ORIGINAL ARTICLE

Frequency and trend of vitamin D deficiency in correlation with demographic and selected biochemical parameters in Karachi, Pakistan

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Abstract

Objective: To evaluate the frequency and trend of vitamin D deficiency, and to find its correlation with demographic and selected biochemical parameters

Method: The retrospective study was conducted at The Indus Hospital, Karachi, and comprised clinical laboratory data of individuals tested for vitamin D from January 2013 to March 2018. The trend of vitamin D deficiency and frequency was assessed in relation to age, gender and serum levels of calcium, phosphorus, magnesium, alkaline phosphatase and parathyroid hormone. Data was analysed using Stata software.

Results: Of the 35,017 tests analysed, 23,522 (67.2%) related to females and 11,495 (32.8%) to males ($p<0.05$). Overall, 25,051 (71.5%) were vitamin D-deficient while 504 (1.4%) had toxic levels. Age had significant correlation with vitamin D deficiency ($p<0.05$). No significant correlation was observed with any of the biochemical parameters studied ($p>0.05$).

Conclusion: Vitamin D deficiency was high among female gender and young population.

Keywords: Vitamin D, Deficiency, Karachi, Risk factors, Gender.

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Introduction

Vitamin D is a fat-soluble vitamin essential for calcium homeostasis. It is primarily synthesised in skin by sunlight and contributes to more than 90% of vitamin D serum concentration. While absorbing solar energies (ultraviolet B), 7-dehydrocholesterol (provitamin D3) converts to vitamin D3 (cholecalciferol). Vitamin D can also be taken by diet through fortified dairy products and fish oils. After entering the circulation, Vitamin D3 is transported to the liver where it is converted to 25-hydroxyvitamin D (25[OH]D), which, although biologically inactive, is currently regarded as the best indicator of vitamin D status. In the kidney, 25(OH)D is metabolised to 1, 25(OH)2D (calcitriol), which is the biologically active form of vitamin D. This unfortunately has a half-life of 4-6 hours, and, hence, is not the best parameter to analyse vitamin D levels.[1,2]

Multiple reviews show a high prevalence of vitamin D deficiency worldwide, even in countries where it was assumed that ultraviolet (UV) B radiation was sufficient to prevent vitamin D deficiency.[3,4] Low vitamin D levels have been found in different ethnicities and age groups. However, data regarding prevalence of Vitamin D deficiency is lacking from many countries.[5]

Avoidance of sunshine or inadequate consumption of vitamin D and malnutrition can potentially be the main causes for deficiency.[6] Vitamin D deficiency can be caused by nutritional factors, reduction in solar exposure, malabsorption resulting from intestinal inflammation, Coeliac disease or gastric surgery and others. Low 25(OH)D status leads to reduced efficiency in intestinal calcium absorption, and the body reacts by increasing the secretion of parathyroid hormone (PTH). Increased serum PTH concentration is known to cause excessive bone turnover and loss, defects in mineralisation, and increased risk of fractures, especially in the elderly and women.[6,7] Literature shows that vitamin D deficiency not only affects bone metabolism and quality, but is also known to be associated with autoimmune diseases, neurological diseases and cancer.[1]

Detection of serum 25(OH)D is a reliable method for evaluating vitamin D reserves in patients. The different ranges vary considerably between populations and are dependent on many geographical, racial and cultural variables.[7] Vitamin D deficiency has been observed in nations, such as the United Kingdom, the United States, Australia, Brazil and China, to state a few.[1,7,8]

There is a lack of studies on the understanding of the association of vitamin D deficiency with patient population has been noted[9,10] and there is a dearth of empirical representation of vitamin D levels in Pakistan. The current study was planned to examine the frequency and trend of vitamin D levels in all patients tested over five years at our hospital, and to study its relation with age, gender and certain biochemical markers among our patient population.

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Materials and Methods

The retrospective study was conducted at The Indus Hospital, Karachi, and comprised clinical laboratory data of individuals tested for vitamin D from January 2013 to March 2018 after exemption from ethical approval was obtained from institutional review board. Data was obtained through the hospital management information system (HMIS) database.

The tests had been performed using cobas e411 (Roche Diagnostics) analyser that utilises electro-chemiluminescence immunoassay technique to detect Vitamin D levels. Data regarding parameters such as calcium (Ca), alkaline phosphatise (ALP), phosphorus (P), magnesium (Mg) and PTH was retrieved to study correlation. Ca, P, ALP and Mg were measured spectrophotometrically on Cobas c311 (Roche Diagnostics), while PTH was analysed on cobas e411 (Roche Diagnostics).[11] The trend and pattern of Vitamin D levels over the study period were determined. Vitamin D levels were categorized in line with Mayo Clinic's reference range[12]. Severe deficiency was defined as <10ng/ml in circulation, while 10-25ng/ml was considered mild to moderately deficiency, 25(OH)D level 25-80 ng/ml was considered normal and levels >80 were toxic.[12]

Data were entered into Microsoft (MS) Excel and was analysed using Stata software. Normality of all quantitative variables was assessed using Kolmogrov-Smirnov and D'Aogstino test. Mann-Whitney U-test and Median test were applied to assess significant differences in quantitative variables between the genders. Kandll tau-b correlation was applied to assess significant association between various quantitative variables. Chi-square test was applied to assess significant association between gender and vitamin D and to assess trend over the years. Gamma test was applied to check any possible correlation of vitamin D levels with the years. P<0.05 was considered statistically significant.

Results

Of the 35,017 tests analysed, 23,522(67.2%) were related to females and 11,495(32.8%) to males (p<0.05). Age had significant correlation with vitamin D deficiency (p<0.05). Median age of the patients tested was 38.3 (interquartile range [IQR]: (20.2-51.6) years; the youngest was aged 47

Table-1: Comparison of study participants' characteristics between the genders.

Variables	Gender	Mean ± SD	Median (IQR)	Min - Max	*p*-value
Age (years)	Female	38.0 ± 18.5	39.6 (25.1-51.0)	0.13-105.62	0.000**
	Male	33.7 ± 23.5	33.2 (10.3-53.6)	0.24-103.6	
	Overall	36.6 ± 20.4	38.3 (20.2 – 51.6)	0.13-105.62	
Alkaline Phosphate (U/L)	Female	178.04 ± 251.5	127.5 (89-194)	8-4198	0.0037*
	Male	198.7 ± 201.5	145 (93-221)	23-2369	
	Overall	188.4 ± 228	135 (91–211)	8-4198	
Calcium (mg/dl)	Female	9.5 ± 0.78	9.6 (9.2-10)	4-16.6	0.3652
	Male	9.5 ± 0.84	9.6 (9.2-10.1)	3.7-16.8	
	Overall	9.5 ± 0.8	9.6 (9.2-10)	3.7-16.8	
Magnesium (mg/dl)	Female	2.1 ± 0.33	2.1 (1.9-2.3)	0.71-3.1	0.0454*
	Male	2.2 ± 0.3	2.2(2-2.3)	1.2-3.1	
	Overall	2.1 ± 0.3	2.1 (2.0-2.3)	0.7-3.12	
Parathyroid Hormone (pg/ml)	Female	170.3 ± 250	93.6 (46.3-193.2)	6.2-3198	0.1783
	Male	149 ± 228.7	80.9 (45.3-172.2)	1.8-3243	
	Overall	159 ± 239.2	86.4 (45.7-184)	1.8-3243	
Phosphorus (mg/dl)	Female	4.5 ± 1.3	4.5 (3.7-5.2)	1.2-10	0.1918
	Male	4.7 ± 1.4	4.6 (3.7-5.3)	0.97-11.3	
	Overall	4.6 ± 1.4	4.5 (3.7-5.3)	1.0-11.3	
Vitamin D (ng/ml)	Female	20.6 ± 34.5	14.2 (7.9-26.2)	3-140	0.000**
	Male	23.3 ± 21.8	18.5 (11.8-28.2)	3-140	
	Overall	21.36 ± 21.38	15.8 (9-27.1)	3-140	

**p*-value<0.05, ***p*-value<0.0001, Mann-Whitney U test; SD: Standard deviation; IQR: Interquartile range

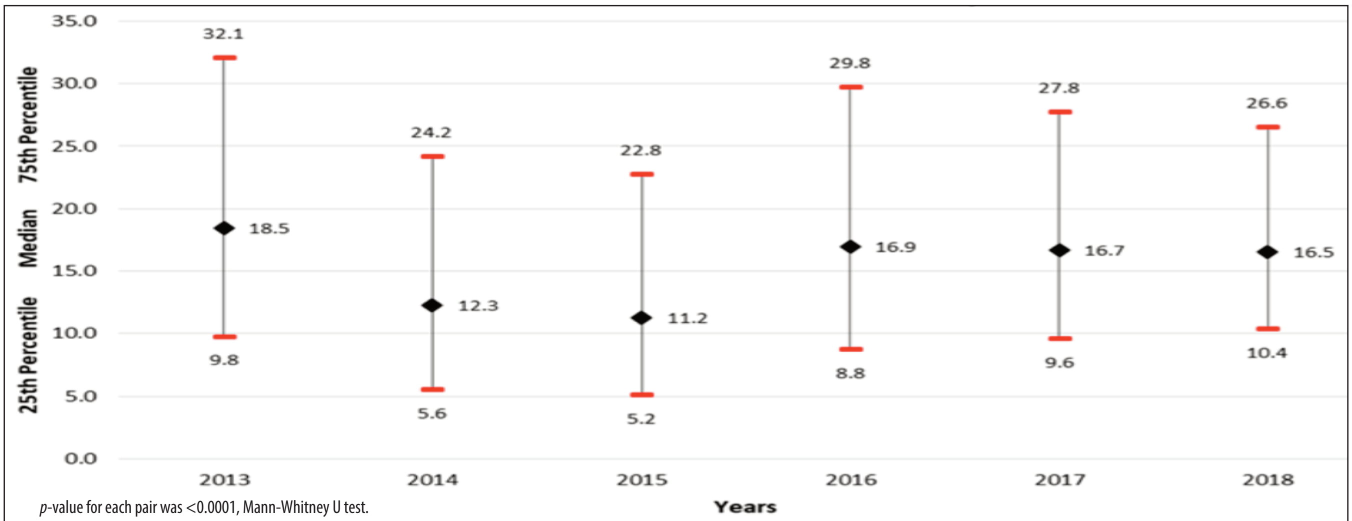

Figure: Trend of vitamin D levels over six years with the median and interquartile values with an upward trend following the year 2015.

Table-2: Association of Vitamin D levels with gender and age groups n (%).

	Vitamin D Status				Total	*p*-value†
	Severe deficiency	Mild to moderate	Normal	Toxicity		
Gender						
Female	8119 (34.5)	9096 (38.7)	5989 (25.5)	318 (1.4)	23522 (100)	0.000**
Male	2116 (18.4)	5720 (49.8)	3473 (30.2)	186 (1.6)	11495 (100)	
Total	10235 (29.2)	14816 (42.3)	9462 (27)	504 (1.4)	35017 (100)	
Age groups (years)						
<5	447 (15.7)	1034 (36.3)	1254 (44)	116 (4.1)	2851 (100)	0.000**
5 to <15	942 (23.6)	1992 (50)	992 (24.9)	61 (1.5)	3987 (100)	
15-24 (youth)	1693 (45.6)	1413 (38.1)	561 (15.1)	42 (1.1)	3709 (100)	
25-35 (young adults)	2045 (36.1)	2407 (42.5)	1167 (20.6)	41 (0.7)	5660 (100)	
36-55 (middle-aged)	3493 (28.1)	5394 (43.4)	3416 (27.5)	135 (1.1)	12438 (100)	
>55 (older people)	1615 (25.3)	2576 (40.4)	2072 (32.5)	109 (1.7)	6372 (100)	
Total	10235 (29.2)	14816 (42.3)	9462 (27)	504 (1.4)	35017 (100)	
Year of registration						
2013	17 (25.8)	22 (33.3)	27 (40.9)	0 (0)	66 (100)	0.000**
2014	1019 (41.8)	833 (34.2)	550 (22.6)	34 (1.4)	2436 (100)	
2015	1917 (46)	1345 (32.3)	880 (21.1)	28 (0.7)	4170 (100)	
2016	1655 (29.3)	2159 (38.2)	1835 (32.5)	2 (0)	5651 (100)	
2017	2960 (26.5)	4823 (43.1)	3200 (28.6)	196 (1.8)	11179 (100)	
2018	2667 (23.2)	5634 (48.9)	2970 (25.8)	244 (2.1)	11515 (100)	
Total	10235 (29.2)	14816 (42.3)	9462 (27)	504 (1.4)	35017 (100)	

***p*-value<0.0001,† Pearson chi-square test.

days and the oldest 105.27 years. Women were older than men (p<0.0001). Overall, 25,051(71.5%) patients were vitamin D-deficient; 10,235(29.3%) severely deficient, 14,816(42.3%) mild to moderate, and 504(1.44%) had toxic levels. Vitamin D toxicity was observed more in those aged <5 years (p<0.0001). Also, women had significantly lower median values than men (p=0.001). ALP values were significantly higher in men, while PTH values were higher than normal in both genders (Table 1).Moreover, women were found to have 2.2 (95%CI: 2.1-2.4) times higher odds ratio of having severe vitamin D deficiency as compared with the men (34.5% vs 18.4% Table 2)

There was increasing vitamin D deficiency seen till 2015, after which there was an upward trend (Figure). In 2015, the median values were the lowest and subsequently showed a consistently higher trend over the next three years, while, toxicity rose sequentially in 2014, 2017 and 2018 (Table 2).

Table-3: Correlation among various variables.

	Age (years)	Alkaline Phosphate	Calcium	Magnesium	Parathyroid Hormone	Phosphate
Age (Year)	1					
Alkaline Phosphate	-0.2 (0.707)	1				
Calcium	-0.33 (0.452)	0.6 (0.133)	1			
Magnesium	0.33 (0.452)	0.47 (0.26)	0.07 (1.00)	1		
Parathyroid Hormone	-0.2 (0.707)	- 0.33 (0.452)	-0.2 (0.707)	-0.33 (0.452)	1	
Phosphate	-0.47 (0.26)	0.73 (0.06) ¤	0.87 (0.024)*	0.2 (0.707)	-0.07 (1.00)	1
Vitamin D	0.73 (0.06)¤	0.07 (1.00)	-0.07 (1.00)	0.6 (0.133)	-0.47 (0.26)	-0.2 (0.707)

Correlation coefficient (*p*-value) * p-value <0.05, ¤*p*-value <0.1 (showing trend), Kandall tau-b correlation test.

No significant correlation was observed between Vitamin D levels and other biochemical parameters studied (p>0.05).

Discussion

Vitamin D deficiency is a global health issue. The median level of 25(OH)D in the current study was 15.8 (IQR: 9-27.1) ng/ml. Other studies conducted in Pakistan have reported similar low references.[13,14] However, to our knowledge, the current is the first to have a large sample (35,017) of patients spread over five years. Our results are consistent with literature, as people from Asian countries are reported to have very low vitamin D levels.[2,15,16] Risk groups are predominantly young children, pregnant women, older individuals, institutionalised people, and non-Western immigrants.[3] Risk factors for vitamin D deficiency include low sun exposure, skin pigmentation, sunscreen coverage, choice of attire and a diet low in fish and dairy products.[2]

25(OH)D levels for both men and women were below normal in our population and 71.5% were either moderately or severely deficient. However, women had a significantly lower vitamin D status than men, as reported earlier,[15] especially by studies done in Brazil,[1] India,[17] China[8] and Wales[18] where a high degree of vitamin D deficiency was seen among the populations, with a lower 25(OH)D status in females. An examination according to region exhibited that females tended to have lower 25(OH)D values, especially in the Middle East, Africa and Asia/Pacific regions.[19] Some have suggested that this finding may be related to cultural factors, such as differences in clothing styles and mobility that may impede vitamin D conversion in the skin.[15] It is surprising to see vitamin D deficiency in a country with abundant sunlight. However, individuals with increased melanin pigmentation require prolonged exposure to sunlight to synthesise vitamin D as well.[3] Some studies have indicated that males have lower fat percentage than females with the same body mass index (BMI), thus showing that less vitamin D is stored in fat and more stays in the blood after cutaneous synthesis, explaining higher vitamin D levels than females.[8,20] However, the existence of vitamin D deficiency in many sun-exposed areas, such as South America, where clothing does not impediment vitamin D activity, is still becoming a major public health problem.[9]

Higher than expected reference levels of PTH was found in the current study. Individuals with low vitamin D levels are known to have higher values of PTH and vice versa.[1] A high level of PTH indicates vitamin D inadequacy even if its blood levels are apparently normal. Use of this biological parameter for the definition of vitamin D adequacy, rather than the absence of rickets/osteomalacia, has been proposed already.[5,7,21] Vitamin D deficiency leads to secondary hyperparathyroidism which results in increased urinary loss and decreased intestinal absorption of phosphorus. Insufficient calcium phosphorus product affects the bone mineralisation process, thus causing rickets in children and osteomalacia in adults.[5]

Our study showed a high rate of vitamin D deficiency. Consistent with literature, this could be due to sedentary lifestyle and lack of daily mobility.[5] Surprisingly, 45.6% of youth and 36.1% of young adults were severely deficient. The routine of a nascent career and the demands of starting a family, associated with individuals in this age group, would not only impact personal nutrition, but also restrict time for outdoor recreational activities, subsequently limiting sun exposure.[19] While vitamin D can be obtained from dietary sources, it is primarily synthesised in the skin as an outcome of UV light exposure.[17] Hence, less exposure to sunlight could result in their low serum 25(OH)D levels.[1] Our study population predominantly belonged to a single socio-economic background that may not be able to consume the adequate recommended vitamin D supplements as well.

In the current study, 2015 showed decreased vitamin D levels which then rose over the next three years to yield higher median values, although the difference was not statistically significant. Increasing awareness of the prevalence of Vitamin D deficiency and possible supplementation could be a potential cause of the gradual rise. Another study conducted in Norway examined trends in 25(OH)D over time, in which 2668 subjects were studied in 1994 and again in 2008. Their 25(OH)D levels were coherent with our results but showed miniscule yet significant increase from 21.5±6.5 ng/ml to 22.1±7.3 ng/ml.[22]

The current study has some limitations. Due to its retrospective nature, it could only observe associations but not establish causal relationships between variables and did not have details on patient illnesses, history and treatment. Also, it was a single-centre study and its findings are not generalizable. More studies with comparisons between institutions and hospitals are necessary to give a relevant representation of the regions affected.

Conclusion

Women were largely at more risk of vitamin D deficiency then men and were found to be more vitamin D-deficient.

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