

Vitamin D Perspective in Front Line Healthcare Workers Amid COVID-19

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ABSTRACT

Deficiency of Vitamin D is very common in Pakistan, even among healthy asymptomatic individuals [1], [2]. Recent studies have shown that the risk of contracting COVID-19 was increased to two-fold, and consequent mortality to 4-fold if the person is Vitamin D deficient [3]. Health care workers including the nursing and administration staff are at a high risk of contracting SARS-CoV2 due to increased regular exposure in a health care setting [4]. Consequently, a convergence of the COVID-19 pandemic, the deficiency of Vitamin D, and the increased exposure can render the health care workers at an additional risk to COVID-19 infection. Our objective was to determine the prevalence of vitamin D deficiency in healthy asymptomatic front-line health care workers and to analyze the change in serum level by loading oral dose of SunnyD STAT softgel capsules (200000 IU Vitamin D3). We followed single centered, cross-sectional, cohort study with subsequent randomized placebo-controlled design for supplementation and follow up. Serum level of 25-hydroxyvitamin D (25OHD) was the main outcome variable, with anthropometric data, nutritional intake, and lifestyle variables analyzed for potential association as risk factors for the outcome. Severe Vitamin D deficiency was found to be prevalent among front line health care workers in this urban hospital-based sample. Serum level of Vitamin D was found to be significantly associated with designation and presence of high blood pressure. The likelihood of increased serum Vitamin D levels was observed with increasing monthly income, higher designation, increasing age and supplementation intake. Mean increase in the serum 25(OH)D3 level after 2 doses of SunnyD STAT softgel capsule (200000 IU Vitamin D3) was 34.22 ng/ml. Public health interventions regarding Vitamin D supplementation and awareness are needed, especially amid COVID-19 pandemic.

Keywords: COVID-19, healthcare workers, Vitamin D deficiency.

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I. INTRODUCTION

Vitamin D is a secosteroid that has a wide spectrum of immunomodulatory, anti-inflammatory, antifibrotic, and antioxidant actions [5]. Epidemiological studies have reported that vitamin D deficiency is associated with viral respiratory tract infections and acute lung injury [5]. Vitamin D supplementation has exhibited protective effects against acute lung injury by modulating the expression of members of the renin-angiotensin system such as ACE2 in lung tissue [7], supporting the role of vitamin D deficiency as a pathogenic factor in COVID-19. Type-II pneumocytes are the primary target of coronaviruses and ACE2 receptors are highly expressed on these cells [9]. Impaired function of type-

II pneumocytes decrease the surfactant level and increase surface tension in COVID-19 [9]. Metabolites of 1,25-dihydroxyvitamin D have been reported to stimulate surfactant synthesis in alveolar type-II cells [10]. Recent studies have shown that the risk of contracting COVID-19 was increased to two-fold, and consequent mortality to 4-fold if the person is Vitamin D deficient [12]. Moreover, optimal levels of Vitamin D in the blood can reduce the risk of ICU admission to up to 97% [13].

Unfortunately, there is a high prevalence of vitamin D deficiency/insufficiency globally, in a very diverse population around the world [14]-[16]. Different studies done in Pakistan also identify this prevalence to be between 78-97% in Pakistani population [1], [2], [17], [20]-[25].

Amid the current pandemic of COVID-19, the health care workers including the nursing staff and administration are at high risk of contracting SARS-CoV2 [4]. With the Vitamin D deficiency already endemic in the society [21], a convergence of the COVID-19 pandemic, the deficiency of Vitamin D, and the increased exposure can render the health care workers at an additional risk to COVID-19 infection. To the best of our knowledge, no study had been done to evaluate the prevalence of Vitamin D deficiency in this particular cohort. This study, therefore, aimed to cover this gap in literature by reporting the prevalence of hypovitaminosis D in this cohort, identifying the potential risk factors and to assess the change in baseline levels of Vitamin D after loading dose of supplementation, so that policy recommendations can be given for adequate public health interventions.

II. METHODS

A. Study Population

We enrolled 256 healthy volunteer front line health care workers as participants for this study. The front-line healthcare workers included all the working doctors, nursing staff, paramedical, administrative, and cleaning staff of the ward who had regular exposure to patients coming to the hospital and did not have any apparent signs and symptoms of active COVID-19 infection. Sample size of 256 participants was calculated according to the formula:

$$n = N \times X / (X + N - 1)$$

where

$X = Z_{\alpha/2} - *p * (1-p) / MOE^2$;

$Z_{\alpha/2}$ = critical value of the Normal distribution at $\alpha/2$

(confidence level of 95%, α is 0.05 and the critical value is 1.96);

MOE = margin of error;

p = sample proportion;

N = population size;

Selected margin of error = 5%;

Selected Confidence level = 95%;

Selected Population size = 1000000;

Sample proportion = 80% (previous studies [17], [21]).

All health care workers of the ward including doctors, nurses and admin staff were offered to be included in the trial after taking informed consent, until the desired sample of 256 was achieved.

B. Consent and Ethical Approval

Consent was obtained by receiving signature or thumb impression of the participant on the consent form. Participants were informed that the dose would be given according to their current serum levels after laboratory testing, in compliance with international guidelines [23], to avoid risk of any toxicity or adverse event. Participants were also informed that, in case of deficiency, they had equal chances of being randomly allotted to either the placebo or the supplementation group. The Institutional Review Board of SIMS hospital approved the protocol.

C. Data Collection

Once enrolled, the participants filled a questionnaire about their current dietary habits and lifestyle. Moreover, a brief medical, surgical and drug history was also be taken to evaluate any association with serum Vitamin D levels.

D. Laboratory Measurements

After filling up of the Questionnaire, participants underwent baseline screening of their serum Vitamin D status through 15 mL blood test sampling of serum 25(OH)D3. All tests were performed by the Chughtai lab, SIMS hospital. Serum 25(OH)D levels were measured by competitive binding assay. Lab results were shared with participants and analysts.

E. Statistical Analysis

A sample size of 256 participants was calculated using the formula specified above, with 95% confidence level, α value of 0.05 and the critical value at 1.96. Descriptive data is expressed in frequencies and percentages while serum 25(OH)D3 levels are also expressed through mean, median and mode.

Data was categorized for statistical analysis. For dietary variables including egg, milk, and fish consumption, “zero consumption” was considered if the participant reported to have never consumed these foods or very rarely (hardly once a month) consumed them. Moreover, for egg consumption, those who consumed an egg daily, or 3-10 times per week were categorized as “frequent eaters” of egg. While “heavy eaters” included consumers of 10 or more eggs per week. Similarly, for milk consumption, 1-2 glasses per week were categorized as “seldom consumers”, while “frequent consumption” referred to 1-2 or >2 glasses of milk every day. For fish intake, “good consumers” referred to consumption of at least 1-2 or > 2 fish per week, or at least 1 fish daily.

For sun exposure, duration was labelled to be “no sun exposure” if the participant has no daily sun exposure or hardly 20 minutes a week. “Regular but low sun exposure” referred to those having 1-10 minutes of sun exposure every day, while 10-20 minutes or >20 minutes of daily sun exposure was considered “regular and good exposure”.

Statistical analyses were conducted with a commercially available software program (SPSS for Windows; Version 25).

Skewed distribution was log transformed for analysis, to prevent undue influence of extreme values. 40 ng/ml or greater was considered optimal level for immune health and values at 39.9 ng/ml or below were considered sub optimal for immune protection for COVID-19 [26]. Prevalence of hypovitaminosis D in subcategories was further displayed in frequencies and percentages.

To further assess simple bivariate associations among serum 25(OH)D level, and predictor variables, we used the χ^2 statistic, likelihood ratio, Fisher exact test, Pearson, and Spearman correlation coefficient as appropriate to the nature and distribution of the variables.

Pearson Chi square statistic was used for categorical (nominal) variables assuming the null hypothesis that no relationship exists between the serum 25(OH)D3 levels and the categorical variables in the population, i.e., they are independent. Cross tabulations (bivariate tables) were used to evaluate tests of independence. Continuity correction was

applied to bivariate variables like gender, designation, taking regular medicines, presence/absence of co morbidities like diabetes, cardiovascular disease, high blood pressure, disability, and chronic body aches and pains to approximate the discrete distribution. $P < 0.05$ was considered to be statistically significant.

Likelihood of having below optimal levels of serum Vitamin D3 was analyzed through ratio (>10 considered high) with a value of $p < 0.05$ considered statistically significant. Fisher exact test was also used for bivariate variables including gender and presence/absence of co morbidities including diabetes, CVD, HBP, physical disability, chronic body aches and pains. The variables went further linear to linear comparison with the serum 25(OH)D3 levels.

To assess the correlation between the interval and ordinal variables and the serum 25(OH)D level, the strength of linear relationship was analyzed using the Pearson and Spearman correlation coefficients. These included age, weight, height, monthly income, length of sun exposure and consumption of egg, milk, fish, and dietary supplements. Pearson's R was calculated for interval variables and serum Vitamin D levels, including age weight and height, based on normal approximation. Spearman's correlation was established for ordinal variables including monthly income, length of sun exposure and intake of egg, milk, fish, and dietary supplements.

III. RESULTS

The final sample was composed of 256 participants. After cleaning of data and removal of missing data, 199 remained valid for analysis. Baseline descriptive characteristics of the participants is given in Table I.

A. Baseline Characteristics of the Participants

The mean age of the participants was 35 years (Range 20-73 years). Majority of the participants were in the younger age group with 89 (44.7%) participants falling between 20-29 years of age, 42 (21.1%) in the 30-39 years age bracket, 34 (17.1%) in the 40-49 years age bracket and just 28 (14.1%) above 50 years of age. 109 (54.8%) participants were male while 90 (45.2%) were females. In designations, the highest number was that of House officers 39 (19.6%) of the total sample, followed by nurses comprising of 11.1% ($n=22$) of the total sample. 46 (23.1%) participants were earning in the salary range between Rs. 20000-50000/month, while just 20 (10.1%) participants had a salary above Rs.100000/month.

71.9% ($n=143$) participants had weight above 50 kg, while 23.6% ($n=47$) had weight between 41-50 kg. Presence of co morbidities including diabetes, cardiovascular diseases, high blood pressure and chronic body aches and pains was 7.5% ($n=15$), 3% ($n=6$), 6.5% ($n=13$) and 12.6% ($n=25$) respectively.

35.2% ($n=70$) participants had nil to minimal sun exposure (hardly 20 minutes/week), 21.1% ($n=42$) had regular but low sun exposure while 24.6% ($n=49$) had regular and good sun exposure (See Methods for definitions of categories).

58.8% ($n=117$) participants were frequent eaters of egg on a daily basis, while 17.1% ($n=34$) seldom or rarely ate eggs. 13.1% ($n=26$) ate 10 or more eggs per week and were

categorized as heavy eaters of egg. 44.7% ($n=89$) almost never drink milk, while 38.7% ($n=77$) consumed only 1-2 glasses per week. Only 13.1% ($n=26$) of the participants regularly drank at least 1 or 2 glasses of milk. Fish consumption was very scarce with 85.9% ($n=171$) of the participants hardly eating 1 or 2 fish in a month, while only 11.1% ($n=22$) reported to consume at least 1-2 fish per week or daily.

TABLE I: BASELINE CHARACTERISTICS OF THE PARTICIPANTS

Characteristics	Value n (%)
Age y. valid=193 missing=6	
Mean +-SD	35.09 +-10.79
Range	20-73
20-29	89 (44.7%)
30-39	42 (21.1%)
40-49	34 (17.1%)
50-59	26 (13.1%)
>60	2 (1%)
Gender Valid= 199 missing=0	
Male	109 (54.8%)
Female	90 (45.2%)
Designation Valid=188 missing=11	
Medical Student	19 (9.5%)
House officer	39 (19.6%)
Resident	20 (10.1%)
Assistant Professor	3 (1.5%)
Professor	4 (2%)
Head of department	3 (1.5%)
Consultant	5 (2.5%)
Nurse	22 (11.1%)
Head Nurse	4 (2%)
Administration Staff	2 (1%)
Nursing Superintendent	8 (4%)
Other	59 (29.6%)
Monthly income Valid= 156 missing=43	
5000-20000	23 (11.6%)
20000-50000	46 (23.1%)
50000-100000	34 (17.1%)
Above Rs. 100000	20 (10.1%)
Other	33 (16.6%)
Serum D3 levels total=160, missing=39	
Below optimal*	118 (59.3%)
optimal*	42 (21.1%)
Mean +- SD	32.03 +- 32.801
Median	18.95
Mode	7.4
Range	5.6-154.2
Weight valid=198 missing=1	
21-30	1 (0.5%)
31-40	1 (0.5%)
41-50	6 (3%)
51-60	47 (23.6%)
Above 60	143 (71.9%)
Diabetes valid=197 missing=2	
No	182 (91.5%)
Yes	15 (7.5%)
CVD valid=196 missing=3	
No	190 (95.5%)
Yes	6 (3%)
HBP valid=196 missing=3	
No	183 (92%)
Yes	13 (6.5%)
Any other Illness/disability valid=159 missing= 40	
No	146 (73.4%)
Yes	13 (6.5%)
Egg consumption valid=177 missing=22	
Zero eaters	34 (17.1%)
Frequent eaters	117 (58.8%)
Heavy eaters	26 (13.1%)
Milk Intake valid=192 missing= 7	
Zero	89 (44.7%)
seldom	77 (38.7%)

TABLE I: CONTD.

Characteristics	Value n (%)
Frequent	26 (13.1%)
Fish intake valid= 193, missing= 6	
Nill to rare	171 (85.9%)
Good consumers	22 (11.1%)
Medicines valid=160 missing =39	
No	159 (99.5%)
Yes	1 (0.5%)
Chronic body aches valid = 171 missing = 28	
No	146 (73.4%)
Yes	25 (12.6%)
Vitamin D supplements intake valid= 187 missing= 12	
No. I don't take any supplement	135 (67.8%)
I take supplements but I don't remember the amount of Vitamin D in it	25 (12.6%)
0-500 IU per day	5 (2.5%)
0-500 IU per week	1 (0.5%)
500-1000 IU per day	4 (2%)
5000-10000 IU per day	3 (1.5%)
200000 IU once a month	12 (6%)
Sun exposure valid=161 missing = 38	
No sun exposure	70 (35.2%)
Regular but low sun exposure	42 (21.1%)
Regular and good exposure	49 (24.6%)

*>40 ng/ml.

**<40 ng/ml.

B. Prevalence of hypovitaminosis D

The prevalence of sub optimal levels of Vitamin D3 in the total sample was 74.8%; with severe deficiency (<10 ng/ml) observed in 26.7% (n=42) of the participants. The lowest value reaching at 5.6 ng/ml, and a mode of 7.4 ng/ml was observed. The mean serum 25(OH)D3 was 32.03 ng/ml and a median serum 25(OH)D3 level of 18.95 ng/ml was calculated in the sample. The prevalence of hypovitaminosis within subgroups is listed in Table III, with the highest prevalence observed in young age participants between 20-29 years of age with 93.4% of them being deficient, zero eaters of egg (82.41% deficient), no supplements intake (88.2% deficient) and with nil to less than 20 minutes per week sun exposure (75.53% deficient).

The serum 25OHD level showed a skewed distribution and was accordingly log transformed for analysis, to prevent undue influence of extreme values.

TABLE II: PREVALENCE OF HYPOVITAMINOSIS D IN SUBGROUPS
FREQUENCY TABLE

Characteristics	Optimal* n (%)	Below optimal** n (%)	Total
Age y.			
20-29	5 (6.5%)	71 (93.4%)	76
30-39	12 (37.5%)	20 (62.5%)	32
40-49	12 (48%)	13 (52%)	25
50-59	11 (47.82%)	12 (52.17%)	23
>60	1 (100%)	0 (0%)	1
Gender			
Male	20 (23.25%)	66 (76.7%)	86
Female	22 (29.7%)	52 (70.27%)	74
Designation			
Medical Student	2 (12.5%)	14 (87.5%)	16
House officer	3 (0.08%)	31 (91.17%)	34
Resident	2 (12.5%)	14 (87.5%)	16
Assistant Professor	0 (0%)	3 (100%)	3
Professor	1 (25%)	3 (75%)	4
Head of department	3 (100%)	0 (0%)	3
Consultant	1 (25%)	3 (75%)	4
Nurse	6 (33.3%)	12 (66.66%)	18
Head Nurse	2 (66.6%)	1 (33.34%)	3
Administration Staff	1 (50%)	1 (50%)	2

Nursing Superintendent	7 (87.5%)	1 (12.5%)	8
Other	12 (30%)	28 (70%)	40
Monthly income			
5000-20000	3 (16.67%)	15 (83.3%)	18
20000-50000	9 (25.71%)	26 (74.29%)	35
50000-100000	10 (35.71%)	18 (64.29%)	28
Above Rs. 100000	11 (57.89%)	8 (42.11%)	19
Other	2 (7.14%)	26 (92.8%)	28
Weight			
21-30	0 (0%)	1 (100%)	1
31-40	0 (0%)	1 (100%)	1
41-50	1 (25%)	3 (75%)	4
51-60	9 (21.9%)	32 (78.04%)	41
Above 60	32 (28.31%)	81 (71.68%)	113
Diabetes			
No	36 (24.65%)	110 (75.34%)	146
Yes	5 (41.66%)	7 (58.3%)	12
CVD			
No	38 (24.6%)	116 (75.3%)	154
Yes	2 (66.6%)	1 (33.3%)	3
HBP			
No	34 (22.97%)	114 (77%)	148
Yes	6 (66.6%)	3 (33.3%)	9
Any other illness/disability			
No	32 (27.1%)	86 (72.8%)	118
Yes	1 (10%)	9 (90%)	10
Egg consumption			
Zero eaters	5 (17.85%)	23 (82.14%)	28
Frequent eaters	23 (24.46%)	71 (75.53%)	94
Heavy eaters	9 (41%)	13 (59%)	22
Milk Intake			
Zero	19 (26%)	54 (73.97%)	73
seldom	16 (27.58%)	42 (72.41%)	58
Frequent	4 (17.4%)	19 (82.6%)	23
Fish intake			
Nill to rare	34 (25.18%)	101 (74.81%)	135
Good consumers	6 (30%)	14 (70%)	20
Chronic body aches			
No	29 (24.7%)	88 (75.2%)	117
Yes	7 (31.8%)	15 (68.18%)	22
Vitamin D supplements intake			
No. I do not take any supplement	13 (11.7%)	98 (88.2%)	11
I take supplements but I do not remember the amount of Vitamin D in it	9 (56.25%)	7 (43.75%)	16
0-500 IU per day	1 (20%)	4 (80%)	5
500-1000 IU per day	1 (25%)	3 (75%)	4
5000-10000 IU per day	3 (100%)	0 (0%)	3
200000 IU once a month	7 (63.63%)	4 (36.36%)	11
Sun exposure			
No sun exposure	14 (24.56%)	43 (75.53%)	57
Regular but low sun exposure	7 (20%)	28 (80%)	35
Regular and good exposure	14 (34.14%)	27 (65.85%)	41

*Optimal = 40 ng/ml and above.

**Below optimal = 39.9 ng/ml and below.

C. Variables Associated with Low 25(OH)D3 Levels

Among the categorical (nominal) variables, the levels of serum 25(OH)D3 did not differ by gender ($X^2=0.861$ $p=0.353$), presence/absence of co morbidities like diabetes ($X^2=1.669$ $p=0.196$), cardiovascular disease ($X^2=2.733$ $p=0.098$), any physical disability ($X^2=1.412$ $p=0.235$) and chronic body aches and pains ($X^2=0.477$ $p=0.49$). However, designation ($X^2=37.113$ $p=0.000$) and high blood pressure ($X^2=8.531$ $p=0.003$), was strongly associated with serum Vitamin D levels.

The likelihood of increased serum Vitamin D levels (high

likelihood ratio >10) was observed with increasing monthly income (likelihood=17.286 p=0.002), higher designation (likelihood=36.785 p=0.000), increasing age (likelihood=34.64 p=0.000) and supplementation intake (likelihood = 46.406 p=0.000).

Using Fisher Exact test, higher odds for hypovitaminosis was seen in patients having chronic body aches and pains

(exact significance 2 sided = 0.596, one sided = 0.327) and those having some form of disability (exact significance 2 sided = 0.451, one sided = 0.215). Designation (12.25 p=0.000), Age (26.968 p= 0.000) and intake of supplements (32.659 p=0.000) showed high linear by linear association and positive correlation with serum Vitamin D3 levels.

TABLE III: CHI SQUARE TESTS

Test	Value	df	Asymptotic significance (2 sided)	Exact sig (2 sided)	Exact sign (1-sided)
Vitamin D*Gender					
Pearson Chi square	0.861 (a)	1	0.353		
Continuity correction (b)	0.559	1	0.455		
Likelihood ratio	0.859	1	0.354		
Fisher Exact test				0.373	0.227
Linear by linear Association	0.856	1	0 (0%)	1	
N of valid cases	160				
Vitamin D3 * designation					
Pearson Chi square	37.113 (a)	11	0.000.		
Likelihood ratio	36.785	11	0.000.		
Linear by linear Association	12.25	1	0.000.		
N of valid cases	151				
Vitamin D3 * Diabetes					
Pearson Chi square	1.669	1			
Continuity correction (b)	0.902	1			
Likelihood ratio	1.524	1			
Fisher Exact Test				0.301	0.169
Linear by linear Association	1.659	1			
N of valid cases	158				
Vitamin D3 * CVDs					
Pearson Chi square	2.733 (a)	1	0.098		
Continuity correction (b)		1	0.325		
Likelihood ratio		1	0.13		
Fisher Exact Test				0.16	0.16
Linear by linear Association		1	0.099		
N of valid cases					
Vitamin D3 * HBP					
Pearson Chi square	8.531 (a)	1	0.003		
Continuity correction (b)	6.385	1	0.012		
Likelihood ratio	7.216	1	0.007		
Fisher Exact Test				0.009	0.009
Linear by linear Association	8.477	1	0.004		
N of valid cases	157				
Vitamin D3 * Disability					
Pearson Chi square	1.412	1	0.235		
Continuity correction (b)	0.659	1	0.417		
Likelihood ratio	1.685	1	0.194		
Fisher Exact Test				0.451	0.215
Linear by linear Association	1.401	1	0.237		
N of valid cases	128				
Vitamin D3 * chronic body aches and pains					
Pearson Chi square	0.477 (a)	1	0.49		
Continuity correction (b)	0.181	1	0.67		
Likelihood ratio	0.460.	1	0.497		
Fisher Exact Test					0.596
Linear by linear Association	0.474	1	0.491		
N of valid cases	139				

b. Computed only for a 2×2 table.

D. Symmetric Measures

Based on normal approximation, statistically significant but moderately positive correlation was seen between age (R= 0.416, p=0.000) and serum 25(OH)D3 levels, through the Pearson R coefficient.

Among ordinal variables, a statistically significant and moderately positive linear correlation was observed between the intake of supplements (R=0.465, p=0.000) and serum Vitamin D levels. Weakly positive association was seen between increasing weight (R=0.084, p=0.290), egg consumption (R=0.150 p=0.073), milk intake (R=0.013

$p=0.873$), fish intake ($R=0.037$ $p=0.649$), duration of sun exposure ($R=0.085$ $p=0.333$ and serum Vitamin D3 levels but were all statistically non-significant ($p>0.05$), using the Spearman's rank correlation. The results of the symmetric measures statistics are summarized in Table IV.

E. Increase in Serum Vitamin D3 Levels

Mean increase in the serum 25(OH)D3 level in the interventional group after 2 doses of SunnyD STAT softgel capsule (200000 IU Vitamin D3) was 34.22 ng/ml. The mean increase in the placebo group was 3.04 ng/ml.

TABLE IV: SYMMETRIC MEASURES

		Value	Asymptotic SE (a)	Appr. T (b)	Appr. sig. (c)
Vitamin D*Monthly income					
Interval by Interval	Pearson's R	-0.014	0.077	-0.158	0.875 (c)
Ordinal by ordinal	Spearman Correlation	0.000.	0.080.	0.000.	1.000. (c)
N of valid cases		160			
Vitamin D3 * Ages					
Interval by Interval	Pearson's R	0.416	0.072	5.692	0.000 (c)
Ordinal by ordinal	Spearman Correlation	0.435	0.067	6.007	0.000 (c)
N of valid cases		157			
Vitamin D3 * Weight					
Interval by Interval	Pearson's R	0.084	0.066	1.062	0.290 (c)
Ordinal by ordinal	Spearman Correlation	0.075	0.075	0.949	0.344 (c)
N of valid cases		160			
Vitamin D3 * Egg consumption					
Interval by Interval	Pearson's R	0.150.	0.084	1.806	0.073
Ordinal by ordinal	Spearman Correlation	0.149	0.083	1.792	0.075
N of valid cases		144			
Vitamin D3 * Milk intake					
Interval by Interval	Pearson's R	0.013	0.082	0.16	0.873
Ordinal by ordinal	Spearman Correlation	0.013	0.082	0.129	0.898
N of valid cases		154			
Vitamin D3 * Fish intake					
Interval by Interval	Pearson's R	0.037	0.084	0.457	0.649
Ordinal by ordinal	Spearman Correlation	0.037	0.084	0.457	0.649
N of valid cases		155			
Vitamin D*Vit D supplements					
Interval by Interval	Pearson's R	0.465	0.079	6.434	0
Ordinal by ordinal	Spearman Correlation	0.515	0.084	7.352	0
N of valid cases		152			
Vitamin D*Sun exposure					
Interval by Interval	Pearson's R	0.085	0.089	0.972	0.333
Ordinal by ordinal	Spearman Correlation	0.08	0.089	0.918	0.36
N of valid cases		133			

a. Not assuming the null hypothesis.

b. Using the asymptotic standard error assuming the null hypothesis.

c. Based on normal approximation.

Apr = Approximate.

SE = Standard Error.

IV. DISCUSSION

To the best of our knowledge, this study was the first to analyze the serum 25(OH)D3 levels in health care workers. The cross-sectional design gave a near-to-real snapshot of the hypovitaminosis picture in this cohort. The triple blinded placebo-controlled intervention added to the reliability of the results.

We found a high prevalence of severe vitamin D deficiency among otherwise healthy, asymptomatic, working health care workers who are regularly exposed to patients from one of the main public sector hospitals of the city. These findings add to growing data of the high prevalence of hypovitaminosis among other young, healthy, asymptomatic adults of Pakistan [17], [24], [25]. Previous studies [18]-[22] highlighted the prevalence among general populations or in different cohorts

of patients, but to the best of our knowledge, this is the first study done in Pakistan to highlight the deficiency faced by those who are the most vulnerable at the front line of this pandemic war. These findings suggest that the problem of Vitamin D deficiency is spanning even the spectrum of healthy adults in the working health care sector.

To our surprise, young doctors were found to be comparatively more deficient than their seniors. Despite the decreasing ability of skin to synthesize Vitamin D from sunlight with age [27], [37], the effect of co morbidities [28], [38] and uptake of medications [29], [30], this finding of the high prevalence of hypovitaminosis in the youth is further alarming.

Another interesting finding was that females were comparatively less deficient than males, contrary to the expected element of more covered clothing [27], [31], lesser

outdoor time [32] and consequently lesser exposure to sunlight [32], [33].

Among dietary habits, low egg consumption was found to be another risk factor for low serum levels of 25(OH)D₃, with statistically significant values and a high prevalence of hypovitaminosis D among participants with zero to minimal egg consumption while fish and milk intake moderately influenced the serum D₃ levels, with no statistically significant values.

Another expected result was that for supplementation intake, with low prevalence of hypovitaminosis D in those taking regular Vitamin D supplements.

Low sun exposure was identified as another major risk factor for hypovitaminosis D. With availability of near to ample sunlight throughout the year in the country, the heliophobic tendency of South Asian culture [34], sun avoidance behavior [35], fear of tanning [34], indoor working hours [32], lack of deliberate sun exposure [32] and covered clothing [27], [31] could account for the high prevalence of Vitamin D deficiency in Pakistan.

All the risk factors identified above are easily modifiable. Therefore, awareness about the high prevalence of Vitamin D deficiency in Pakistan should be prioritized especially for at-risk population which is most vulnerable during this pandemic.

V. WHAT THIS STUDY ADDS

Contrary to most studies done in this region on the prevalence of hypovitaminosis in patients coming to health care facilities or general population, our sample was composed of those who are at greatest risk during any epidemic. To the best of our knowledge, this was the first study done on healthy, asymptomatic, health care workers of the region. The findings of such high prevalence of hypovitaminosis more than expected for this cohort. This study also contradicts the results of previous studies³⁶ of the higher prevalence of hypovitaminosis in females compared to males, and young compared to elderly [37], [38].

VI. LIMITATIONS

The study was cross sectional; therefore, causality cannot be inferred. Future longitudinal studies analyzing the identified risk factors can confirm the influence of these variables with more definite interpretations. Additionally, the inherent limitations of reporting bias in a questionnaire-based data collection tool could be present. Secondly, some participants didn't answer the questionnaire completely or were lost at follow up, resulting in a decrease in the data remaining valid for final analysis. Moreover, the sample was limited to health care workers so generalizability of the results to general population should be extrapolated with caution.

VII. CONCLUSIONS

There is a high prevalence of severe Vitamin D deficiency in front line, apparently healthy, asymptomatic health care workers in Pakistan. This study can provide grounds for

public health interventions like Vitamin D supplementation and raising awareness among this cohort.

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