

Correlation of 25-Hydroxyvitamin D3 Serum Level with Levator Ani Muscle and Gastrocnemius Soleus Muscle Strength in Patients with Pelvic Organ Prolapse and Patients without Pelvic Organ Prolapse in Postmenopausal Women

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Abstract

Introduction: The aim of this study was to evaluate the correlation of 25-Hydroxyvitamin D3 serum level with levator ani muscle and gastrocnemius soleus muscle strength in patients with pelvic organ prolapse (POP) and patients without POP in postmenopausal women.

Materials and Methods: This study was an observational analytical cross-sectional study. The subjects of study were postmenopausal women consisted of 22 patients with POP and 22 patients without POP. 25-Hydroxyvitamin D3 serum level, levator ani muscle and gastrocnemius soleus muscle strength were measured in all women. Spearman's correlation test was used for data analysis.

Results: The mean age of POP group was 59.4 years while non-POP group was 55 years. The age of POP group and non-POP group showed significant differences, while BMI in both groups did not show significant differences so that it could be compared ($p>0.05$). In the non-POP group, the mean and median of all variables were greater than POP group ($p<0.05$). There were no significant correlation ($p>0.05$) between 25-Hydroxyvitamin D3 serum level with levator ani muscle and gastrocnemius soleus muscle strength in POP and non-POP group.

Conclusion: No significant correlation of 25-Hydroxyvitamin D3 serum level with levator ani muscle and gastrocnemius soleus muscle strength was observed in patients with POP and without POP in postmenopausal women.

INTRODUCTION

Pelvic organ prolapse (POP), a part of pelvic floor disorder, is a major clinical problem in postmenopausal women.¹ The etiology of POP are multifactorial and associated with aging, multiparity, and women's reproductive history, especially trauma of levator ani muscle during childbirth.¹⁻⁴ The levator ani has been believed to play an important role in the pathophysiology of POP.⁴⁻⁸ The weakness of levator ani muscle is clinically observed in women with POP and may be impacted by vitamin D deficiency.⁹

Vitamin D is a fat soluble vitamin that plays a vital role in

calcium homeostasis in smooth and skeletal muscle.^{9,10}

Vitamin D deficiency is very common among women with age 65 years or older.⁹ It is associated to the development of poor muscle strength and loss of muscle mass, which in turn leads to pelvic floor disorders such as urinary/fecal incontinence and POP.^{4,10-13}

The bond of $1.25(\text{OH})_2\text{D}_3$ at vitamin D receptor (VDR) triggers protein transcription involved in calcium metabolism and promotes the rapid activation of mitogen-activated protein kinase (MAPK) signaling pathway, myogenesis, cell proliferation or differentiation or apoptosis.

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Though this mechanism, 1,25(OH)₂D₃ stimulates cell proliferation and growth of muscle cells.^{4,14}

Aging women are at increased risk for both pelvic floor disorders and Vitamin D deficiency. The age-related decline skeletal muscle mass and strength accelerates with the beginning of menopause. Consistently, vitamin D deficiency is common in postmenopausal women due to reduced capacity of vitamin D production, reduced renal function, lower absorption of vitamin D by gastrointestinal tract, and use of multiple drugs that may interfere with the absorption and metabolism of vitamin D.^{15,16} Considering the association between 25-hydroxy-vitamin D₃ serum level with muscle strength of pelvic organ,¹⁷ this study aimed to observe the correlation of 25-hydroxy-vitamin D₃ serum level with levator ani muscle and gastrocnemius soleus muscle strength in patients with POP and without POP in postmenopausal women.

MATERIALS AND METHODS

This study was an observational analytical cross-sectional study. This study has been approved and was recommended by Medical Research and Ethical Committee, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia. Informed consent was obtained from all participants before and during the study when needed. Privacy is guaranteed, during and after the study.

The subjects of study were postmenopausal women consisting of 22 patients with POP and 22 patients without POP. Participants were excluded from the study if the medical record was not complete, had unstable vital signs or poor general health condition, and had other comorbidities such as diabetes mellitus, heart diseases, hypertension, stroke, neuropathy and impaired renal function. 25-Hydroxyvitamin D₃ serum level were measured by electrochemiluminescence immunoassay (ECLIA). Levator ani muscle strength was measured by perineometerTM and gastrocnemius soleus muscle strength was measured by hand held dynamometer. This study was conducted in RS Dr. Hasan Sadikin Gynecologic Clinic, within the period of December 2016 – January 2017.

Statistical Analysis

Data analysis in this study was divided into univariate and bivariate analysis. Univariable data analysis for age and BMI was described as mean and range. The distribution of data

was determined using Shapiro-Wilk test. The statistical test to compare the characteristics of two groups was done by using Mann-Whitney test, with p<0.05 was considered statistically significant. Then, the correlation between 25-hydroxy-vitamin D₃ serum level and levator ani and gastrocnemius soleus muscle strength was analyzed using Spearman's correlation test. P <0.05 was considered statistically significant. Data analysis was done by using SPSS version 25.0 for Windows.

RESULTS

Table 1
Characteristics of Subjects

Variable	Group		p-value
	POP n= 22	Non-POP n= 22	
Age (year)			0.021
Mean (SD)	59.4 (5.6)	55.0 (6.5)	
Range (min-max)	50-70	46-73	
BMI (Kg/m²)			0.431
Mean (SD)	26.1 (3.6)	25.3 (3.2)	
Range (min-max)	18.5-32.6	18.8-30.2	

Note: *Analyzed by unpaired t-test

The baseline characteristics of each group included age and body mass index (BMI), were presented in Table 1. The mean age of POP group was 59.4 years while non-POP group was 55 years. The age of POP group as well as non-POP group showed significant differences (p<0.05), while BMI in both groups did not show significant differences so that it could be compared (p>0.05).

Table 2

Comparison of 25-Hydroxyvitamin D₃ Serum Level with Levator Ani Muscle and Gastrocnemius Soleus Muscle Strength in Patients with Pelvic Organ Prolapse and Patients without Pelvic Organ Prolapse Group

Variable	Group		p-value ^{*)}
	POP n= 22	Non-POP n= 22	
Vitamin D₃ (ng/ml)			<0.001
Mean (SD)	8.8 (3.3)	15.1 (3.2)	
Median	8.6	13.9	
Range (min-max)	4.0-17.7	11.5-24.3	
Perineometer (cmH₂O)			<0.001
Mean (SD)	24.2 (5.8)	45.5 (14.2)	
Median	23	38.6	
Range (min-max)	11.3-37.6	29.3-77.1	
Dynamometer (kg)			<0.001
Mean (SD)	10.6 (4.7)	13.7 (1.2)	
Median	9.0	13.6	
Range (min-max)	6.7-28.2	10-15.3	

Note: *)Analyzed by Mann-Whitney test

Table 2 showed the comparison of 25-Hydroxyvitamin D₃ serum level, levator ani muscle and gastrocnemius soleus

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muscle strength. In the non-POP group, the mean and median of all variables were greater than POP group. The difference of both groups is statistically significant ($p < 0.05$).

Table 3

Correlation of 25-Hydroxyvitamin D3 Serum Level with Levator Ani Muscle and Gastrocnemius Soleus Muscle Strength in Patients with Pelvic Organ Prolapse and Patients without Pelvic Organ Prolapse Group

Correlation of Vitamin D ₃ with	POP		Non-POP	
	r _s	p-value	r _s	p-value
Perineometer	0.166	0.461	0.368	0.092
Dynamometer	0.231	0.301	0.228	0.309

Note: *Analyzed by Spearman

Table 3 revealed that there were no significant correlation ($p > 0.05$) between 25-Hydroxyvitamin D3 serum level with levator ani muscle and gastrocnemius soleus muscle strength in POP and non-POP group.

DISCUSSION

In this study, POP and non-POP group had the mean age of more than 50 years. Previous studies revealed that woman's age is one of the important cause for POP, almost half of all women older than 50 years have POP symptoms. This might be due to age-related changes in neuromuscular function and connective tissue in elderly women.^{1,18} A study by Kaur et al on 200 geriatric women revealed there was a visible increasing trend in vitamin D deficiency with increase in time since menopause.¹² Aging process also weakens the levator ani muscle and muscle regeneration and healing process.⁴ However, a previous study involving 375 women revealed that pelvic floor muscle strength was weakly associated with patient age ($r = -0.25$, $p < 0.01$).¹⁹ The average BMI of both POP and non-POP group were classified as overweight (25 to < 30 kg/m²). Similarly, previous study by Kudish et al on a group of 16,608 women found a progression of POP with increasing body weight.²⁰ Study by Young et al showed that there was a positive association between BMI and posterior compartment prolapse, but not for the anterior and central compartment prolapse.²¹

POP group had 25-Hydroxyvitamin D3 serum level, levator ani and gastrocnemius soleus muscle strength which were lower than non-POP group ($p < 0.001$). All of POP subjects were vitamin D deficient; about 77.3% of POP group were severely deficient (< 10 ng/mL) and 22.7% were moderately deficient (10-19.9 ng/mL). In addition, about 90.9% of non-POP group were moderately deficient and 9.1% were

slightly deficient (20-29 ng/mL). This study had the same result with study conducted by Navaneethan et al that revealed vitamin D level were significantly lower in women with pelvic floor disorder than those without pelvic floor disorder.¹ Similarly, other previous studies also showed that vitamin D levels were associated with a decreased risk of pelvic floor disorders.^{11,12}

Levator ani defect had been believed to have an important role in the pathophysiology of POP.⁷ The muscle contraction strength of levator ani muscle in POP group was significantly lower than non-POP group. The gastrocnemius soleus and levator ani muscle had similar muscle fiber. Previous study revealed there was a correlation between levator ani muscle and gastrocnemius soleus muscle contraction strength ($r = 0.52$, $p < 0.001$). The gastrocnemius soleus muscle contraction strength among women with POP were lower than women without POP.⁸ In this study, gastrocnemius soleus muscle contraction strength in POP group was also lower than non-POP group.

The effect of vitamin D has been shown to be related to growth and musculoskeletal function, although the exact mechanism can not be clearly explained. Vitamin D receptors have been identified in the skeletal muscles. Recent studies on the role of vitamin D in maintaining muscle strength, neuromuscular function, and body stability have been evaluated. Vitamin D also plays a role in calcium absorption, protecting muscle cell from insulin resistance and inflammation. Muscle weakness was a prominent clinical feature of vitamin D deficiency. Levator ani muscle and gastrocnemius soleus muscle consist of skeletal muscle, possibly affected by vitamin D levels.^{17,22}

Several previous studies found that there was a positive correlation between vitamin D and levator ani muscle strength in postpartum women.^{4,23} Vitamin D supplementation has been proven in improving muscle strength among postmenopausal women.^{24,25} Study by Beaudart et al also found that vitamin D supplementation has a small positive impact on muscle strength and seems more effective in elderly.²⁶ However, our study found that there was no significant correlation of 25-Hydroxyvitamin D3 serum level with levator ani muscle and gastrocnemius soleus muscle strength in POP and non-POP patients among postmenopausal women ($p > 0.05$). Similarly, study on 88 postmenopausal women revealed that after vitamin D supplementation, the change in 25-Hydroxyvitamin D3

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serum level was not correlated with the change in muscle mass and muscle strength.¹⁵ Study by Granlund et al that revealed the association between vitamin D deficiency and reduced lower limb muscle strength did not reach statistical significance ($p=0.052$).²⁷ Consistently, previous study of Asians elderly included 354 elderly men and 328 postmenopausal women, also found there was no association of 25-Hydroxyvitamin D3 serum level with the risk of low muscle strength in both genders. These results suggested that 25-Hydroxyvitamin D3 serum level could not be a useful predictor of low muscle strength during aging in Asians elderly.²⁸

Although we can not determine the exact reason for this result in the current study, we speculate that this finding might be explained by the dominant effect of age on determination of muscle strength. In postmenopausal women, there were several mechanisms that were thought to play a role in the regeneration process of muscle including loss of the number or function of satellite cells, decreased myoblast proliferation, or weakening of the differentiation process.²² However, according to some previous studies, there is still possibility that vitamin D can play beneficial role on muscle strength among postmenopausal women, particularly levator ani muscle strength. Additional studies are needed to find out the effect of vitamin D supplementation toward levator ani muscle strength in POP patients among postmenopausal women. Being a cross-sectional study and a relatively small sample size were the limitations of this study.

CONCLUSION

No significant correlation of 25-Hydroxyvitamin D3 serum level with levator ani muscle and gastrocnemius soleus muscle strength was observed in patients with POP and without POP among postmenopausal women.

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