Review Article

Vitamin D Status in Women with Pelvic Floor Disorders: A Meta-Analysis of Observational Studies

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Abstract

The current evidence regarding the association between vitamin D status and pelvic floor disorder (PFD) are inconclusive. This meta-analysis was aimed to summarize existing data demonstrating the association between Vitamin D status and PFD using published observational studies. All national and international databases including Web of Science, PubMed, Google Scholar, and Scopus were searched up until January 30, 2018, and related published studies retrieved for meta-analysis. The effect sizes of Vitamin D status were presented as standardized mean difference (SMD) with 95% confidence interval (CI), using random-effect models and inverse variance method. The Cochran Q statistic and I^2 tests were used to evaluate the heterogeneity across included studies. Seven studies with 3219 women were included our meta-analysis. There was heterogeneity existing among included studies (I^2 = 96.4%, P < 0.001), so a random-effect model was used. The findings of this meta-analysis revealed that the mean serum Vitamin D levels in women with PFD were significantly lower than healthy women (SMD −0.60; 95% CI, −1.06, −0.13; P = 0.01). This meta-analysis demonstrates lower levels of serum Vitamin D in women with PFD rather than healthy women. Additional prospective studies regarding the association between Vitamin D status and PFD are required to confirm our findings.

Keywords: *Meta-analysis, observational studies, pelvic floor disorder, Vitamin D levels*

Introduction

Pelvic floor disorder (PFD), the major clinical problem in postmenopausal women, includes pelvic organ prolapse (POP), urinary incontinence (UI), and fecal incontinence (FI).[1] More than 24% of nonpregnant women suffer from PFD,[2] which almost doubles by aging, with its prevalence being 36%–49% after the age of 60 years.[3] PFD might be significantly associated with other morbidities and affect woman's quality of life.[4] PFD poses economic burden on healthcare because of complex medical conditions and coincident morbidities which lead to subsequent diagnostic and therapeutic issues.[4-6]

Vitamin D plays a critical role in bone growth and preserving bone mineral density.[7] The current evidence has shown that less concentrations of serum 25-hydroxyvitamin D are correlated with reduced postural stability[8] and increased risk of falls.[9] The prevalence of low Vitamin D status among postmenopausal women worldwide is ranged from 1.6% to 86% depending on the regional location and seasonal variation.[10] Earlier studies demonstrating the impact of Vitamin D on skeletal muscle strength and function are inconsistent.[11,12] However, it is highly suggested that Vitamin D has a considerable effect on the function and efficiency of skeletal muscle. Recent literature has proposed the contribution of low Vitamin

Access this article online

Quick Response Code:

Website: www.jmidlifehealth.org

DOI: 10.4103/jmh.JMH_9_19

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How to cite this article: Ghanbari Z, Karamali M, Mirhosseini N, Akbari M, Tabrizi R, Lankarani KB, *et al.* Vitamin D status in women with pelvic floor disorders: A meta-analysis of observational studies. J Mid-life Health 2019;10:57-62.

D status in the incidence of PFD. The weakness of pelvic floor muscle which is noticed in women suffering from PFD symptoms might probably be related to low Vitamin D status. Further, detrusor muscles in bladder wall have Vitamin D receptor (VDR);[13] therefore, Vitamin D deficiency may impair the function of urinary bladder leading to paravaginal defect (PVD) symptoms. Navaneethan *et al*.[14] have shown a high prevalence of low Vitamin D status and its significant association with PFD among postmenopausal women. In another study, increased FI symptoms were shown to be associated with hypovitaminosis D.[15]

There are several studies that have confirmed the association between serum Vitamin D levels and PFD; however, we did not find any meta-analyses to summarize the findings of existing publications. Considering the disagreements among the current evidence regarding the association of serum Vitamin D levels and PFD, the aim of the study was to systematically review existing evidence and to summarize the available findings in a meta-analysis, if possible.

Materials and Methods

Search process

The related studies were detected by searching in the national and international online databases including Web of Science, PubMed, Google Scholar, and Scopus until January 30, 2018. Two independent authors (MA and RT) performed the search process. The search keywords were selected using MeSH terms and text words: exposure ("Vitamin D status" OR "Vitamin D levels" OR "Vitamin D concentrations") and outcomes ("PFD" OR "POP" OR "UI" OR "FI" OR "stress urinary incontinency" OR "urge incontinency" OR "vaginal apex prolaps" OR "anterior vaginal wall prolaps" OR "posterior vaginal wall prolaps" OR "rectocele" OR "perineal defect" OR "anterior colporraphy" OR "custocele" OR "paravaginal defect (PVD)" OR "lower urinary tract dysfunction"). The reference list of the selected studies was hand searched to include the articles which were not captured in the primary electronic search. Further, authors contacted with appropriate research institutes, centers, experts, and researches for gray literatures and unpublished studies. Articles published in English were used in this meta-analysis.

Study selection

Relevant studies were included in the meta-analysis, after screening for the title, abstract, and the full text of the articles and excluding irrelevant and duplicate papers. Studies were selected according to the following inclusion criteria: original observational studies with cross-sectional, case–control and cohort design, studies related to PFD among women diagnosed based on the national guidelines,[16] however, women without PFD were considered as control group, and studies that reported the mean changes of serum Vitamin D (ng/mL), along with standard deviation (SD) for both case and control groups. Articles not reporting the mean differences and SD of Vitamin D, case reports or case series, the abstracts with no available full text, and articles with low score of quality assessment were excluded from the meta-analysis.

Quality assessment

STROBE checklist, specified for observational studies, was applied to evaluate the quality of selected studies. This checklist examined different methodological aspects (with 12 questions) including total sample size, study design, sampling methods, study participants, the method and tool of data collection, the definitions of different variables, the assessment of samples, statistical analyses, the aims of study, the appropriate style to report findings based on the goals of the study.[16] One score was devoted to each item, and the studies with at least 8 points were included in this meta-analysis.[17]

Data extraction

Two independent authors (MA and RT) extracted data from observational studies using the standard Excel spreadsheets. The extracted data included; first author's name, country study conducted, publication date, study method, sample size in intervention and control groups, outcomes, and the mean and SD of serum Vitamin D (ng/mL) in both groups.

Data analysis

All statistical analyses were conducted using STATA version 12.0 (Stata Corp, College Station, TX, USA). The Cochrane's Q test and the I^2 statistic were applied to assess the heterogeneity among included studies. On heterogeneous studies, random effect model was used to pool data in the meta-analysis. Cohen statistics and inverse variance method were applied to calculate standardized mean difference (SMD) and 95% confidence interval. Further, to evaluate the source of heterogeneity, subgroup analyses were conducted based on the potential confounders such as country (the USA vs. India vs. other), and outcome (PFD vs. other related conditions). Moreover, the sensitivity analysis was conducted to evaluate the contribution of each study in the pooled effect size (SMD) and Egger's test was used to examine the publication bias among the included studies.

Results

Overall, 321 articles were found through database search. After screening the title, abstract, and the full-text of the articles and removing non-relevant and

duplicate studies, seven observational studies, with 3219 women included, were eligible to be included in our meta-analysis. Flowchart of step by step detailed study identification and selection are depicted in Figure 1. The study characteristics assessing the relationship between serum Vitamin D levels and PFD are indicated in Table 1. The study sample size ranged between 60 and 1674. These studies were published between 2012 and 2017. Out of seven included studies, two had cohort design and five case–controls.

The relationship between Vitamin D status and pelvic floor disorder

Seven studies assessed the association between Vitamin D levels and PFD among women. A random-effect model was used due to the heterogeneity among included studies (I^2 = 96.4%, P < 0.001). The findings indicated that the mean of serum Vitamin D levels was significantly lower in cases with PFD rather than healthy women in control group (SMD − 0.60; 95% confidence interval (CI), −1.06, −0.13; P = 0.012) [Figure 2].

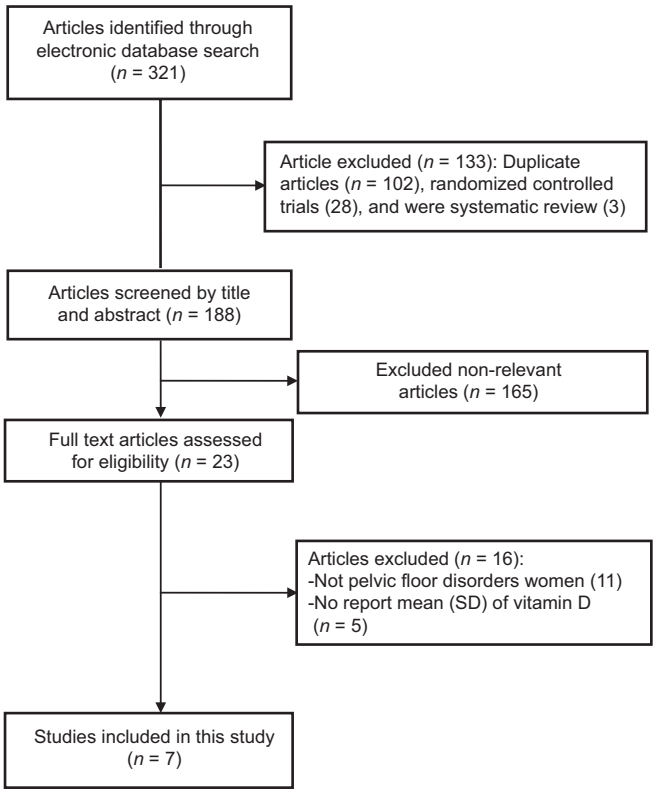

Figure 1: Flowchart for the selection of eligible studies

Because of existing heterogeneity among included studies, subgroup analyses were conducted based on the country and outcome to specify the relation between Vitamin D levels and PFD. We found a reduction of heterogeneity for some of the strata of these variables. Our finding revealed a significant association between Vitamin D levels and risk of PFD, using trials performed in India (SMD = −0.37, 95% CI: −0.67, −0.07; I^2 = 0.0%) versus those in the United States (SMD = −0.29, 95% CI: −0.61, 0.04; I^2 = 81.5%) or other locations (SMD = −1.29, 95% CI: −3.82, 1.23; I^2 = 99.4%). Considering type of outcome, three studies conducted in women with PFD showed significant association between Vitamin D levels and disease (SMD = −0.43, 95% CI: −0.60, −0.25; I^2 = 0.0%) when compared to other pelvic conditions SMD = −0.74, 95% CI: −1.49, −0.00; I^2 = 98.1%).

The significant results demonstrating the association between Vitamin D status and risk of PFD remained unchanged after applying sensitivity analysis. However, the lower and upper pooled SMD for the relation between Vitamin D levels and risk of PFD in the sensitivity analysis were −0.70 (95% CI: −1.34, −0.06) after excluding Lee and Lee[19] and −0.23 (95% CI: −0.42, −0.04) after removing Nseir *et al*.[20] [Figure 3].

Publication bias

Egger's regression tests were used to assess any significant evidence of publication bias, and we did not find any bias among included studies assessing the relationship between Vitamin D levels and risk of PFD (B = −5.97, P = 0.126).

Discussion

This systematic review and meta-analysis, to our best knowledge, is the first report demonstrating the relationship between serum Vitamin D levels and PFD. The current meta-analysis revealed that Vitamin D status

Table 1: The characteristics of included studies

Authors (references)	Publication year/ country	Type of study	Intervention/control (sample size)	Target population
Parker-Autry *et al*.[18]	2012/United states	Cohort	268/126	Women with pelvic floor disorder
Lee *et al*.[19]	2017/Korea	Cross-sectional	558/1116	Women with urinary incontinence
Parker-Autry *et al*.[15]	2014/United states	Cross-sectional	31/81	Women with fecal incontinence symptoms
Nseir *et al*.[20]	2013/Israel	Cross-sectional	93/93	Women with recurrent urinary incontinence
Navaneethan *et al*.[14]	2015/India	Case-control	51/69	Women with pelvic floor disorders
Sharma *et al*.[21]	2013/Delhi	Cross-sectional	30/30	Women with pelvic organ prolapse
Parker-Autry *et al*.[22]	2017/California	Cross-sectional	223/450	Women with incident urinary incontinence

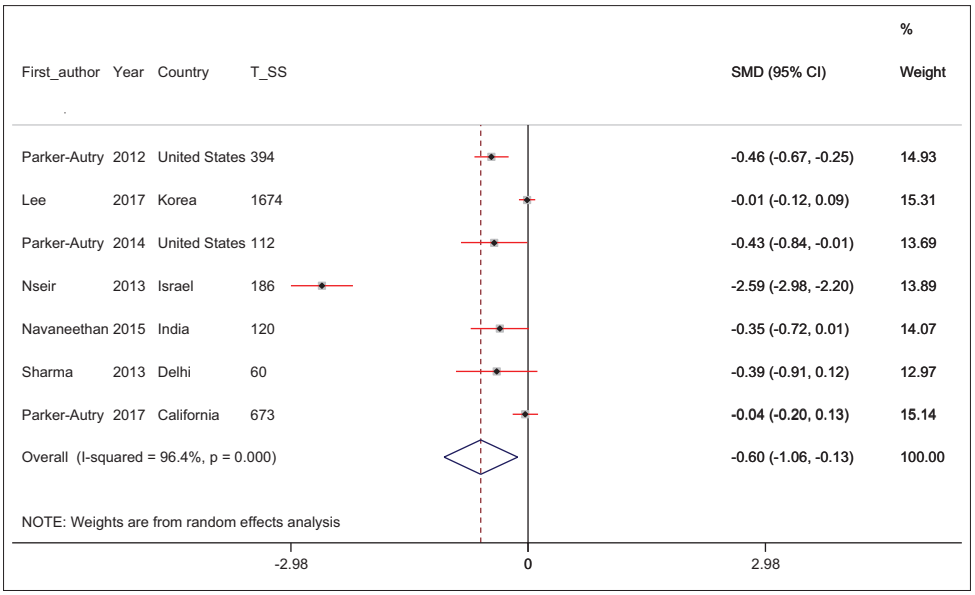

Figure 2: The forest plot of the association between Vitamin D status and pelvic floor disorders by using the random effect model

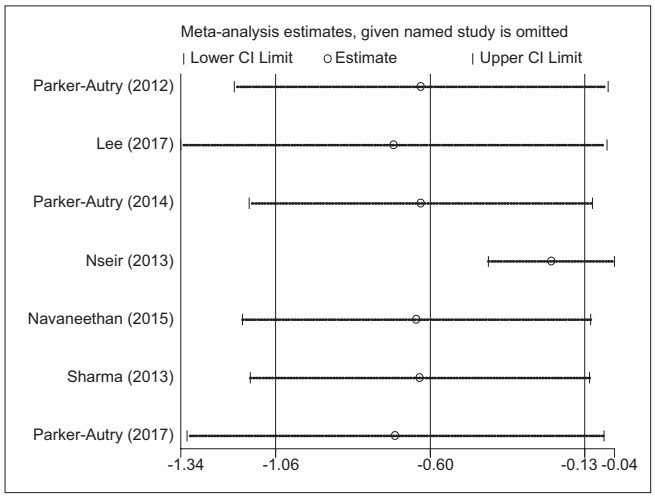

Figure 3: Sensitivity analysis based on the contribution of each study on pooled standard mean difference

is significantly compromised among women with PFD rather than healthy women.

Improved Vitamin D status has been shown to be significantly associated with muscle strength, better neuromuscular function, and postural stability.[23,24] Muscle weakness, which is common among elderly people, is correlated with hypovitaminosis D,[25] because the ability of skin to synthesize provitamin D (25-hydroxycholecalciferol) reduces with aging. Since pelvic floor muscle is composed of skeletal muscles with VDR, their function might be affected by the circulating concentrations of Vitamin D. There are a few retrospective and two epidemiological studies (including community-dwelling women) have shown the association between Vitamin D deficiency and PFD.[18,26,27] The Leicestershire MRC Incontinence Study Group (a longitudinal cohort study) indicated that the consumption of higher doses of Vitamin D was significantly correlated with lower risk of overactive bladder.[27] Further, UI symptoms, but not FI symptoms, were less common in Vitamin D sufficient group, even after controlling for demographic factors which might confound the link between PFD and Vitamin D concentrations.[26] With increasing serum Vitamin D concentrations, the risk of PFD decreased significantly, irrespective of the age. Elderly women have shown to be more prone toward Vitamin D deficiency due to decreased outdoor activity and attenuated function of the skin to change 25-hydroxycholecalciferol into active form of Vitamin D.[23] Hence, Vitamin D deficiency is a precipitating factor for PFD in postmenopausal women.

The suggested mechanisms involving Vitamin D in the effective function of musculoskeletal system include promoting calcium metabolism and absorption, protecting muscle cell against hyperinsulinemia, insulin resistance, and increased inflammation.[23,28,29] VDRs play an important role in the function of smooth and skeletal muscles.[30,31] Randomized studies have provided controversial evidence, however, many observational studies support the beneficial effects of Vitamin D on muscle function and efficacy.[32,33] The advantages of Vitamin D have been proven in proper functioning of both skeletal and smooth muscles.[34,35] Improved serum Vitamin D levels stimulate skeletal muscle proliferation and contribute to proper function of muscle cells via binding to VDR.[18] Specifically, the levator ani and coccygeus muscles (intra-pelvic skeletal muscles) have been shown to be influenced by increased Vitamin D intake.[32]

The weakness of pelvic floor musculature might contribute to the symptoms related to pelvic floor dysfunction including; urinary and FI. Pelvic floor muscles are composed of both smooth and skeletal muscles; therefore, the physiological function of pelvic floor can be modulated through improving Vitamin D status. The variation in geographical regions and subsequently different baseline levels of Vitamin D might complicate its impact on muscle function in these patients. Furthermore, study designs, sample size along with participants' characteristics might explain the discrepancies between different studies.

Conclusions

This meta-analysis revealed Vitamin D status is significantly compromised among women diagnosed with PFD, compared to healthy women. Additional prospective studies regarding the association between Vitamin D status and PFD are necessary.

Acknowledgments

The present study was supported by a grant from the Vice-chancellor for Research, SUMS, Shiraz, and Iran.

Financial support and sponsorship

The present study was founded by a grant from the Vice Chancellor for Research, Shiraz University of Medical Sciences, in Iran.

Conflicts of interest

There are no conflicts of interest.

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