The levels of vitamin D fell as the severity of SUI increased but it was not statistically significant ($P = 0.62$).

Grading of SUI by pad test and relative Vitamin D levels in different grades of SUI are shown in Table 5. Thus, as per pad test, 3 patients (7.9%) had mild SUI (13–19 g urine leak in 24 h) with mean vitamin D levels of 14.0 ± 5.29 ng/ml. A total of 33 (86.8%) patients had moderate SUI (20–74 g urine leak in 24 h) with mean vitamin D levels being 17.91 ± 8.15 ng/ml),

Table 1: Characteristics of women in study

Age	Range	Mean
Mean of	31-61	41.6 years
Parity	1-6	
Mean parity	2.73	
Duration of symptoms	6 months-14 years	4.14 years
Mode of delivery	**Number**	**Percentage**
i) All vaginal delivery	34	85
ii) vaginal delivery and cesarean section	5	12.5
iii) Only cesarean section	1	2.5

Table 2: Vitamin D levels in SUI patients

Characteristics	Vitamin D levels	
Range	6-38 ng/ml	
Mean Vitamin D	17:15±8.1 ng/ml	
Vitamin D Level (ng/ml)	**Number**	**Percentage**
i) Deficient <20 ng/ml	30	7.5%
ii) Insufficient 20-30 ng/ml	7	17.5%
iii) Sufficient >30 ng/ml	3	7.5%

Table 3: Incontinence severity index (15+) in study patients (n=40)

Group	Category	1st score	Number	Percentage
1.	Moderate SUI	3-6	11	27.5
2.	Severe SUI	8-9	24	60.0
3.	Very severe SUI	12	5	12.5

Table 4: Relative vitamin D levels as per ISI index

Group	1st	Number	Percentage	Mean Vitamin D level (ng/ml±SD)
1	Moderate (3-6)	11	27.5	19.18±6.76
2.	Severe (8-9)	24	60.0	16.96±9.03
3.	Very severe (12)	5	12.5	13.60±2.09
4.	Overall	40	100	17.15±8.12

Pearson correlation 0.8 P=0.62

Table 5: Grading of SUI by Pad test and vitamin D levels

24-h Pad test (g)	Number	Percentage	Mean Vitamin D levels±ng/dl
Mild (13-19 g)	3	7.9	14.0±5.29
Moderate (20-74 g)	33	86.8	17.91±8.15
Severe (0.775 g)	2	5.3	15.0±2.82

while 2 (5.3%) patients had severe SUI (>75 g urine leak in 24 h) with mean vitamin D levels being 15.0 ± 2.82 ng/ml. Hence, as per pad test, the levels of vitamin D were less in all patients, but were not significantly different in different grades. It could be due to very smaller number of patients (only 3 in mild and 2 in very severe SUI).

Hence, levels of vitamin D were lower (either deficient or insufficient) in most (92.5%) women with SUI and there was no significant decrease in vitamin D levels with increase in levels of SUI.

Discussion

Stress urinary incontinence is the most common form of transurethral urinary incontinence in women, mainly seen in the reproductive age group and post-menopausal women and is underdiagnosed and underreported.[1] Hampel *et al*.[19,20] in a large meta-analysis in 1997 and then in 2004 reported an estimated prevalence of urinary incontinence of 30% in women aged 30–60 years, with approximately half of the cases attributed to SUI.

SUI worsens with age and child birth.[1,2] In the present study mean age was 41.6±8.4 years and mean parity was 2.73. Women with SUI often suffer in silence before presenting. In the present study average duration of stress incontinence was 4.14 years.

The relationship between SUI and Vitamin D and improvement after vitamin D supplementation is not known. Vitamin D is a fat-soluble vitamin whose active metabolite [1,25(OH) D3] plays a vital role in calcium homeostasis and thus is important in overall health. Because Vitamin D receptors are present in human muscle tissue,[12] a direct effect of vitamin D on muscle physiology is biologically plausible. Our study confirms very high prevalence of vitamin D deficiency in women with SUI. Our results are similar to other authors who reported lower vitamin D in various urogynaecological disorders. In the present study, over 40 women with SUI, the mean vitamin D levels were 17.15 ± 8.12 ng/ml. Only 3 (75%) women had normal vitamin D levels but 30 (75%) were vitamin D deficient, while 7 (17.57%) had insufficient vitamin D levels.

In the present study, ISI was taken to define the grading of SUI[21] and vitamin D levels were correlated with the severity of SUI as per ISI. There was trend toward falling mean vitamin D levels as severity increased being 19.18 ng/ml in moderate, 16.96 ng/ml in severe, and 13.60 ng/ml in very severe SUI. However, there was no significant difference (P = 0.62). Grading of SUI was done as per ISI and which are well established and validated in quantification and grading of urinary incontinence by different studies using pad test.[21,22] Majority (86.8%) women have moderate SUI as per pad test. The mean vitamin D levels were low in most cases of SUI being 14.0 ng/ml in mild SUI, 17.91 ng/ml in moderate SUI, and 15.0 ng/ml in severe SUI, but it was not statistically different. It could be due to in very few cases, mild and severe SUI categories (3 in mild and 2 in severe SUI).

Pal *et al*.[23] demonstrated a strong relationship between moderate to severe POP and low bone mineral density in postmenopausal women enrolled in the Women's Health Initiative Estrogen Plus Progestin trial. Badalian *et al*.[17] had done a cross-sectional study in 2010 and found that Mean vitamin D levels were significantly lower for women reporting at least one PFD and for those with urinary incontinence, irrespective of age. The likelihood of urinary incontinence was significantly reduced in women 50 and older with vitamin D levels 30 ng/ml or higher. Gau in 2010[24] observed improvement of urinary incontinence after supplementation of vitamin D.[24]

Cardace *et al*.[25] observed mean vitamin D levels of 29.3 ± 11.5 ng/ml in their study on PFD.

However, vitamin D deficiencies are pandemic and are underdiagnosed and undertreated nutritional deficiency in the world.[7] Vitamin D deficiency is common in India despite plentiful sunshine in India.[3-6] High prevalence of vitamin D deficiencies was observed in India.[3-6] Tando *et al*.[26] observed mean vitamin D of 23.3 ng/ml in women while Goswami *et al*.[27] observed mean vitamin D to be only 8.76 ng/ml in women in 2000 and even lower 6.8 ng/ml in 2009.[28] Similarly Marwaha *et al*.[5] observed vitamin D level of only 9.79 ng/ml with 91.2% women being deficient in vitamin D.

Conclusion

To conclude, vitamin D levels were low in the majority of SUI patients (92.5%) being deficient in 75% women. There is a need to improve vitamin D levels in the population by vitamin D supplementation. However, large multicentric studies are recommended to confirm the findings of the present study.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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