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Elleah Chin April 3, 2024

The Correlation between Life Quality of Female Patients with Cystic Fibrosis and Vitamin D Level

by

Elleah Chin

Vin Tangpricha MD, Ph.D.
Adviser

Department of Biology

Vin Tangpricha, MD, Ph.D.

Adviser

Michal Arbilly, Ph.D.

Committee Member

William Hunt, MD

Committee Member

2024

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Vin Tangpricha MD, Ph.D.

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An abstract of
a thesis submitted to the Faculty of Emory College of Arts and Sciences
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Department of Biology

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Abstract

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Importance

Vitamin D deficiency occurs frequently in patients with cystic fibrosis often due to pancreatic exocrine insufficiency and lack of outdoor activity**.** However, previous research showed that vitamin D deficiency is associated with an increase in the risk of health issues such as cancer, osteomalacia, and rickets. Investigating the correlation between vitamin D levels in females with cystic fibrosis and their life quality might improve their daily lives.

Objective

To determine if there is a positive correlation between vitamin D status in female patients with cystic fibrosis and their life quality, sexual function, and mobility.

Design/Setting

Quantitative Studies using Survey and Data from Blood Samples

Participants

26 consented women with cystic fibrosis, aged between 16-50 years, who were treated at Children's Hospital of Atlanta, Emory Clinic, and Emory Hospital from January 1, 2000, to August 10, 2018. Participants should be patients who are not in critical condition, on steroids, and post-liver or lung transplantation.

Measure

25-hydroxyvitamin D Concentration using 25 VitD^{s}, an FDA-cleared and CE-marked machine that uses an automated Chemiluminescence Immunoassay (CLIA) format. 3 surveys that each measures different criteria: quality of life, female sexual function, and mobility.

Results

Unfortunately, there was no significant difference between vitamin D status and life quality scores, sexual activity scores, and mobility scores of female patients with cystic fibrosis. In other words, we did not find any correlation between the vitamin D status and life quality scores, sexual activity scores, and mobility scores of female patients with cystic fibrosis.

Conclusion and Relevances

We reported that vitamin D status is unlikely to have a correlation between the life quality, sexual activity, and mobility of female patients with cystic fibrosis.

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By Elleah Chin

Biology Department Honors Thesis

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Conclusion and Relevance

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Introduction and Background

Vitamin D is a fat-soluble vitamin and seco-steroid hormone that plays a major role in calcium and phosphate homeostasis and bone metabolism for humans. Vitamin D is found in the diet from a few foods such as salmon, tuna, liver, and egg yolk in trivial amounts and mostly through supplements (Lamberg-Allardt, 2006). However, the major source of vitamin D comes from exposure to the skin to ultraviolet light. 5-dehydrocholesterol in the skin is converted to vitamin D3 upon exposure to UV light. The produced vitamin D3 then circulates to the liver and is hydroxylated in the 25-position to form 25(OH)D and then to the kidney to be hydroxylated in the 1-position to form 1,25-dihydroxyvitamin D (1,25(OH)2D) (Lips, 2006).

Researchers have recently reported a high prevalence of vitamin D deficiency (defined as a 25(OH)D below 30 ng/mL) (Holick and Chen, 2008). Recent studies have demonstrated that vitamin D deficiency is associated with an increase in the risk of cancer, osteomalacia, and rickets (Charoenngam and Holick, 2020). Furthermore, additional research has shown a relationship between low vitamin D levels and mental health problems such as depression, fatigue, anxiety, and stress (Almuqbil et al., 2023).

Vitamin D deficiency occurs frequently in patients with cystic fibrosis. Low levels of vitamin D in patients with cystic fibrosis could be caused by pancreatic exocrine insufficiency and lack of outdoor activity (Chesdachai and Tangpricha, 2015). Thus, many patients with cystic fibrosis are encouraged to take vitamin D supplements to maintain adequate vitamin D status. Improved vitamin D status is associated with decreased inflammation and improved lung function in patients with cystic fibrosis (Pincikova et al.,

2016). Moreover, previous studies have found that estrogen levels in patients with cystic fibrosis are associated with higher quality of life test scores, female sexual function index, and mobility test scores(Wu et al., 2022).

The purpose of this research is to examine the relationship between vitamin D status and several factors such as quality of life score, female sexual function index, and mobility scores in female patients with cystic fibrosis. We plan to explore relationships between vitamin D status and quality of life, sexual function, and mobility of female patients with cystic fibrosis.

Material and Method

Study Protocols

This was a secondary analysis in an Emory IRB-approved study that examined the relationship between estrogen levels and the quality of life scores in female patients with cystic fibrosis. This proposal will focus on vitamin D status as assessed by serum 25-hydroxyvitamin D concentrations in the participants recruited in the parent study.

Participants

This study involves 22 consented women with cystic fibrosis, aged between 16-50 years, who were treated at Children's Hospital of Atlanta, Emory Clinic, and Emory Hospital from January 1, 2000, to August 10, 2018. Participants should be patients who are not in critical condition, on steroids, and post-liver or lung transplantation. Moreover, out of the 22 participants, 7 participants were taking estrogen supplements. However, there were no significant differences between baseline demographics between the participant group that takes estrogen supplements and the group that does not take estrogen supplements.

25-hydroxyvitamin D Concentration

Serum 25-hydroxyvitamin D (Cacifediol) is the best marker of vitamin D status in our body. To measure serum 25-hydroxyvitamin D level, we will collect at least 10 µL of stored blood from each participant. Then, we will run them through 25VitD^{S}, an FDA-

cleared and CE-marked machine that uses an automated Chemiluminescence Immunoassay (CLIA) format.

Surveys

We are focusing on 3 different criteria: quality of life, female sexual function, and mobility.

CFQ-R: To measure the score of quality of life, we asked the participants to self-report through surveys called CFQ-R (Cystic fibrosis-specific health-related quality of life instrument). CFQ-R, a Food and Drug Administration-approved questionnaire, measures the quality of life in 12 areas and is scored on a scale of 1-100 (100 being the greatest life quality).

FSFI-6: FSFI-6 (Female Sexual Function Index-6) to measure sexual function index. It measures sexual function on a scale of 1-30 and 1-19 is considered sexual dysfunction.

LSA: LSA (measurement of person's mobility) to measure the how far the patient travels from their residential place. It measures how far away the participants get from their bedroom on a scale of 1-120 in which the higher the score is, the greater the mobility.

Results

Baseline Demographic Result

Table 1 reports the baseline demographic characteristics for 22 female patients with cystic fibrosis. Results show most of our participants are in their middle adulthood stage (mean=30.91 years), Caucasian (86%), mostly single and never married (64%), and working fully or part-time (50%). Moreover, the table reports that the majority of them have either homozygous mutation(45%) or heterozygous mutation(41%) in delta F508 and pancreatic insufficiency. However, only a small number of participants had cystic fibrosis-related diabetes (18%).

CFQ-R Survey Result

CFQ-R survey results are shown in Table 2 and Figure 1. Table 2 explains the statistical comparison between the CFQ-R score, or life quality score, of the low vitamin D group, middle vitamin D group, and high vitamin D group. It shows that there is no significant difference between all 3 vitamin D groups in any of the life quality measuring categories: physical functioning, vitality, emotional state, eating disturbances, treatment burden, health perceptions, social, body image, role/school, weight, respiratory, and digestion (all p-values > 0.05). Although there were slight differences in emotional state between the middle vitamin D level group and high vitamin D level group(p-value = 0.96), health perception between the low vitamin D level group and middle vitamin D level group(p-value = 0.96), and body image between low vitamin D level group and two other groups (between middle vitamin D level group, p=0.51; between high vitamin D level

group, p-value = 0.91), there is still no significant statistical difference between the scores (p-values > 0.05). Moreover, the difference in median scores between the 3 groups are a mixture of positive and negative values. In other words, they do not show a consistent trend of one group always having a higher score.

In Figure 1, the CFQ-R survey score data is represented in a bar graph for easier comparison between the 3 vitamin D status groups by different CFQ-R survey categories. The graph also indicates that there is no statistical difference between the high-level vitamin D group, middle-level vitamin D group, and low-level vitamin D group through overlap in standard deviation between the groups. Moreover, the bar does not show a consistent trend of one group always being the highest or one group always being the lowest.

FSFI-6 Survey Result

FSFI-6 survey results are shown in Table 3 and Figure 2. Table 3 reports the statistical comparison between the FSFI-6 score, or female sexual function index score, of the low vitamin D group, middle vitamin D group, and high vitamin D group. FSFI-6 survey also shows no significant difference between all 3 vitamin D groups in any of the sexual function measuring categories: Libido, Arousal, Lubrication, Orgasm, Satisfaction, and Dyspareunia (all p-values > 0.05). Although there is a slight difference in FSFI-6 score between libido between middle vitamin D level group and the 2 other groups (p-value = 0.47 between low vitamin D group, p-value = 0.7 between high vitamin D group), there is still no significant difference between the 3 groups (p-value > 0.05). However, the percentage of participants who were engaged in sexual activity was highest in the high

vitamin D group(86%), followed by the low vitamin D group(63%), and lowest in the middle vitamin D group(29%).

In Figure 2, the FSFI-6 survey score data is displayed in a bar graph to facilitate the comparison between the low vitamin D group, middle vitamin D group, and high vitamin D group by different indications of sexual functions of women. The graph indicates that there is no significant difference between the 3 groups through a large overlap in the standard deviation bar. However, a slight trend in the middle vitamin D level group showing low FSFI-6 scores compared to the low vitamin D level group and high vitamin D level group is shown in Libido, Arousal, Lubrication, Satisfaction, and Dyspareunia. Out of the categories that showed such a trend, only lubrication showed a slightly higher median score in the low vitamin D level group than the high vitamin D level group.

LSA Survey Result

LSA survey results are shown in Table 4 and Figure 3. Table 4 reveals the statistical comparison between the LSA score, or mobility score, of the low vitamin D group, middle vitamin D group, and high vitamin D group. LSA survey shows no significant difference in composite life space score between the 3 groups(p-value > 0.05). In terms of composite life space score, there was a slight difference between the low vitamin D level score and middle vitamin D level score(p-value = 0.27), it is still not significantly different from each other (p-value > 0.05). To go into specifics, there were slight differences between the groups in each LSA question. However, all of them indicated no significant difference between the two groups that were compared (p-value > 0.05).

In Figure 3, the LSA survey score data is represented in a bar graph to compare the 3 vitamin D status groups in the mobility of the participants. The graph indicates that there is no significant difference between the low vitamin D level group, middle vitamin D level group, and high vitamin D level group through overlap in the standard deviation bar.

Discussion

This research is a subsequent study of “Use of estrogen supplementation is associated with higher quality of life scores in women with cystic fibrosis” by Dr. Malinda Wu and her team. In Dr. Wu’s study, they divided the participants by whether the participants were taking estrogen supplements or not. However, our study divided the same participants into 3 groups depending on their vitamin D status to find the correlation between the vitamin D level in female patients with cystic fibrosis and their life quality, sexual function, and mobility. The reason for choosing vitamin D was because previous studies show that patients with cystic fibrosis tend to have vitamin D deficiency due to pancreatic exocrine insufficiency and lack of outdoor activity (Chesdachai and Tangpricha, 2015). However, other research reported that D deficiency is associated with an increase in health risks such as cancer, osteomalacia, and rickets (Charoenngam and Holick, 2020). Furthermore, additional research has shown a relationship between low vitamin D levels and mental health problems such as depression, fatigue, anxiety, and stress (Almuqbil et al., 2023). Thus, our objective was to see if there was any correlation between the life quality of people with cystic fibrosis and the low vitamin D level to possibly reduce the inconvenience in their lives.

For this study, we divided 22 participants into 3 groups: low vitamin D level group, middle vitamin D level group, and high vitamin D level group. The vitamin D level of the low vitamin D level group with 8 participants (N=8) ranged from 15 ng/mL to 46 ng/mL, the middle vitamin D level group (N=7) ranged from 50 ng/mL to 63 ng/mL, and high vitamin D level group (N=7) ranged from 64 ng/mL to over 120 ng/mL. Then, we compared the CFQ-R score(life quality score), FSFI-6 score(sexual function index), and LSA

score(mobility) of the 3 groups and determined the p-value to find the significance between the groups.

First, according to Table 2, there is no significant difference between the life quality of low vitamin D level group, middle vitamin D level group, and high vitamin D level group(p-value > 0.05). In other words, there is no difference in physical functioning, vitality, emotional state, eating disturbances, treatment burden, health perceptions, social, body image, role/school, weight, respiratory, and digestion between the 3 groups. Additionally, using the difference in the median as evidence, there is no trend between the 3 groups. To explain, in Table 2, the difference in median is a mixture of positive and negative values which means that sometimes the median of the second group was higher than the first group and sometimes it was lower. To support this point, Figure 1 also shows that there is no consistent trend of one group always having higher scores than the other group. This shows that vitamin D status in patients with cystic fibrosis is highly likely not the factor that affected the life quality of the participants.

Second, Table 3 shows that there is also no statistically significant difference between the sexual function in 3 different vitamin D level groups(p-value > 0.05). This tells us that there is no correlation between vitamin D status and sexual function categories such as Libido (or sexual desire), Arousal, Lubrication, Orgasm, Satisfaction, and Dyspareunia (or lasting or recurrent genital pain that occurs just before, during, or after sex) (Mayo Clinic, 2024). Although FSFI-6 results show a minor trend of the low vitamin D level group and the high vitamin D level group showing higher sexual function scores than the middle vitamin D level group in all of the categories except orgasm, it is

still statistically insignificant. This result reveals that there is no major correlation between vitamin D status and the sexual function of female patients with cystic fibrosis.

Lastly, Table 4 shows that there is no statically critical difference in mobility between the low vitamin D level group, middle vitamin D level group, and the high vitamin D level group (p-value > 0.05). To clarify, the results reveal the fact that there is no difference in the participant's distance traveled from their bedroom to other locations between the 3 different vitamin D level groups. This indicates that vitamin D will be least likely associated with the composite life space or mobility of female patients with cystic fibrosis.

Unlike the previous research that showed some kind of correlation between people's health and vitamin D status, our research showed no significant correlation between feelings about the health status of female participants with cystic fibrosis and vitamin D status (Charoenngam and Holick, 2020) (Almuqbil et al., 2023). Moreover, although previous research stated that many patients with cystic fibrosis have vitamin D deficiency, most of our participants who are patients with cystic fibrosis did not show low vitamin D levels (Chesdachai and Tangpricha, 2015). For someone to be considered vitamin D deficient, they must have less than 30 ng/mL of vitamin D. However, only 2 out of 22 participants were tested to have insufficient amount of vitamin D levels through serum tests.

These differences in results between the previous research and our research might have been caused by the small sample size (n=22) which led us to divide the vitamin D status groups within the normal vitamin D level range instead of having a group with insufficient amount of vitamin D and sufficient amount of vitamin D. In addition to the small

sample size, the data of rather the participants are taking vitamin D supplements or not might have explained the reason for 91% of our participants having sufficient amount of vitamin D while 82% showed pancreatic insufficiency (Table 1).

Thus, future studies should continue studying the difference between the life quality of female patients with cystic fibrosis and vitamin D deficiency and cystic fibrosis and vitamin D sufficiency. This will provide a clearer correlation between vitamin D status and life quality, sexual function, and mobility status of female patients with cystic fibrosis. Moreover, studying the relationship between vitamin D status and homozygosity in gene mutation delta F508, a common genetic mutation found in patients with cystic fibrosis will also be a good future research topic. If a correlation is found between the homozygosity in mutation and vitamin D level, that finding might allow the prediction of low vitamin D levels in patients with cystic fibrosis which might reduce the chance of health risks that are often caused by vitamin D deficiency.

Conclusion

The present study showed no statistically significant correlation between life quality, sexual function, and mobility and vitamin D status in female patients with cystic fibrosis. This result could be interpreted as life quality, sexual function, and composite life space are independent of vitamin D status. Therefore, vitamin D status does not affect how female patients with cystic fibrosis feel about their own health. The findings of this study provide a better understanding of the impact of vitamin D on the life of female patients with cystic fibrosis and provide us with further research directions.

Tables and Figures

Table 1: Participants Baseline Demographics by Vitamin D Status

Baseline Demographics by Level of Vitamin D level

Charactersticis	All Participants (N=22)		Low Vitamin D level (N=8)		Middle Vitamin D level (N=7)		High Vitamin D level (N=7)		*p-value*			
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**L,M**	**M,H**	**L,H**	
Age (years)	30.91	7.12	30.25	7.54	33.67	7.3	29	6.71	0.06	0.25	0.37	*
FEV1 (% predicted)	74.62	29.95	74.88	32.63	68.17	32.23	79.86	28.43	0.71	0.51	0.76	*
BMI (kg/m2)	22.88	5.33	22.63	6.59	24.29	5.29	21.76	4.1	0.60	0.34	0.76	*
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**				
Delta F508 status												
Homozygous	10	45%	3	29%	4	57%	3	43%				
Heterozygous	9	41%	4	57%	2	29%	3	43%				
No copies	3	14%	1	14%	1	14%	1	14%				
Race (Caucasian)	19	86%	5	63%	7	100%	7	100%				
Pancreatic insufficient	18	82%	7	88%	6	86%	5	71%				
Have CF-related diabetes	4	18%	2	25%	2	29%	0	0%				
Marital status												
Single/Never married	14	64%	4	50%	6	86%	4	57%				
Widowed	0	0%	0	0%	0	0%	0	0%				
Married	4	18%	2	25%	1	14%	1	14%				
With a partner	4	18%	2	25%	0	0%	2	29%				
Education												
Professional or graduate degree	1	5%	1	13%	0	0%	0	0%				
College degree	8	36%	1	13%	5	71%	2	29%				
Some college	8	36%	4	50%	0	0%	4	57%				
High school diploma/GED	4	18%	1	13%	2	29%	1	14%				
Some high school or less	1	5%	1	13%	0	0%		0%				
Occupation status												
Working full time or part-time	11	50%	4	50%	4	57%	3	43%				
Attending school outside home	7	32%	2	25%	2	29%	3	43%				
Seeking work	2	9%	0	0%	1	14%	1	14%				
Not attending school or working due to health	2	9%	2	25%	0	0%	0	0%				

Table 2: The statistical comparison between CFQ-R score of low vitamin D group, middle vitamin D group, and high vitamin D group. The statistical significance (p-value) was found using Bonferroni correction of Kruskal Wallis test.

CFQ-R Results																
CFQ-R Domain	All Participants (N=22)		Low Vitamin D level (N=8)		Middle Vitamin D level (N=7)		High Vitamin D level (N=7)		*p-value*			Difference in median scores		
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	L, M	M, H	L, H	L, M	M, H	L, H
Physical Functioning	75	34.35, 98.95	85.4	44.8, 96.85	45.80	35.4, 93.75	75.00	35.4, 93.75	1.00	1.00	1.00	-39.60	29.20	-10.40
Vitality	58.3	35.38, 72.92	54.15	37.45, 77.08	50.00	33.3, 62.5	58.30	33.3, 62.5	1.00	1.00	1.00	-4.15	8.30	4.15
Emotional State	76.65	66.7, 91.65	80	66.7, 93.3	66.70	63.35, 86.65	80.00	63.35, 86.65	1.00	0.96	1.00	-13.30	13.30	0.00
Eating disturbances	100	77.8, 100	94.45	75.03, 100	77.80	72.25, 100	100.00	72.25, 100	1.00	1.00	1.00	-16.65	22.20	5.55
Treatment burden	66.7	44.4, 75.03	50	33.3, 80.56	66.70	44.4, 72.25	66.70	44.4, 72.25	1.00	1.00	1.00	16.70	0.00	16.70
Health perceptions	66.7	47.2, 88.9	83.35	61.13, 91.68	55.60	50, 72.25	66.70	50, 72.25	0.96	1.00	1.00	-27.75	11.10	-16.65
Social	72.2	56.98, 83.3	80.55	48.6, 90.28	72.20	58.35, 77.75	77.80	58.35, 77.75	1.00	1.00	1.00	-8.35	5.60	-2.75
Body image	77.8	66.7, 100	66.7	55.6, 83.35	88.90	77.8, 94.45	100.00	77.8, 94.45	0.51	1.00	0.91	22.20	11.10	33.30
Role/School	75	58.3, 91.7	66.65	39.6, 87.48	83.30	66.65, 87.5	75.00	66.65, 87.5	1.00	1.00	1.00	16.65	-8.30	8.35
Weight (symptom scale)	100	41.65, 100	100	58.35, 100	66.70	66.7, 100	100.00	66.7, 100	1.00	1.00	1.00	-33.30	33.30	0.00
Respiratory (symptom scale)	52.8	40.27, 81.92	50	38.9, 80.58	50.00	41.65, 69.45	72.20	41.65, 69.45	1.00	1.00	1.00	0.00	22.20	22.20
Digestion (symptom scale)	77.8	66.7, 100	94.45	63.93, 100	77.80	66.7, 88.9	77.80	66.7, 88.9	1.00	1.00	1.00	-16.65	0.00	-16.65
Overall between groups									0.23*	0.16*	0.87*			

Figure 1: Bar graph about difference in CFQ-R score of low vitamin D group, middle vitamin D group, and high vitamin D group. x-axis shows each of the question or life quality criteria and y-axis indicates the CFQ-R score. Line in the middle of the bar represents the standard deviation of each data.

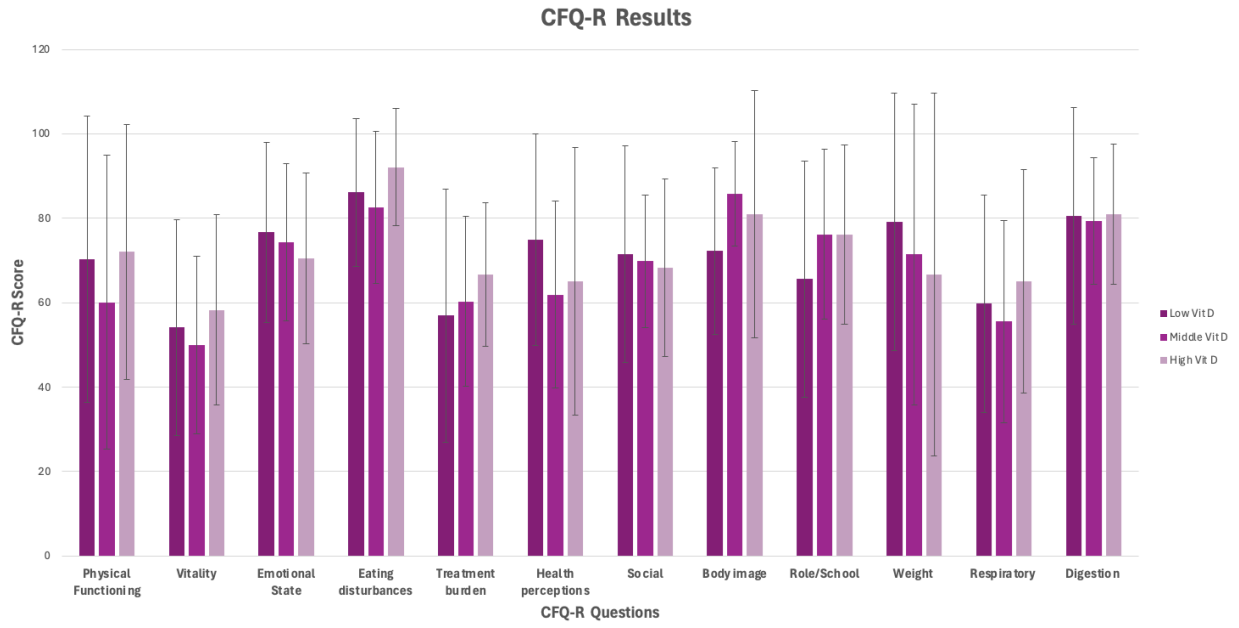


Table 3: The statistical comparison between FSFI-6 score of low vitamin D group, middle vitamin D group, and high vitamin D group. The statistical significance (p-value) was found using Bonferroni correction of Kruskal Wallis test.

Female Sexual Function Index-6 Results

	All Participants (N=13)		Low Vitamin D level (N=5)		Middle Vitamin D level (N=2)		High Vitamin D level (N=6)		*p-value*		
	Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**L, M**	**M, H**	**L, H**
Libido	4	3, 4	4	3,4	2.5	2.25, 2.27	4	3.25, 4.75	0.47	0.70	1.00
Arousal	4	3, 5	4	4,4	3	2.5, 3.5	4.5	3.25, 5	1.00	1.00	1.00
Lubrication	4	4, 5	4	4,5	3	2, 4	4.5	2.5, 5	1.00	1.00	1.00
Orgasm	3	2, 4	3	2,4	3.5	2.75, 4.25	3.5	2.25, 4.75	1.00	1.00	1.00
Satisfaction	5	2, 5	5	4.75, 5	3	2, 4	4.5	2.5, 5	1.00	1.00	1.00
Dyspareunia	4	3, 5	5	2,5	3.5	2.75, 4.25	4	4, 4.75	1.00	1.00	1.00

	All participants (N=22)	**Low Vitamin D level (N=8)**	**Middle Vitamin D level (N=7)**	**High Vitamin D level (N=7)**
Sexual active	59%	63%	29%	86%

Figure 2: Bar graph about difference in FSFI-6 score of low vitamin D group, middle vitamin D group, and high vitamin D group. x-axis shows each of the question or sexual function criteria and y-axis indicates the FSFI-6 score. Line in the middle of the bar represents the standard deviation of each data.

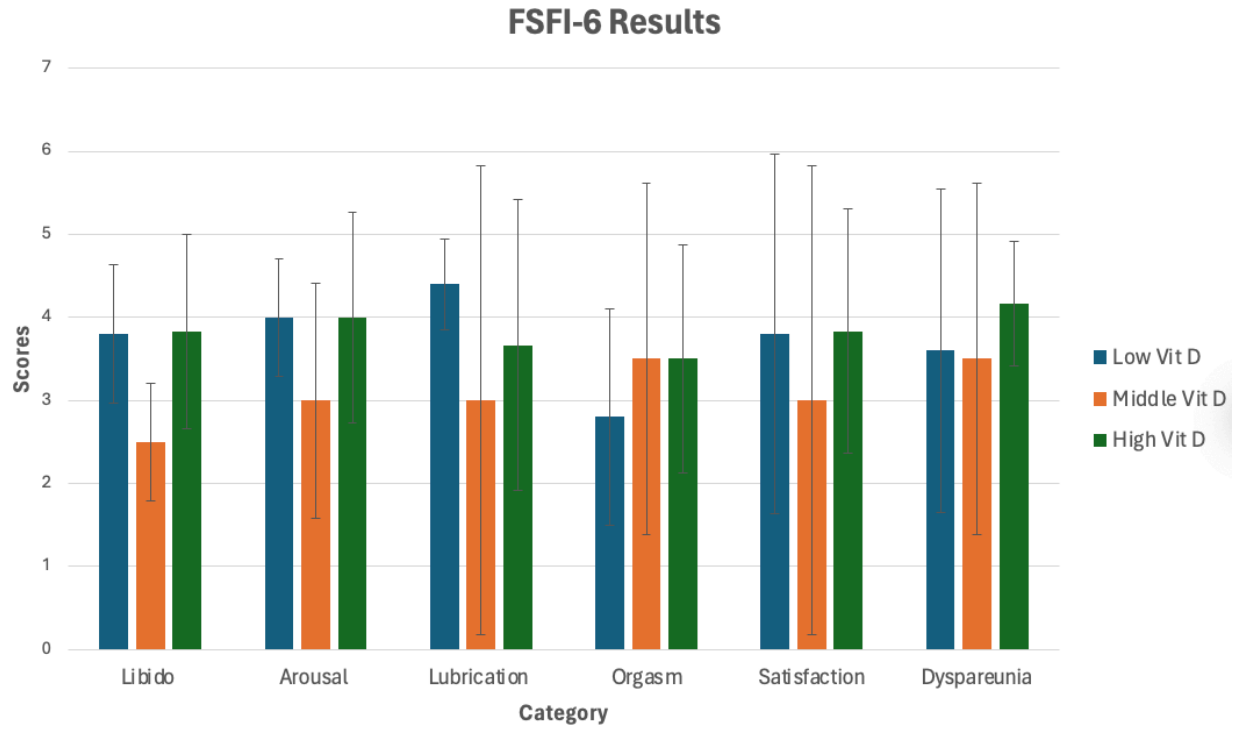
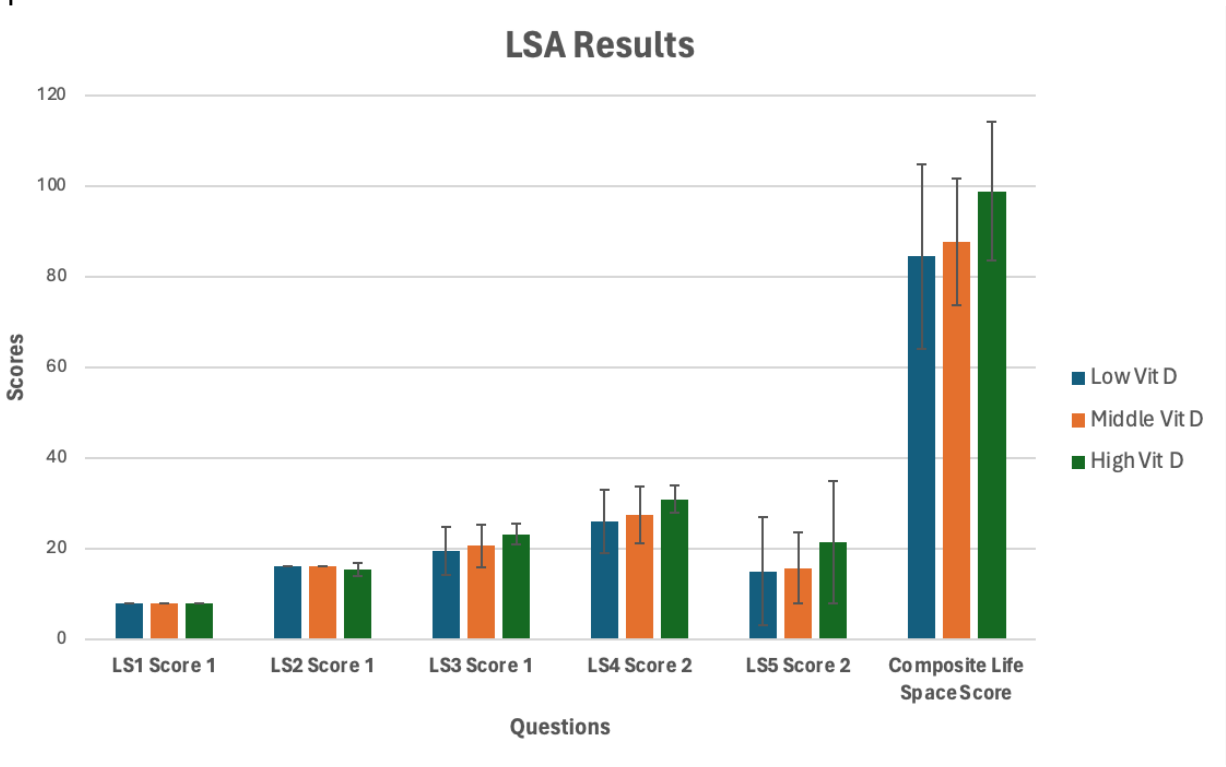


Table 4: The statistical comparison between LSA score of low vitamin D group, middle vitamin D group, and high vitamin D group. The statistical significance (p-value) was found using Bonferroni correction of Kruskal Wallis test.

LSA Results

	All Participants (N=22)		Low Vitamin D level (N=8)		Middle Vitamin D level (N=7)		High Vitamin D level (N=7)		*p-value*		
	Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**L, M**	**M, H**	**L, H**
LSA Q1	8	8,8	8	8,8	8	8, 8	8	8, 8	N/A	N/A	N/A
LSA Q2	16	16,16	16	16,16	16	16,16	16	16,16	N/A	0.78	0.70
LSA Q3	24	18,24	21	16.5, 24	24	18, 24	24	24, 24	1.00	0.78	0.44
LSA Q4	32	24, 32	28	22, 32	32	24, 32	32	32, 32	1.00	1.00	0.93
LSA Q5	15	10, 20	10	10, 20	10	10, 20	20	15, 30	1.00	0.74	0.44
Composite Life Space Score	83	75, 92.5	90	83, 98	100	86, 110	100	86, 110	0.27	1.00	1.00

Figure 3: Bar graph about difference in LSA score of low vitamin D group, middle vitamin D group, and high vitamin D group. x-axis shows each of the question or mobility criteria and y-axis indicates the LSA score. Line in the middle of the bar represents the standard deviation of each data.



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