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Original Article

Muscle strength and quality of life improved after vitamin D supplementation among adult Saudi females

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SUMMARY

Background & aims: Physical and mental well-being following vitamin D supplementation shows contradictory data in the literature. We aimed to explore this more among young and middle-aged Saudi females suffering from vitamin D deficiency by analyzing handgrip strength and self-reported quality of life.
Methods: Fifty-eight females with bone or muscle aches attending the outpatient orthopedics clinic of an area hospital were enrolled after informed consent. Each participant filled out the SF-8™ questionnaire for quality of life (QOL) and was assessed for demographic/behavioral data, serum level of 25-hydroxyvitamin D (25(OH)D), and handgrip (HG) for both hands at baseline and 3 months after standard 25(OH)D oral supplementation.
Results: The mean age was 31.9 ± 7.3 years; serum 25(OH)D values increased significantly after the oral supplementation (11.28 ± 4.1, range 4.2–22 vs. 23.98 ± 6.81, range 7–41.4 μg/dl, $P < 0.001$) The handgrip mean for both hands after 25(OH)D supplementation also showed statistically significant higher values (13.24 ± 4.95, range 5–25.33 vs. 17.76 ± 4.39, range 9.5–27.33 kg/m^2, $P < 0.001$). The SF-8™ QOL questionnaire results showed an overall statistically significant improvement ($P < 0.001$). 25(OH)D baseline values

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; HG, handgrip; PTH, parathyroid hormone; QOL, quality of life; T3, triiodothyronine; T4, thyroxine; TSH, thyroid stimulating hormone.

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predicted muscle weakness; area-under-the-curve was 63% (95% CI: 47–79%) with the best cut-off value at 17.17 μg/dl (sensitivity 64% and specificity 62%).
Conclusion: Adult Saudi females showed improved muscle strength and quality of life following standard 25(OH)D oral supplementation.

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1. Introduction

Vitamin D deficiency (Serum 25(OH)D level < 20 μg/dl) [1] is a known risk factor for both musculoskeletal (e.g., osteoporosis) and non-musculoskeletal disorders (e.g., cardiovascular diseases, diabetes mellitus, and cancer) [2,3]. The high prevalence of vitamin D deficiency among Saudi adults poses a major public health problem. The fortification of food with vitamin D (i.e., primary prevention) and early detection of this condition (i.e., secondary prevention) are effective strategies to reduce its adverse health outcomes [4].

Serum 25(OH)D is generally low among Saudi women. The limited sunlight exposure due to prevalent social and religious norms (women cover themselves up from head to toe in public) likely contributes, among other factors, to their low vitamin D levels [5]. The situation is similar for school-aged adolescent girls [6]. Data on the gender distribution of hypovitaminosis D is mixed. It ranges from studies where it was found to be higher among females [7], to studies that showed no difference by sex [8], to studies where it was found to be higher among males [9].

A typical manifestation of hypovitaminosis D in adults is skeletal muscle weakness. Vitamin D receptors have been identified in muscle cells, and in a large majority of the cases, a positive correlation has been shown between low serum vitamin D and muscle weakness [10–13], with a few exceptions [14,15]. Many of these studies, however, were conducted on elderly people, who are prone to muscle weakness due to aging.

Besides skeletal muscle, serum vitamin D is also positively correlated with respiratory muscle strength; its deficiency thus leads to impaired respiratory muscle strength, which in turn is responsible for poor pulmonary function and quality of life (QOL) [2,16]. There is evidence that vitamin D deficiency affects quality of life and physical fitness [17].

The treatment of vitamin D deficiency with oral supplementation is well established [1]. Data indicate that supplementation improves both muscle weakness and QOL in patients with vitamin D deficiency [2]. However, the data for Saudi Arabia about the effect of 25(OH)D supplementation on muscle strength and QOL is limited, particularly among young adults.

There is reason to believe that the vitamin D deficiency problem is more pronounced in the Qassim region of Saudi Arabia. The weather gets very hot during the summer, and residents avoid going outside during the daytime, which limits sun exposure. Additionally, Qassimis are religiously conservative, and women strictly follow the modest dress code of covering the entire body and face, which further limits their sun exposure.

Therefore, we selected a sample of young Saudi females who had vitamin D deficiency or insufficiency, treated them with vitamin D supplementation, then assessed whether their muscle strength and/or quality of life improved.

2. Materials and methods

2.1. Study design and participants

Fifty-eight adult Saudi females aged 18–25 years with low backache and/or other bone or muscle aches from Qassim, Saudi Arabia who were attending the outpatient orthopedics clinic of one area

hospital were enrolled in the study from February 2017 and December 2017. Laboratory tests confirmed that all of them had 25(OH) D deficiency <20 μg/dl. After they met the eligibility criteria and agreed to participate through informed consent, this quasi-experimental study tested whether their muscle weakness or QOL improved after vitamin D supplementation, Other patients with similar complaints but who were already taking 25(OH)D or calcium supplementation, had abnormal liver, renal, thyroid or parathyroid function tests, high serum albumin, bilirubin, ALT, AST, BUN, serum creatinine, total T4, TSH and PTH, known malignancy or chronic granulomatous disorders, or who were pregnant were excluded from this study. This study was approved by the Local Ethical Committee Review Board of Qassim Region, Ministry of Health, Saudi Arabia.

2.2. Measurements

2.2.1. Clinical data

Participating patients' socio-demography, such as age, marital status, number of children, dietary habits, residence, and education were recorded along with some information on physical activity and sun exposure duration per week. Anthropometric measures (weight in kg, height in cm), resting blood pressure and heart rate were measured [7]. A musculoskeletal examination was performed for all subjects.

2.2.2. Laboratory testing

For serum level of 25(OH) D estimation, we used Bachman Coulter, Inc. (250 S. Kraemer Blvd., Brea, CA 92821, USA) immunoassay system. Serum 25(OH)D was estimated as a 2-step competitive binding immune-enzymatic assay from a collected blood sample. The unit of measurement was μgm/dl.

2.2.3. Handgrip (HG)

HG strength was assessed for both right and left hands. After giving instructions as per standardized protocol [18], a total of three readings of standard handgrip measurements were taken for each hand. The highest dynamometer reading was taken into account for the analysis. The procedure was performed using a dynamometer machine (Baseline® HD Hydraulic Hand Dynamometer; product 12−0221, SR 12203449, White Plains, NY 10602, USA). The normal range of handgrip for Middle Eastern young females is (22−30 kg/m^2) [18].

2.2.4. Quality of life (QOL)

We used the Optum™ SF-8™ Health Survey to test participants' well-being and functional health as a measure of QOL [19]. The eight questions included.

1) Overall health: How would you rate your health during the past 4 weeks?

   Excellent, very good, good, fair, poor, or very poor.

2) During the past 4 weeks, how much did physical health problems limit your physical activities (such as walking or climbing stairs)?

   Not at all, very little, somewhat, quite a lot, or could not do physical activities.

3) During the past 4 weeks, how much difficulty did you have doing your daily work, both at home and away from home, because of your physical health?

   Not at all, very little, somewhat, quite a lot, or could not do daily work.

4) How much bodily pain have you had during the past 4 weeks?

   None, very mild, mild, moderate, severe, or very severe.

5) During the past 4 weeks, how much energy did you have?

   Very much, quite a lot, some, a little, or none.

6) During the past 4 weeks, how much did your physical health or emotional problems limit your usual social activities with family or friends?

   Not at all, very little, somewhat, quite a lot, or could not do social activities.

7) During the past 4 weeks, how much have you been bothered by emotional problems (such as feeling anxious, depressed or irritable)?

   Not at all, slightly, moderately, quite a lot, or extremely.

8) During the past 4 weeks, how much did personal or emotional problems keep you from doing your usual work, school or other daily activities?

   Not at all, very little, somewhat, quite a lot, or could not do daily activities.

2.3. Vitamin D supplementation

We followed the running standard of care according to Saudi Arabian Ministry of Health management protocol, and all patients received 50,000 units of 25(OH)D oral supplementation weekly for 8 weeks [1].

2.3.1. Procedure

The above mentioned measures (clinical data, laboratory investigations including serum 25(OH)D, HG, and SF-8™ questionnaire for QOL) were performed twice; first at enrollment following the diagnosis of 25(OH)D deficiency, and the second assessment 3 months after the start of 25(OH)D supplementation.

2.3.2. Statistical methods

Statistical analyses were performed using SPSS Statistics, version 25 (SPSS Inc., Chicago, Illinois, USA). Qualitative variables were presented as frequency and proportion, while the quantitative ones were presented as mean ± SD. We used Mann–Whitney U and Krushkal–Wallis tests as applicable. The pre- and post-intervention values of vitamin D, HG, and QOL were tested with Wilcoxon signed rank test. To assess treatment adherence, we checked the vitamin D change by baseline vitamin D classified into below and above median. A receiver operating characteristic (ROC) curve was generated, and area-under-the-curve (AUC) was assessed for vitamin D cut-off values. A p-value ≤ 0.05 was considered significant.

3. Results

3.1. Patients' characteristics at baseline (before vitamin D supplementation)

Table 1 shows the baseline characteristics of patients. The age of the patients was 30.82 ± 7.5 years, ranging from 18 to 45 years. They had an overall BMI of 25.76 ± 3.84. Sixty-nine percent of them came from urban areas, 71% had a college education while others had only school level education, 78% had no job, and half of them were married. Sixty percent of them had no positive history of osteoporosis, 60% reported walking and 32% regularly ran as a part of their activity; 74% said that their hands were regularly exposed to sun, and only 14% had sun exposure to both hands and face. Only single women

Table 1
Baseline characteristics of patients with muscle weakness (n = 58).

Variables	Mean ± SD or number (%)
Age (years)	30.82 ± 7.53
Height (cm)	161.09 ± 5.60
Weight (kg)	66.98 ± 11.36
BMI (kg/m^2)	25.76 ± 3.84
Residence	
Urban	40 (69.0)
Education	
College level	41 (70.7)
Occupation	
No job	45 (77.6)
Marital status	
Married	30 (51.7)
Family history of osteoporosis	
No	34 (58.6)
Activity	
Walking	35 (60.3)
Running	19 (32.8)
Sun exposure type	
Hand	43 (74.1)
Hand and Face	8 (13.8)

BMI, body mass index.

and women with a family history of osteoporosis had significantly low HG scores compared to women who were married and who had no family history of osteoporosis.

3.2. Vitamin D, HG and QOL Change Following Vitamin D Supplementation

Table 2 shows pre- and post-supplementation values of serum level of vitamin D, right HG, left HG, mean HG (MHG) and QOL (including each questionnaire question and the mean of the eight questions). It shows that mean 25(OH) significantly increased by > 13 μgm/dl, mean HG increased by 4 kg/m^2, and the QOL also increased significantly from the pre-intervention value.

3.3. Assessing Treatment Adherence and Impact of Treatment

Treatment adherence was evident by the significant improvement of vitamin D change in below median baseline vitamin D category patients ($P < 0.05$) compared to those of the higher category (Table 3).

3.4. Vitamin D Cut-off Value for Muscle Weakness

A receiver operating characteristic (ROC) curve was generated (Fig. 1) to evaluate 25(OH)D values at baseline as a predictor for muscle weakness; AUC was 63% (95% CI: 47–79%) with the best cut-off value at 17.17 μg/dl (sensitivity 64% and specificity 62%).

4. Discussion

To our knowledge, this is the first study to test the effect of vitamin D supplementation on muscle strength and QOL standards in Saudi Arabia. In addition, this study highlighted the value of handgrip measurement as a simple, feasible and reproducible tool that could be used to screen for muscle weakness.

Despite the ample sunshine in Saudi Arabia, young women are suffering from hypovitaminosis D mostly due to acquired and genetic risk factors, including those related to skin type, diet, exercise, and cultural and religious beliefs that can augment the problem [4,5,7,8,20].

Table 2
The research parameters before and after intervention.

Variable	Before	After	Change	Improvement (%)	*p*-value
25(OH)D (μg/dl)	11.33 ± 4.06	24.66 ± 6.98	13.33 ± 6.84	54.06	<0.001
Right HG (kg/m^2)	13.16 ± 5.52	17.85 ± 4.77	4.69 ± 3.52	26.27	<0.001
Left HG (kg/m^2)	13.14 ± 4.95	17.65 ± 4.42	4.51 ± 2.68	25.55	<0.001
Mean HG (kg/m^2)	13.18 ± 5.09	17.49 ± 4.40	4.57 ± 2.90	26.13	<0.001
QOL1	2.24 ± 0.60	2.67 ± 0.69	0.43 ± 0.60	16.10	<0.001
QOL2	1.98 ± 0.83	2.59 ± 0.59	0.60 ± 0.84	23.17	<0.001
QOL3	1.86 ± 0.87	2.55 ± 0.71	0.69 ± 0.84	27.06	<0.001
QOL4	2.26 ± 0.91	2.84 ± 0.67	0.59 ± 0.94	20.77	<0.001
QOL5	1.76 ± 0.76	2.66 ± 0.64	0.90 ± 0.77	33.83	<0.001
QOL6	2.34 ± 0.85	2.88 ± 0.68	0.53 ± 0.75	18.40	<0.001
QOL7	1.76 ± 0.87	2.72 ± 0.83	0.97 ± 0.92	35.66	<0.001
QOL8	2.17 ± 0.88	2.93 ± 0.86	0.76 ± 0.87	25.94	<0.001
Total QOL	16.34 ± 4.27	21.84 ± 3.44	5.5 ± 5.07	25.18	<0.001

HG, handgrip; QOL, quality of life.

Table 3
Assessment of change in Vitamin D by the baseline median vitamin D level.

	< Median	> Median	*p*-value
Change in Vitamin D (μg/dl)	15.36	11.29	<0.05

Our sample showed 25(OH)D deficiency in 95% (10.8 ± 3.41 μg/dl) of patients and insufficiency in 5% (21.2 ± 0.9 μg/dl), which reflects other published research results from Saudi Arabia. Siddiqui and Kamfar (2007) found that 81% of Saudi girls had low 25(OH)D levels [6]. Alsuwadia et al. (2013) studied 488 middle-aged Saudi patients and found lower percentages for 25(OH)D deficiency and insufficiency (29%, 22.7% respectively); moreover, they found that females were at higher risk for both 25(OH)D deficiency and insufficiency [7].

Vitamin D deficiency among the population in the Qassim region was highlighted in some studies with variant magnitude and distribution. Hussain et al. (2014) showed that the prevalence of 25(OH)D deficiency was 83.6%, and the Saudi adolescents showed more significant values [21]. Naeem et al. (2011) showed that in 180 Saudi patients living in Qassim, 28.3% had 25(OH)D deficiency, 39.4%showed insufficiency, and 32.2% had normal 25(OH)D levels [22]. Elshafie et al. (2012) also found a significantly higher prevalence of 25(OH)D deficiency in women compared to men (70%,40% respectively) [23]. Recently, Fayed and Saleh (2017) studied 60 Saudi patients who presented with musculoskeletal complaints at a tertiary hospital in Qassim. Their results showed that the mean age of the patients was 43.2 ± 6.4 years; 90% had lower 25(OH)D values (70% deficiency and 20% insufficiency) [24]. They concluded that 25(OH)D deficiency was not restricted to females but extended to affect males living in Qassim, which further shows the magnitude of the problem.

Our results showed insignificant impact of patients' different behavioral aspects, including area of residence, education, occupation, daily activity, or sun exposure on the serum level of 25(OH)D. Alsuwadia et al. (2013) also showed insignificant impact of different behaviours among Saudi patients, including marital status, education level, socioeconomic status, activity level, smoking or dietary habits [7]. Al-Shaikh et al. (2016) had similar findings except that being middle-aged or unemployed were significant risk factors for low serum 25(OH)D among Saudi female patients ($P < 0.05$) [25]. ElShafie et al. (2012) showed different results; among 50 married Saudi couples, they found that men were at lower risk for 25(OH)D deficiency due to some protective behaviours like sun exposure and milk intake, which was reflected and proved by a multivariate regression analysis [23].

After standard oral 25(OH)D supplementation, our results showed a statistically significant increased 25(OH)D serum level (11.28 ± 4.1 vs. 23.98 ± 6.81 μg/dl, $P < 0.001$) with an overall improvement of 48.2%. Not only 25(OH)D levels, but also mean handgrip showed a statistically significant increase (13.24 ± 4.95 vs. 17.76 ± 4.39 kg/m^2, $P < 0.001$). The prevalence of muscle weakness for

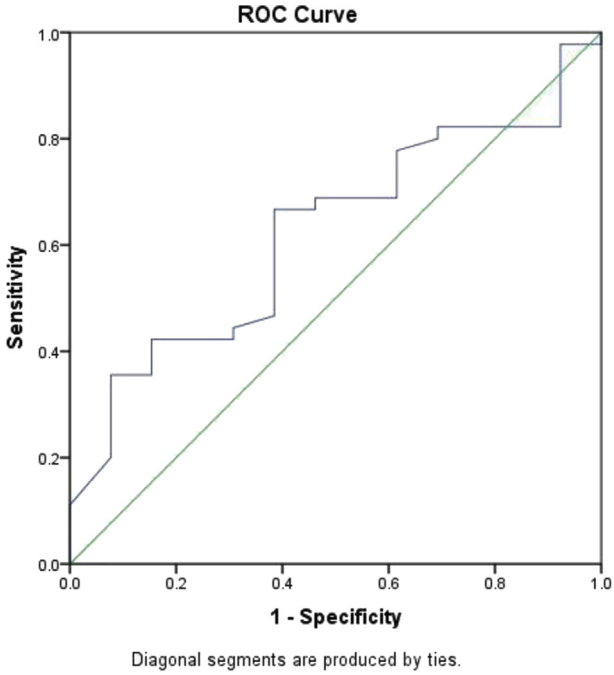

Fig. 1. ROC curve for detection of 25(OH)D as a predictor of muscle weakness.

both hands among patients was 93%, but after supplementation, it improved to be 81% ($P < 0.05$). Our results showed that the baseline values of 25(OH)D could predict muscle weakness with the best cut-off value at 17.2 μg/dl, a moderate sensitivity of 64% and specificity of 62%.

Our results aligned with Gumieiro et al. (2015), who found that in 100 patients with a mean age of 80 ± 7 years (73% females), 37% had 25(OH)D deficiency and were at more risk for low handgrip values in univariate analysis [26]. Also, Hirani et al. (2014) found that 25(OH)D deficiency and insufficiency are significantly correlated to physical disability; disability was tested by a modified Katz Index of Independence in Activities of Daily Living (Katz ADL) scale, and muscle weakness was tested by handgrip. They also found that low 25(OH)D levels were correlated to mortality in the studied sample. Moreover, they found that the cut-off value for all complications, including physical disability, muscle weakness, and poor general health was <50.0 nmol/L for 25(OH)D levels, and the risk was eliminated with improved 25(OH)D levels with a cut-off value at 75 nmol/L.

As QOL and mental health has tremendous effect on productivity and physical health, we investigated that point in our study and found that standard oral 25(OH)D supplementation significantly improved QOL items tested by the SF-8™ Health Survey ($P < 0.05$). Our results matched a cross-sectional study done by Chao et al. (2014) on 1,493 Canadian subjects; they found a positive correlation between higher levels of 25(OH)D and mental health and QOL standards [17]. In a local study, Fayed and Saleh (2017) showed that following significant improvement of serum 25(OH)D after 12 weeks of supplementation, there was a significant decrease in the Numeric Rating Pain Scale (7.42 ± 2.12 vs. 2.06 ± 2.04, $P < 0.001$), and functional status scores of the participants significantly improved (93.95 ± 23.56 vs. 203.1 ± 58.6, $P < 0.001$) [24]. In a more recent meta-analysis done by Hoffmann et al. (2015) where they analyzed previous QOL trials related to vitamin D supplementation published between 1950 and May 2014, vitamin D supplementation was found to have a positive correlation with QOL, and they recognized the need for more research to evaluate long-term effects [27].

On the other hand, some studies showed no correlation between 25(OH)D level and muscle strength, including the Rafiq et al. (2017) study on 1,200 patients with chronic obstructive pulmonary disease; although the participants' serum 25(OH)D levels were significantly improved following supplementation, handgrip strength, QOL, and other study outcomes failed to show significant improvement after 6 months [16]. The same result was reproduced by Grimnes et al. (2017); they found that in a sample of 275 postmenopausal women with osteopenia or osteoporosis, no improvement in handgrip strength or QOL occurred following 12 months of calcium plus vitamin D3 supplementation [2].

This discrepancy in results among studies of vitamin D supplementation's effect on both physical and mental health is related to differences in the selected samples, especially in age group with variable general health status and comorbidities. For example, some studies enrolled elderly, frail, or postmenopausal subjects while others enrolled young and middle-aged healthy subjects. In addition to diverse samples, variable methodologies, doses of vitamin D supplementation and follow-up periods affected the various outcomes of the studies.

The limited number of patients in this study is considered a limitation, but the follow-up on 25(OH)D levels and other study outcomes in the enrolled sample reduced the biased results.

5. Conclusions

Both muscle strength and quality of life showed statistically improved values after standard oral 25(OH)D supplementation. Baseline vitamin D levels predicted muscle weakness with moderate sensitivity and specificity.

Vitamin D supplementation should be advised as a routine supplement for young and middle-aged Saudi females whose serum 25(OH)D level is < 20 μg/dl. This recommendation mirrors that in Al-Daghri et al. (2017), who recommended 25(OH)D therapy for all persons in Saudi Arabia with a serum 25(OH)D level of <20 μg/dl; a target of 30 μg/dl was advised for elderly osteoporotic patients [28].

Conflicts of interest

None.

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CRediT authorship contribution statement

Mohammed Ewid: Conceptualization, Methodology, Validation, Writing - original draft, Writing - review & editing. **Mohammed AlTelbany:** Methodology, Investigation, Formal analysis, Writing - review & editing. **Syed Muhammad Baqui Billah:** Investigation, Formal analysis, Writing - original draft, Writing - review & editing. **Nazmus Saquib:** Conceptualization, Writing - original draft, Supervision, Writing - review & editing. **Akram Helmy:** Methodology, Investigation, Formal analysis, Writing - review & editing. **Saadi AlJundi:** Investigation, Formal analysis, Writing - review & editing. **Tawfik Rajab:** Investigation, Formal analysis, Writing - review & editing. **Saed Enabi:** Investigation, Formal analysis, Writing - review & editing. **Ahmed AlShwaikh:** Investigation, Formal analysis, Writing - review & editing. **Abdullah Morhaf:** Investigation, Formal analysis, Writing - review & editing. **Hossam Sherif:** Conceptualization, Methodology, Writing - original draft, Writing - review & editing.

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Appendix A. Supplementary data

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