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Pelvic floor prolapse and vitamin D levels: are we doing enough? A research paper

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ABSTRACT

Objective. Pelvic organ prolapse (POP) is a common problem that negatively affects the quality of life of women and requires a wide range of management steps that can involve serious surgical interventions. This study aims to evaluate a possible relation between pelvic organ prolapse presence and severity, and vitamin D levels. We don't aim to assess the incidence of pelvic floor prolapse in Jordan in this study.
Materials and Methods. This was a cross-sectional study of non-pregnant females with pelvic organ prolapse presented to gynecology outpatient clinics for a 1-year duration. Full clinical history and gynecological evaluation were recorded and correlated to plasma vitamin D levels. An independent t-test was used to analyse the possible relationship between vitamin levels and POP.
Results. One hundred forty women were recruited, with an average age of 42.1 ± 13.3 and a mean parity of 5.73 ± 1.88. The mean vitamin D levels were 12.8 ± 11.4, lower than the international standards. The serum levels of vitamin D were markedly lower in the prolapse group than in the non-prolapse group ($p = 0.046$). Moreover, lower vitamin D levels correlate with multisite manifestation ($p = 0.022$), rectocele ($p = 0.007$), and advanced stage ($p = 0.053$).
Conclusions. The study concluded that patients with pelvic organ prolapse showed lower vitamin D levels than those without prolapse. Moreover, it seems that vitamin D deficiency can be independently correlated to multisite prolapse and advanced grades.

INTRODUCTION

Pelvic organ prolapse (POP) or genital prolapse is a pathological condition affecting the uterus, the vagina, or both [1]. In uterine prolapse, the uterus falls into the vaginal canal.
Levator ani muscle (LAM) has an essential role in pelvic organ support [2]. Loss of LAM function in addition to other factors such as aging lead to pelvic organ prolapse (POP) and/or pelvic floor dysfunction syndrome with its adverse effect on the female quality of life.

In vaginal prolapse, one or more parts of the vaginal wall project into the vaginal canal: a cystocele and/or a ureterocele if involving the upper anterior vaginal wall and/or the lower anterior vaginal wall respectively; a rectocele and/or enterocoele if involving the lower posterior vaginal wall and/or the upper posterior vaginal wall respectively, or apical prolapse, which is a descent of the uterus, cervix or rarely the vaginal cuff after hysterectomy, then it is called a vault prolapse [1].
POP is a common complaint in gynecological clinics, affecting 32% to 76% of female patients [3, 4].

It is estimated to be diagnosed in 40% to 60% of parous women [4]. Moreover, the incidence is likely to increase because of the aging population.

Pelvic floor dysfunction (POP) leads to surgery in 11% of women's lifetime. Recurrence risk of 25% within 5 years and the need for repeat surgery is 17% [5]. It is the main indication for about 15-18% of hysterectomies and is the most common indication for hysterectomy in postmenopausal women [6].

Mild genital prolapse may be asymptomatic; symptoms when present can be non-specific, such as pelvic heaviness, genital bulge, and difficulties during sexual intercourse. Advanced stage prolapse can be associated with urinary incontinence (in the case of cystocele), incomplete urinary emptying (associated with cystocele and/or uterine prolapse), the need for manual pressure to the perineum or the posterior vaginal wall for defecation (associated with rectocele) [7], vaginal discharge and/or bleeding.

The leading cause of POP is weakness or damage to the supporting pelvic floor muscles which is primarily provided by the levator ani muscles and the connective tissue attachments of the vagina to the sidewalls and pelvis.

This damage can be caused by pregnancy, childbirth, or chronic increases in intra-abdominal pressure such as lifting, coughing, straining, connective tissue conditions, and menopause [8].

On the other hand, vitamin D maintains the homeostasis of phosphorous and calcium and through vitamin D receptors (VDRs), the biological effects are exerted from its active form [1,25$(OH)_2D_3$]. These VDRs are present in skeletal and smooth muscles [9, 10]. They help in the contractility of skeletal muscles and the maintenance of an anti-inflammatory cell environment by regulating calcium homeostasis [11]. The insufficiency or deficiency of vitamin D causes a decrease in type 2 muscle fibers causing muscle weakness [12]. In POP, degenerative changes in the connective tissue are accelerated as well [13]. Increased type III collagen and decreased ratio of type I to type III collagen has been found in women with POP compared to those without it [14].

A recent study in the Sylvanian female population showed that lower vitamin D levels might be systematically associated with POP [15]. It seems that lower levels of vitamin D stores were related to the risk of pelvic floor disorders (PFD) at all ages in adult women. Therefore, vitamin D deficiency might be an influencing cause leading to POP. Hence, the present study is trying to evaluate the relationship between vitamin D deficiency and pelvic floor prolapse in Jordanian women. The results will be an essential addition to understanding the possible role of vitamin D diffeciey in patients with POP if any, such an observation may help in reducing the risk of developing prolapse and possibly managing early stages.

MATERIALS AND METHODS

Study design

This cross-sectional study was conducted on healthy, non-pregnant females who visited the general outpatient clinics of the gynecological department over a 1-year duration and they were assessed based on clear inclusion and exclusion criteria. Women fulfilling inclusion criteria were included in the study and upon examination, if they were found to have POP ie asymptomatic they were assigned to the study group, and those without POP on clinical examination were assigned to the control group.

This study aimed to compare vitamin D levels between the two groups of patients *i.e*. with POP and without among Jordanian women.

One hundred forty (n = 140) non-pregnant married or previously married Jordanian women were interviewed and included in the present study. Women needed to provide informed written consent to participate in the study. They had to be 18 years old or above, confirmed non-pregnant, with no known history of POP or of previous POP surgery. Women who refused to participate, were underage, or were pregnant regardless of their age were excluded from the study. All chronic illnesses or complaints were noted, with a particular focus on those that could potentially harm directly or indirectly the musculature of the pelvic region, such as chronic cough, obstructive pulmonary disease, asthma, muscle or connective tissue disorder, or nerve disease. Those who were getting treatment for osteoporosis and taking vitamin D supplements were excluded as well.

Clinical data and examination

Demographic data and medical history of each woman were completed or retrieved from the hospital records. The collected demographic data included age, BMI, and menopausal status. Parity, mode of child delivery, history of stress and urge urinary incontinence, vaginal discomfort, dyspa-

reunia, and other medical procedures and conditions (*e.g.*, hypertension, diabetes).
Two experienced gynecologists evaluated the patients for prolapse type and degree according to clear examination guidelines and protocols to minimize bias. Prolapse types were categorized as cystocele, rectocele, and uterine prolapse, no enterocoeles were reported during the study period. There are two central systems for grading the severity of genital prolapse, the Baden-Walker halfway system (1) and the Pelvic Organ Prolapse Quantification system (POP-Q) (2).
Baden-Walker halfway system is a simple grading system that was followed here since more elaborate assessment methods would lay beyond the scope of the present study on vitamin D levels and POP. Thus, grade 0 – no prolapse, grade 1 – or mild = 2 cm away from the introitus (halfway to hymen) grade 2 – within 2 cm of the introitus/hymen, grade 3 – passing the introitus/hymen, grade 4 – maximum descent/or non-reducible prolapse passing the introitus [1]. Reports suggest that the estimations with either method coincide [16]. Since all our subjects were unaware of prolapse, none was classified as grade 4.
The control group was patients whom upon examination were found not to have prolapse

Laboratory testing

The plasma levels of total vitamin D [1,25$(OH)_2D_3$] were assessed at the Clinical Chemistry Laboratory of the King Abdulla University Hospital (KAUH), Jordan. The sample was obtained the same day the clinical examination was conducted. According to the manufacturer's instructions, blood was obtained by venipuncture, and vitamin D was measured in duplicate. The commercial kit Elecsys vitamin D total II (Reference number: 07464215 190, Roche, USA) was used on a COBAS Automatic Analyzer.
A previously reported national vitamin D average level for Jordanian females of (31.1 ± 12.0 nmol/l) was used as a cut-off level for this study [17].

Statistical analysis

Statistical analysis was performed using the Jamovi 1.2.27 software. Descriptive statistics of mean, standard deviation, frequency, and percentages were used to describe the variables measured in this study. Shapiro-Wilk Test of Normality was used to check the normality of the data distribution. An Independent T-test was used to analyse the effect of vitamin D on POP. Non-parametric one-way ANOVA (Kruskal-Wallis) correlated varied factors with prolapse incidence. A P-value of less than 0.05 was considered significant.

RESULTS

This study included one hundred and forty women. The mean age of our participants was 42.1 ± 13.3 (range 21-67 years old), and the mean parity was 5.73 ± 1.88 (range 0-13 children/woman) (**Table 1**).The mean value for vitamin D levels was 12.8 ± 11.4.
Almost half of the participants (54.5%) were premenopausal, 97% had given birth naturally, 62.12% felt vaginal discomfort, while 31.82% complained of dyspareunia. Stress urinary incontinence and urge urinary incontinence were 68.8% each.
Only one patient was a smoker and 3 had thyroid problems (thyroidectomy, hypothyroidism).
Out of the 140 subjects, 104 had POP at the time of examination, while 36 did not. Of those with POP, 51.92% had more than one type of POP; 75% had cystocele; 68.27% had rectocele and 9.62% had uterine prolapse.
Only one case was diagnosed as cervical prolapse, grade 3. As far the grade goes, grade 1 (mild prolapse) was found in 52 patients (50%); grade 2 (moderate) in 44 (42.31%) and grade 3 (advanced) in 26 women (25%). The exact size and grade are shown in **Table 2**.
Non-parametric one-way ANOVA (Kruskal-Wallis) showed that age, menopause, parity, number of natural births, foetal weight, vaginal discomfort and urge urinary incontinence statically correlate with having POP (**Table 3**).
Moreover, advanced grade correlates with lower vitamin D levels (**Table 4**). Additionally, multisite prolapse and rectocele correlate with lower vitamin D (**Table 5**). The vitamin D levels did not cor-

Table 1. *Characteristics of the participants.*

Variable (n = 140)	Mean	SD	P-value
Age	42.1	13.3	
Prolapse (n = 104)	43.4	13.9	0.41
No prolapse (n = 36)	40.8	12.7	
Parity	5.73	1.88	
Prolapse (n = 104)	6.12	2.31	0.12
No prolapse (n = 36)	5.34	1.45	
Vitamin D	12.8	11.4	
Prolapse (n = 104)	9.1	8.1	0.046
No prolapse (n = 36)	16.5	14.7	

relate with any of the other risk factors. From the set of dependent variables (vitamin D, age, body mass index, parity), two important predictive variables were extracted from multivariate discriminant analyses to predict whether having prolapse or not. These were vitamin D and age. The multivariate discriminant analysis on POP and these two variables (Wilks $\lambda = 0.801$, $p = 0.03$; structure matrix coefficients regarding the mathematical function of POP are: for vitamin D = -0.59, for age = 0.67) showed that vitamin D and age are predictive factors for correctly placing the patient in the POP.

DISCUSSION

We studied serum 25-hydroxy vitamin D levels in POP patients', 140 women were included with and without prolapse. Apart from the known, well-established risk factors such as parity, age, and menopausal status [18], we identified vitamin D levels as a possible independent predictor of prolapse incidence and degree. In a prospective study of 120 postmenopausal women with or without symptoms of pelvic floor dysfunction (PFD), in association with serum 25-hydroxy vitamin D levels, it showed that vitamin D levels were significantly lower in women with PFD than those without PFD [18]. Moreover, the menopausal status of more than five years was also significantly associated with PFD, suggesting that long-term vitamin D deficiency may have a cumulative effect [19].

Table 2. *Grade of the prolapse found on examination.*

Variable	Percentage (%)*
Cystocele	75.00
Grade 1	30.77
Grade 2	32.69
Grade 3	11.54
Rectocele	68.27
Grade 1	35.58
Grade 2	20.19
Grade 3	12.5
Uterine prolapse	9.62
Grade 1	1.92
Grade 2	1.92
Grade 3	5.77

Table 3. *Kruskal-Wallis ANOVA with grouping according to prolapse (Y/N).*

Variables	χ^2	P-value
Age	10.192	0.001
Menopause	14.913	< 0.001
Natural birth	11.477	< 0.001
Parity	10.641	0.001
Foetal weight	3.698	0.054
Vaginal discomfort	11.974	< 0.001
Dyspareunia	2.194	0.139
Stress Urinary Incontinence	2.010	0.156
Urge Urinary Incontinence	7.295	0.007
Vitamin D levels	3.991	0.046

Another study [20] on the general health of geriatric women showed that normal vitamin D levels were associated with a decreased risk of PFD and that vaginal health index (MVHI) was found to improve with vitamin D supplementation at 3 and 6 months follow-up. Vitamin D also affects the pathophysiology of overactive bladder syndrome in postmenopausal women, so it is common that urinary incontinence and POP to coexist [21]. In this study, the serum levels of vitamin D were markedly lower in the prolapse group than in the non-prolapse group. It can suggest that vitamin D acts independently from the other risk factors. This is in accordance with previous reports that linked vitamin D levels with pelvic floor muscle strength and found lower levels related to decreased strength of pelvic floor muscle [22], PFD [23, 24], and levator ani and coccygeus skeletal muscles weakness [25].

The novelty of this study's findings lies in the connection between low vitamin D levels and the presence of advanced prolapse stage and their association with multisite manifestation. However, it is limited as the number of participants is relatively low to permit definite conclusions. It is recommended that POP pathophysiology should be investigated further on a large sample size to account for these findings.

Previous studies have shown that vitamin D levels in Jordanian women are lower than the international standard [16]. This study was also limited in its study design as all possible risk factors were not assessed, which wasn't our aim. Therefore, a more extensive longitudinal study is needed to evaluate the impact of supplementing vitamin D in Jordan women. Given the additive effect of vitamin D in many medical conditions associated with women's health, it would be beneficial to supplement women from puberty to prevent future medical problems.

CONCLUSIONS

It was concluded that patients with POP showed lower vitamin D levels than those without prolapse. Moreover, it suggests that vitamin D deficiency is possibly independently correlated to prolapse severity, site and multiplicity. Despite

Table 4. *P-value for vitamin D levels and prolapse grade comparison between control and study group subgroups.*

Grade	P-value
Mild	0.341
Moderate	0.630
Advanced	0.043

Table 5. *P-value for vitamin D levels and prolapse site comparison between control and study group subgroups.*

Grade	P-value
Multisite	0.022
Cystocele	0.270
Rectocele	0.007
Uterine prolapse	0.311

the limitations of this study, it provides more evidence on the possible role of vitamin D in prolapse pathophysiology and warrants further research to strengthen the validity of the observations. Research over the supplementary administration of vitamin D as a preventative measure among women at risk would significantly determine its clinical value which can have social, psychological, and financial grat impact worth taking into action.

COMPLIANCE WITH ETHICAL STANDARDS

Authors contribution

LA-M entirely contributed to this work.

Funding

None.

Study registration

N/A.

Disclosure of interests

The author declares that she has no conflict of interests.

Ethical approval

This study was approved by the Ethical Review Committee, High Education Deanship of the Jordan University for Science and Technology. It adhered to the principles of the Declaration of Helsinki and conforms with the equator guidelines as an observational study.

Informed consent

Informed consent was obtained from all the patients before participation. The names and other identifiers were covered and not divulged to researchers involved in the data analysis.

Data sharing

Data are available under reasonable request to the corresponding author.

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