

Association of 25(OH)D Serum Concentrations on Health-Related Quality of Life among Patients with Low Vitamin D

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Abstract

Objective. To determine the association between 25-hydroxyvitamin D [25(OH)D] serum concentrations and health-related quality of life (HRQoL) among patients with low vitamin D levels.

Methodology. This prospective cohort study included 76 patients (ages 18 to 59; 54 females and 22 males) who had baseline 25(OH)D below 30 ng/ml and were prescribed a Vitamin D supplement for eight weeks. HRQoL was assessed at baseline and after 8 weeks through the Functional Assessment of Non-Life Threatening Conditions (FANLTC) questionnaire.

Results. HRQoL of the participants who were Vitamin D deficient and insufficient at baseline were basically the same (p-values > 0.05). After supplementation, the personal well-being and overall HRQoL of the participants who were Vitamin D sufficient were significantly higher than those who were Vitamin D deficient or insufficient (p-values < 0.05). Moreover, after supplementation, all the HRQoL subscale scores as well as the total HRQoL scores of the participants were significantly higher than their baseline HRQoL scores (p-values < 0.05).

Conclusion. The improved HRQoL scores after Vitamin D supplementation showed that there is a significant association between 25(OH)D serum concentrations and HRQoL.

Key words: *Vitamin D, 25(OH)D, health-related quality of life*

INTRODUCTION

Vitamin D is produced in the skin during sun exposure. Season, latitude, time of day, skin pigmentation, aging and sunscreen use all influence the cutaneous production of vitamin D₃.¹ For most inherently medium to dark-skinned ethnic groups like Filipinos, a half-hour under the tropical sun produces 20,000 to 30,000 IU vitamin D within 24 hours of exposure.² However, despite having year-round sunshine in the Philippines, there are plenty of Vitamin D deficient patients with different symptoms and presentations at diagnosis. In December 2010, Vitamin D deficiency was flagged as a major health concern in South Asia.³

Vitamin D deficient patients may present with muscle aches, unexplained weakness, bone pains and psychological disturbances which may suggest other diseases (fibromyalgia, chronic fatigue, age-related weakness, or even depression) due to the nonspecific nature of its symptoms.⁴ Because of this, patients are subjected to a multiple diagnostic exams to determine the cause of symptoms that may be debilitating enough to affect the patient's daily life. Moreover, low levels of

vitamin D are also linked to other conditions including increased risk of fracture, abnormal bone metabolism, diabetes mellitus, asthma and susceptibility to infections.⁵

The Endocrine Society Clinical Practice Guideline (CPG) released in July 2011⁶ recommends using the serum circulating 25(OH)D level, measured by a reliable assay, to evaluate vitamin D status. The Institute of Medicine (IOM) committee has determined that the level of 25(OH)D that is needed for good bone health for most individuals is 20 ng/ml. However, several sources say that this cut-off is too low. The aforesaid CPG reported that a 25(OH)D equal to or less than 20 ng/ml is considered as Vitamin D Deficiency while a 25(OH)D level of 21 to 29 ng/ml is considered as Vitamin D insufficiency and provided recommendations for its management.

The wide range of manifestations of Vitamin D deficiency and the financial burden of multiple diagnostic examinations for nonspecific signs and symptoms could potentially affect the quality of the patients' lives. To date, there is a dearth of published studies along this line in the foreign, and more so, in the local setting, hence the impetus for this study which has the following objectives:

1. To determine the association between 25(OH)D serum concentrations and health-related quality of life (HRQoL) among patients with low vitamin D.
2. Specifically, this study compared the baseline HRQoL of patients with different Vitamin D levels.

METHODOLOGY

Study design

The investigation was a prospective cohort study.

Participants

Private patients of Makati Medical Center (MMC) endocrine consultants and Health Services Program (HSP) patients from the Outpatient Department of MMC who were suspected to have low Vitamin D levels such as the elderly, obese, those with limited sun exposure, and those with limited dietary intake of foods rich in Vitamin D as assessed by their doctors were requested to have a Vitamin D assay.

Patients who were 18 to 60 years old with a baseline Vitamin D level below 30ng/ml who were prescribed vitamin D supplementation between 2000 IU to 6000 IU daily were included. The dosage per patient varied according to the clinical practice guidelines.⁶

Patients who had cancer, uncontrolled hypertension, congestive heart failure, chronic kidney disease requiring dialysis, poorly controlled diabetes, chronic lung disease, those who had hyperphosphatemia, and/or hypercalcemia, who were bedridden, with known psychiatric illness, or who needed assistance in everyday living were excluded in the study.

Qualified patients who agreed to participate were asked to sign a written informed consent form.

Sample size

Using a 95% CI for the proportion of eligible patients who will complete the assessment form, with a margin of error (ME) of 0.05 and an estimated completion rate of 75%, the required sample for this study was at least 75 patients.

Measures

Serum 25(OH)D concentrations were analyzed using Electro-chemiluminescence binding assay (ECLIA) (Cobas, Roche). Results are determined via an instrument-specific calibration curve which is generated by 2-point calibration and a calibration master curve provided via the reagent barcode.

To measure HRQoL, the Functional Assessment of Non-Life Threatening Conditions (FANLTC) questionnaire

from the Functional Assessment of Chronic Illness Therapy (FACIT) measurement system, a collection of validated HRQoL questionnaires targeted to the management of different types of illnesses, was used.⁷ The FANLTC has also been used in other studies (e.g. involving patients who underwent bilateral breast reduction surgery,⁸ among persons with disabilities).⁹

The FANLTC measures HRQoL in patients with non-life threatening illnesses on four aspects (subscales) – *physical well-being* (I have a lack of energy; I have nausea; Because of my physical condition, I have trouble meeting the needs of my family; I have pain; I am bothered by side effects of treatment, I feel ill, I am forced to spend time in bed), *social/family well-being* (I feel close to my friends; I get emotional support from my family; I get support from my friends; My family has accepted my illness; I am satisfied with family communication about my illness; I feel close to my partner or the person who is my main support; I am satisfied with my sex life), *emotional well-being* (I feel sad, I am satisfied with how I am coping with my illness, I am losing hope in the fight against my illness, I feel nervous, I worry that my condition will get worse) and *functional well-being* (I am able to work, My work is fulfilling, I am able to enjoy life, I have accepted my illness, I am sleeping well, I am enjoying the things I usually do for fun, I am content with the quality of my life right now).

Response categories for the foregoing items consisted of the following: not at all, a little bit, somewhat, quite a bit, and very much, referring to how often they have experienced the statements in the questionnaire 7 days prior to answering. For positively stated items, the said response categories yielded scores of 4, 3, 2, 1, and 0, respectively. For negatively stated items, the scores were reversed. Answers to individual items per subscale were summed after performing the necessary reversals. The sum of the item scores were then multiplied by the number of items in the subscale, then divided by the number of items answered. This produced the subscale score. The subscale scores were then added to derive the total FANLTC score. Higher scores meant better HRQoL.⁹

The subjects were asked to answer the same questionnaire twice- at baseline and after 8 weeks of vitamin D supplementation. The questionnaire took 10 minutes to answer.

FACIT provided the validated questionnaire in English version as well as the translated version in Filipino.

Data analysis

Mean \pm standard deviation, median (interquartile range) and count (percentage, %) were computed for normal, non-normal, and categorical data, respectively. Shapiro-Wilk's test for normality was employed.

Independent samples t-test and Mann-Whitney tests were carried out to test differences between groups in terms of mean or median HRQoL scores, respectively. For comparisons of pre- and post-Vitamin D supplementation data on HRQoL, Wilcoxon Signed Ranks test was used.

A p-value less than 0.05 was considered significant. All statistical computations were performed using Stata/IC 13.

RESULTS

Out of 94 patients screened for eligibility, 82 patients were initially included but only 76 patients completed the study. Baseline demographics showed predominance of females (71% vs. 29%). Patient age range was 18 to 59 years, with a mean age of 40 ±10.7 years and median age of 45 years. [Table 1]

Table 1. Baseline Characteristics of Participants

Characteristics		(n = 76)
Age (years)	Mean (Standard Deviation)	40.67 (10.79)
	Median (Interquartile Range)	45 (13)
	[Minimum, Maximum]	(18, 59)
Sex	Female (n, %)	54 (71%)
	Male (n, %)	22 (29%)
Co-morbidities	Diabetes Mellitus Type 2 (n, %)	49 (64%)
	Hypertension (n, %)	27 (36%)
	Thyroid (Nodular nontoxic goiter, Graves' disease) (n, %)	17 (22%)
	Others (n, %)	3 (4%)

Out of the 62 patients who were Vitamin D deficient at baseline, 46 (74%) had sufficient Vitamin D levels after supplementation, 13 (21%) improved from deficient to insufficient, while 3 (4.8%) remained deficient. The 14 patients who had insufficient Vitamin D at baseline had sufficient Vitamin D levels after supplementation. [Table 2]

Table 2. 25(OH)D Levels Before and After Supplementation

Baseline 25(OH)D Level	25(OH)D Level after Supplementation		
	Deficient	Insufficient	Sufficient
Deficient	3	13	46
	4.8%	21.0%	74.2%
Insufficient	0	0	14
	.0%	.0%	100.0%
Total	3	13	60
	3.9%	17.1%	78.9%

The HRQoL of the study participants who were Vitamin D deficient and insufficient at baseline were basically the same (p-values > 0.05) except for their social/family well-being where a slightly higher median score was noted for those who were Vitamin D insufficient as compared to those who were Vitamin D deficient (15 vs. 13, p=0.031). All the median / mean HRQoL subscale and total scores were below half of the maximum score except for the median for social/family well-being, which was slightly above 14 [Table 3].

After supplementation, the personal well-being and overall HRQoL of the study participants who were Vitamin D sufficient were significantly higher than those who were Vitamin D deficient or insufficient (p-values < 0.05). The social/family well-being, emotional well-being, and functional well-being of both groups were approximately the same (p-values > 0.05) [Table 4].

Moreover, after supplementation, all the HRQoL subscale scores as well as the total HRQoL scores of the study participants were significantly higher than their baseline HRQoL scores (p-values < 0.05). [Table 5]

DISCUSSION

This study examined the association between Vitamin D level and HRQoL. Data obtained at the start of the study showed that patients with Vitamin D level less than 30

Table 3. Comparison of HRQoL Scores at Baseline

HRQoL Subscale	25(OH)D Level	N	Median (Range = 0 to 28)	Interquartile Range	p-value
Personal Well-Being	Deficient	62	5.5	6	.265 ^M
	Insufficient	14	8	8	
HRQoL Subscale Social / Family Well-Being	25(OH)D Level	N	Median (Range = 0 to 28)	Interquartile Range	p-value
	Deficient	62	13	4	.031 ^{*M}
	Insufficient	14	15	9	
HRQoL Subscale Emotional Well-Being	25(OH)D Level	N	Median (Range = 0 to 20)	Interquartile Range	p-value
	Deficient	62	3	2	.665 ^{*M}
	Insufficient	14	3.5	3	
HRQoL Subscale Functional Well-Being	25(OH)D Level	N	Mean (Range = 0 to 28)	Standard Deviation	p-value
	Deficient	62	13.37	3.137	0.516 ^t
	Insufficient	14	12.79	2.486	
Total	25(OH)D Level	N	Median (Range = 0 to 104)	Interquartile Range	p-value
	Deficient	62	35	8	.059 ^M
	Insufficient	14	40	11	

*Significant at $\alpha=0.05$ level; ^M – Mann Whitney U test; ^t – Independent t test

Normality is determined per variable. There are variables which are normally distributed and those which are not. The mean and SD were used to describe normally distributed data while the median (IQR) were used to describe non-normally distributed data.

Table 4. Comparison of HRQoL Scores after Vitamin D Supplementation

HRQoL Subscale	25(OH)D Level	N	Mean (Range = 0 to 28)	Standard Deviation	p-value
Personal Well-Being	Deficient / Insufficient	16	14.31	3.11	.008 ^{*t}
	Sufficient	60	16.93	3.49	
HRQoL Subscale	25(OH)D Level	N	Median (Range = 0 to 28)	Interquartile Range	p-value
Social / Family Well-Being	Deficient / Insufficient	16	24.50	4	.277
	Sufficient	60	25	4	
HRQoL Subscale	25(OH)D Level	N	Median (Range = 0 to 20)	Interquartile Range	p-value
Emotional Well-Being	Deficient / Insufficient	16	9.50	9	.394
	Sufficient	60	11	8	
HRQoL Subscale	25(OH)D Level	N	Median (Range = 0 to 28)	Interquartile Range	p-value
Functional Well-Being	Deficient / Insufficient	16	24.50	5	.306
	Sufficient	60	24	4	
Total	25(OH)D Level	N	Mean (Range = 0 to 104)	Standard Deviation	p-value
	Deficient / Insufficient	16	71.75	6.42	.039 ^{*t}
	Sufficient	60	75.67	6.66	

*Significant at $\alpha=0.05$ level; ^{MM} – Mann Whitney U test; ^t – Independent t test

Table 5. Comparison of HRQoL Scores before and after Vitamin D Supplementation

	Baseline		After Supplementation		p-value
	Median	Interquartile Range	Median	Interquartile Range	
Personal Well-being (Range = 0 to 28)	6.00	6	16.00	6	0.000 ^{*W}
Social / Family Well-being (Range = 0 to 28)	14.00	4	25.00	4	0.000 ^{*W}
Emotional Well-being (Range = 0 to 20)	3.00	2	11.00	8	0.000 ^{*W}
Functional Well-being (Range = 0 to 28)	13.00	3.75	24.00	4	0.000 ^{*W}
Total (Range = 0 to 104)	35.00	10	75.00	8.5	0.000 ^{*W}

*Significant at $\alpha=0.05$ level; ^W – Wilcoxon signed ranks test

ng/ml had lower HRQoL scores. In a report on the association of mood and vitamin D levels presented at the 94th Endocrine Society Congress in Houston, Texas in June 2012,¹⁰ vitamin D deficiency was correlated with exacerbation of depression with improvement in the mood in patients with vitamin D supplementation. The patients' mood and outlook as reflected by their social disposition and attitude towards their family were reflected in this study by the low HRQoL scores.

After receiving vitamin D supplementation for 8 weeks, the repeat HRQoL test showed significant improvement. Other studies also reported positive benefits of correcting Vitamin D deficiency or insufficiency with regards to patients' symptoms such as lack of energy, nausea, pain, body weakness and fatigue. In a case series by Huang, et.al.,¹¹ vitamin D supplementation in vitamin D deficient or insufficient patients resulted to improvement in pain, sleep, and QoL except for role-functioning and emotional QoL relative to baseline. In another study involving patients with mild-to-moderate Crohn's disease, quality-of-life scores also improved following vitamin D supplementation.¹² The present study reflected similar results as evidenced by the significant improvement in the HRQoL scores of patients from baseline to 8 weeks, although other factors that might have contributed in the patients' improved HRQoL scores cannot be totally ruled out.

The main limitation of this study is that the HRQoL questionnaire tool used is not specific for patients with

Vitamin D deficiency. Although it has been used for patients who underwent bilateral breast reduction surgery⁸ and among persons with disabilities,⁹ no other study evaluating Vitamin D deficient patients with this questionnaire has been found. Moreover, this study may be improved with a control group (with sufficient vitamin D at baseline), longer study duration for more stable results in the HRQoL and vitamin D level difference, larger sample size, and controlled intervention i.e., dose of vitamin D given to patients.

Nevertheless, this study reinforces that vitamin D acts as an indicator of overall health and well-being. Vigilance in maintaining a normal vitamin D status should be a high priority for physicians. Surveillance for vitamin D deficiency, with measurement of 25(OH)D concentrations should be part of yearly physical examinations.¹ Findings of this study indicate that correcting vitamin D deficiency or insufficiency in our patients may prove beneficial not only for good bone health but in improving their quality of life as well.

CONCLUSION

The improved HRQoL scores after Vitamin D supplementation showed that there is a significant association between 25(OH)D serum concentrations and HRQoL among patients with low vitamin D.

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