RESEARCH ARTICLE

Vitamin D status of patients visiting a private endocrinology clinic: a retrospective analysis from Karachi, Pakistan

Tasnim Ahsan[1], Saima Ghaus[2], Erum Sohail[3], Wasfa Aijaz[4], Uzma Erum[5], Samar Abbas Jaffri[6]

Abstract

Objective: To estimate the burden of vitamin D deficiency and its association with chronic diseases in patients visiting a private endocrinology clinic in an urban setting.

Method: The retrospective study was conducted at the Medicell Institute of Diabetes Endocrinology & Metabolism, Karachi, and comprised medical records of adult patients of either gender between January 2000 and December 2019.Vitamin D status of the patients and its association with various chronic disorders were investigated. Data was analysed using SPSS 21.

Results: Of the 2,854 patients with mean age 40.87±15.1 years, 2,302(80.7%) were females, and 552(19.3%) were males. There were 1055(37%) patients with vitamin D deficiency, 1,040(36.7%) with severe deficiency, 462(16.2%) with insufficiency, 295(10.3%) with normal status, and 2(0.1%) with vitamin D toxicity. Vitamin D deficiency was observed more frequently in those aged<40 years, and the deficiency was significantly related to type 2 diabetes, impaired glucose tolerance, dyslipidaemia and autoimmune disorders (p<0.05).

Conclusion: The burden of vitamin Deficiency was found to be alarmingly high at a private endocrine and medicine clinic serving a middle and upper socioeconomic class population in an urban setting.

Key Words: Vitamin D deficiency, Metabolic disorder, Diabetes mellitus, Hypertension.

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Introduction

Vitamin D receptors have been identified in almost all tissues of the body, thereby suggesting its role in various physiological functions. Vitamin D deficiency (VDD) has been related to various systemic diseases, such as rickets, musculoskeletal problems, reduced immunity for pneumonia and other respiratory infections, asthma and coronavirus disease-2019 (COVID-19), leading to increased mortality.[1-3] Globally increasing prevalence of VDD is an important public health concern in developing as well as developed countries.[1,4] Commonly identified causes of VDD include insufficient sun exposure, increasing age, workplace environment, outdoor activities, skin pigmentation, genetic factors or ethnicity, and inadequate intake of vitamin D.[5] A systematic review has identified the excess burden of VDD in one or more population subgroup(s) of many low- and middle-income countries (LMICs), including Afghanistan, Pakistan, India, Tunisia and Mongolia.[6] Southeast Asia is also a geographical area from where a high occurrence of VDD has been reported.[7,8]

A high burden of VDD is evident in the National Nutrition Survey-2018 (NNS-2018), with 79.7% of all reproductive-age women having VDD, and severe deficiency being recorded in 25.7% (vitamin D <8.0ng/ml). The prevalence of VDD was higher in urban versus rural populations, indicating the potential role of differences in lifestyle.[9]There is still limited evidence regarding the role of chronic diseases and VDD among urban adults in the Pakistani city of Karachi, which is a densely populated metropolitan centre with a diverse population, making it an ideal location to study VDD occurrence in a cosmopolitan setting.

The current study was planned to estimate the burden of VDD and its association with chronic diseases in patients visiting a private endocrinology clinic in an urban setting.

Materials and Methods

The retrospective study was conducted at the Medicell Institute of Diabetes Endocrinology & Metabolism (MIDEM), Karachi, and comprised medical records of adult patients of either gender between January 2000 and December 2019. MIDEM is a private healthcare facility providing specialised outpatient care services for the upper and middle socioeconomic class for all kinds of endocrine, metabolic and internal medicine disorders.

[1,]Medicell Institute of Diabetes, Endocrinology and Metabolism (MIDEM), OMI Hospital, [2-6]Medicell Institute of Diabetes, Endocrinology and Metabolism (MIDEM), Karachi, Pakistan.

Correspondence: Erum Sohail. **Email:** erum_nathani@yahoo.com

ORCID ID: 0000-0003-3100-236X

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Data was retrieved from the institutional health information management system (HMIS). Indications for investigating serum vitamin D levels included comprehensive health assessment, pregnancy/lactation, backache, generalised body aches, arthralgias, unexplained fatigue/lethargy, unexplained proximal myopathy, recurrent infections, chronic diarrhoea, senility/frailty, autoimmune diseases and previous history of VDD or malnutrition.

Vitamin D levels had been estimated using the chemiluminescence method before and after supplementation. Serum 25-hydroxyvitaminD (25[OH]D) concentration of <10ng/ml defined severe VDD, <20ng/ml VDD, <30ng/ml insufficiency, >30ng/ml normal, and >150ng/ml constituted vitamin D toxicity.[10]

Data about health-related characteristics, and demographic data, such as age, gender, body mass index (BMI), marital status, parity and history of lactation, as well as a history/diagnosis of chronic diseases, including hypertension (HTN), type 2 diabetes mellitus (T2DM), impaired glucose tolerance (IGT), dyslipidaemia, thyroid disorder, metabolic syndrome (MetS) and autoimmune diseases, was collected using a structured format. Being a secondary analysis, exemption from the institutional ethics review board obtained.

Being a retrospective study, exemption from the institutional ethics review board obtained. All the available charts that had vitamin D level recorded were included, while the rest were excluded.

Data was analysed using SPSS 21. Descriptive statistics were calculated for demographic and health-related characteristics. Continuous variables were presented as means ± standard deviations, while categorical variables were expressed as frequencies and percentages. Chi-square and Fisher exact tests were applied, as appropriate, to assess differences in demographic and health-related characteristics among patients with different levels of vitamin D. Paired-sample T test was used to compare vitamin D levels before and after supplementation. Binary logistic regression was applied to assess the association between VDD and different non-communicable diseases P< 0.05 was considered statistically significant.

Results

Of the 2,854 patients with mean age 40.87±15.1 years, 2,302(80.7%) were females, and 552(19.3%) were males. The mean BMI was 26.08±12.09kg/m^2 (Table 1).

There were 1055(37%) patients with VDD, 1,040(36.7%) with severe VDD, 462(16.2%) with insufficiency, 295(10.3%) with normal status, and 2(0.1%) with vitamin D toxicity. VDD was more common among males, but severe VDD was found more in females (Figure).

Table-1: Baseline characteristics (n=2854).

Variables	Mean±SD
Age (years)	40.87±15.14
BMI (kg/m2)	28.54±6.69
Ca (mg/dL)	8.61±3.03
PO4(mg/dL)	2.68±1.67
Alk.PO4(U/L)	77.96±165.26
PTH (pg/mL)	41.13±136.99
Cr (mg/dL)	0.71±0.41
HbA1c (%)	6.41±3.41
Hb (g/dL)	12.88±46.30
FBS (mg/dL)	102.70±56.97
Age Group (n=2809)	
<20 years	211(7.4)
21-40 years	1250(43.8)
41-60 years	1050(36.8)
>60 years	298(10.4)
Gender	
Male	552(19.3)
Female	2302(80.7)
BMI Classification (n=290)	
<18.5 kg/m^2	20(0.7)
18.5-22.9 kg/m^2	41(1.4)
23-24.9 kg/m^2	31(1.1)
≥25 kg/m^2	198(6.9)
Co-morbid conditions	
Hypertension	661(23.2)
Obesity	291(10.2)
Lipid Dysfunction	547(19.2)
Diabetes Mellitus	550(19.3)
IGT	67(2.3)
Thyroid Disorder	614(21.5)
Autoimmune Disorder	228(8.0)
Metabolic Syndrome	136(4.8)

BMI: Body mass index, Ca: Calcium, PO4: Phosphate, Alk.PO4: Alkaline phosphatase, PTH: Parathyroid hormone, Cr: Creatinine, HbA1cGlycated haemoglobin, Hb: Haemoglobin, FBS: Fasting blood sugar, IGT: Impaired glucose tolerance, SD: Standard deviation.

VDD was found to be significantly associated with T2DM, IGT, dyslipidaemia and autoimmune disorders (Table 2).

Regression analysis Indicated that for every one-unit increase in age, the odds of having sufficient Vitamin D levels decreased by 2.7% (dds ratio [OR]: 0.973;p=0.009), indicating a significant negative association. Each unit increase in BMI increased the odds of sufficient vitamin D levels by 2.8% (OR: 1.028;p=0.010), showing a significant positive association. T2DM was associated with higher odds of sufficient vitamin D levels (OR: 1.266; p=0.388). A one-unit increase in calcium levels was marginally associated with higher odds of sufficient vitamin D levels

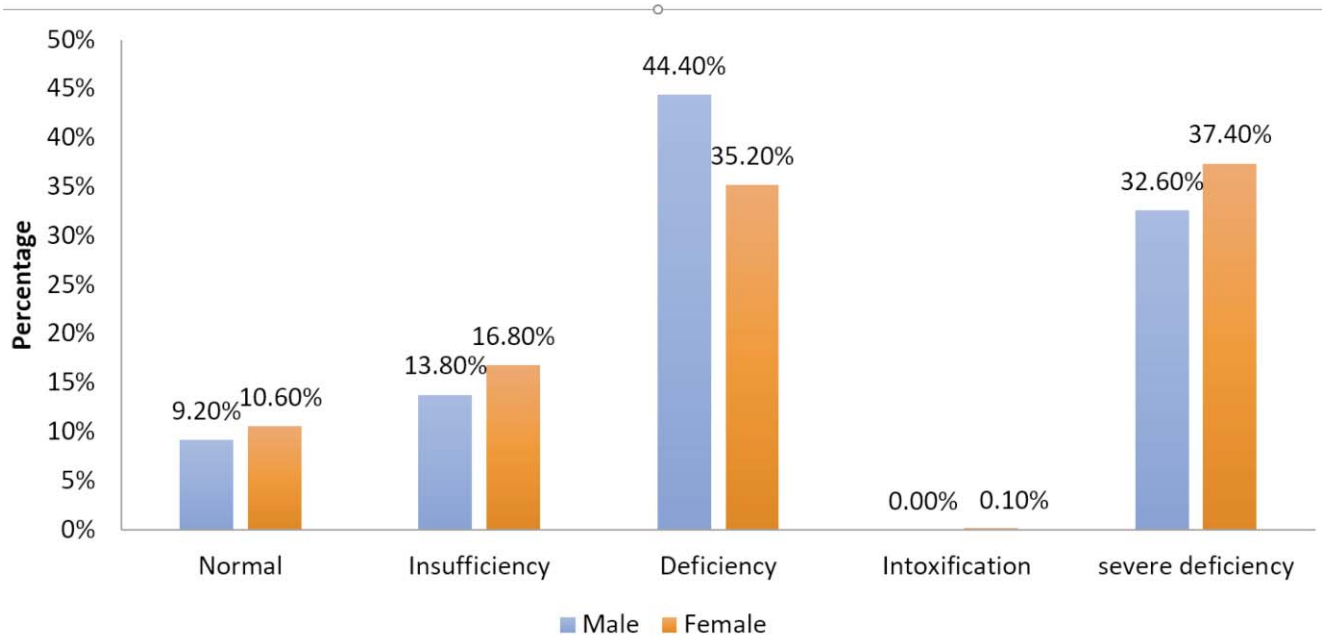

Figure: Stratification of vitamin D deficiency (VDD with respect to gender.

(OR: 1.066;p=0.064) (Table 3).

Post-supplementation data was available for 370(13%) patients. The mean Vitamin D level before supplementation was 14.6±10.8, which improved to 32.52±18.2 after supplementation with 2000-5000 IU/day (p<0.001).

Discussion

Comparatively higher prevalence of VDD has been reported among South Asian populations, identifying it as a public health problem of significance, particularly in countries with relatively limited resources.[7] A recently published meta-analysis of studies from South Asian countries estimated a pooled VDD prevalence of 68% (95% CI: 64-72%), with statistically significant differences among various countries of the region. Pakistan was identified as a South Asian country with the highest burden of VDD (73%; 95%CI: 63-83%), followed by Bangladesh, India, Nepal and Sri Lanka. In addition, a significantly higher prevalence of VDD was reported in females compared to males living in South Asia (76% versus 51%).[8] The current study reported a very high burden of VDD (89.6%) among patients presenting at a private endocrine clinic in Karachi. This high prevalence of VDD was comparable to previous estimates in recently published national as well as local studies, specifically representing the urban population of Sindh, with a prevalence of 79.7%,[9] 84.2%[11]and 78.3%.[12]The slight differences in these estimates, including the current study, can be attributed to the differences in study settings and target population.

Surprisingly, both the prevalence and severity of VDD in the elderly were less than in the younger cohort, with a statistically significant association between VDD and age <40 years (OR:3.9;95%CI: 1.5-9.8). This is contrary to the general observation of more VDD in the elderly population.[13,14] This may be attributed to better elderly care in multigenerational family homes, in keeping with the cultural norms in Pakistan. This finding is in line with previous studies in the Pakistani and other Asian populations reporting a relatively higher burden of VDD in the younger population of age up to 40 years.[14-16] However, in the current study, males were marginally more affected, and had more deficiency compared to women (Figure 1). This is unexpected as many of the factors associated with VDD are specific to women, like purdah, multiple pregnancies, lactation, and relatively less time spent outdoors. This positive association of the male gender with VDD in the current study is contrary to prior local and international evidence identifying a causal association between VDD and female gender except one study.[14-17] The positive association of VDD with the male gender in the current study can be explained by the possible role of concurrent diagnosis of a metabolic disorder, higher prevalence of smoking among male patients, and lifestyle-related risk factors.[13,16] In addition, the comparison of study estimates for the association of

Table-2: Association of patient baseline demographic and clinical characteristics with vitamin D status.

Variables	Vitamin D Status					
	Normal	Insufficiency	Deficiency	Toxicity	Severe Deficiency	p-value
Demographic characteristics						
Age Group						
<20	8(2.7)	17(3.7)	79(7.6)	-	107(10.5)	<0.01*
21-40	99(33.8)	171(37.5)	447(43.1)	1(50.0)	532(52.1)	
41-60	144(49.1)	190(41.7)	395(38.1)	1(50.0)	320(31.3)	
>60	42(14.3)	78(17.1)	116(11.2)	-	62(6.1)	
BMI						
<18.5	4(8.7)	2(3.3)	7(7.4)	-	7(7.9)	0.164
18.5-22.9	2(4.3)	7(11.7)	14(14.7)	-	18(20.2)	
23-24.9	8(17.4)	8(13.3)	11(11.6)	-	4(4.5)	
>=25	32(69.6)	43(71.7)	63(66.3)	-	60(67.4)	
Comorbid conditions						
Hypertension						
Yes	62(21.0)	116(25.1)	268(25.4)	1(50.0)	214(20.6)	0.075
No	202(68.5)	295(63.9)	652(61.8)	1(50.0)	714(68.7)	
Not known	31(10.5)	51(11.0)	135(12.8)	-	112(10.8)	
Obesity						
Yes	41(13.9)	58(12.6)	90(8.5)	-	102(9.8)	0.109
No	223(75.6)	353(76.4)	830(78.7)	2(100.0)	826(79.4)	
Not known	31(10.5)	51(11.0)	135(12.8)	-	112(10.8)	
Lipid Dysfunction						
Yes	78(26.4)	102(22.1)	214(20.3)	-	153(14.7)	<0.01*
No	60(20.3)	65(14.1)	153(14.5)	-	156(15.0)	
Not Done	157(53.2)	295(63.9)	688(65.2)	2(100.0)	731(70.3)	
Diabetes Mellitus						
Yes	55(18.6)	115(24.9)	211(20.0)	-	169(16.3)	0.008*
No	209(70.8)	296(64.1)	709(67.2)	2(100.0)	759(73.0)	
Not known	31(10.5)	51(11.0)	135(12.8)	-	112(10.8)	
IGT						
Yes	15(5.1)	8(1.7)	27(2.6)	-	17(1.6)	0.043*
No	249(84.4)	403(87.2)	893(84.6)	2(100.0)	911(87.6)	
Not known	31(10.5)	51(11.0)	135(12.8)	-	112(10.8)	
Thyroid Disorder						
Yes	73(24.7)	99(21.4)	216(20.5)	1(50.0)	225(21.6)	0.361
No	127(43.1)	181(39.2)	411(39.0)	-	411(39.5)	
Not known	95(32.2)	182(39.4)	428(40.6)	1(50.0)	404(38.8)	
Autoimmune Disorder						
Yes	40(13.6)	55(11.9)	74(7.0)	-	59(5.7)	<0.01*
No	224(75.9)	356(77.1)	846(80.2)	2(100.0)	869(83.6)	
Not known	31(10.5)	51(11.0)	135(12.8)	-	112(10.8)	
Metabolic Syndrome						
Yes	10(3.4)	18(3.9)	56(5.3)	-	52(5.0)	0.628
No	254(86.1)	393(85.1)	864(81.9)	2(100.0)	876(84.2)	
Not known	31(10.5)	51(11.0)	135(12.8)	-	112(10.8)	
Clinical parameters						
HBA1c						
<5.7	45(30.4)	71(30.3)	116(25.6)	-	110(29.7)	0.178
5.7-6.4	55(37.2)	65(27.8)	154(34.0)	1(100.0)	104(28.1)	

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male gender with VDD revealed that most of the local and international research has majorly focused on VDD among women, resulting in limited evidence about men. Hence, further research is required to assess the association of male gender with VDD while taking into account all the relevant confounders, including education, socioeconomic class, dietary habits, smoking, sun exposure, and usage of vitamin D supplements.

In a meta-analysis comprising 21 studies, individuals with obesity demonstrated a 35% higher VDD prevalence compared to those with normal body weight, regardless of age group (95%CI: 1.21-1.50).[18] The current study also revealed a notable connection between VDD and BMI. Various theories have been posited to elucidate the correlation between excess body fat and vitamin D levels. One hypothesis suggests that vitamin D, either produced through the skin or obtained from the diet, is partly stored in body fat before being transported to the liver for initial hydroxylation.[19] Moreover, obese individuals exhibit a significant presence of the vitamin D activation enzyme 1-alpha-hydroxylase in their adipose cells, potentially accounting for the heightened local utilisation of 25(OH)D. According to this proposition, alterations in

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6.5-7	13(8.8)	30(12.8)	37(8.2)	-	38(10.3)	
7.1-9	24(16.2)	45(19.2)	79 (17.4)	-	62(16.8)	
>9	11(7.4)	23(9.8)	67(14.8)	-	56(15.1)	
Ca						
<8.6	59(26.6)	63(18.4)	133(16.9)	-	137(18.0)	0.003*
8.6-10.5	155(69.8)	276(80.5)	639(81.1)	-	615(80.9)	
>10.5	8(3.6)	4(1.2)	16(2.0)	-	8(1.1)	
PO4						
<2.5	69(56.1)	65(35.9)	91(22.1)	-	83(24.1)	0.01*
2.5-4.5	50(40.7)	105(58.0)	297(72.1)	-	239(69.5)	
>4.5	4(3.3)	11(6.1)	24(5.8)	-	22(6.4)	
PTH						
<16	70(87.5)	62(80.5)	81(68.1)	-	67(54.5)	0.01*
16-87	9(11.3)	8(10.4)	25(21.0)	-	30(24.4)	
>87	1(1.3)	7(9.1)	13(10.9)	-	26 (21.1)	

BMI: Body mass index, Ca: Calcium,PO4: Phosphate,Alk.PO4: Alkaline phosphatase, PTH: Parathyroid hormone, Cr: Creatinine,HbA1c: Glycated haemoglobin, IGT: Impaired glucose tolerance.

Table-3: Regression analysis of vitamin D status with study variables.

Variables	B	S.E.	p-value	Exp(B)	95% C.I.	
					Lower	Upper
Demographic characteristics						
Age	-.028	.011	.009	.973	.953	.993
Gender(male)	.396	.405	.328	1.486	.672	3.290
BMI	.028	.011	.010	1.028	1.007	1.050
Comorbid conditions						
Hypertension (Yes)	.194	.275	.480	1.214	.709	2.079
Obesity (Yes)	.104	.273	.705	1.109	.649	1.895
Lipid Dysfunction (Yes)	.071	.243	.769	1.074	.667	1.729
Diabetes Mellitus (Yes)	.236	.273	.388	1.266	.741	2.162
IGT (Yes)	-.386	.441	.382	.680	.286	1.614
Thyroid Disorder (Yes)	-.171	.257	.505	.843	.509	1.395
Autoimmune Disorder (Yes)	.283	.512	.580	1.328	.487	3.621
Clinical parameters						
Ca	.064	.035	.064	1.066	.996	1.141
PO4	.019	.243	.939	1.019	.633	1.640
Alk.PO4	.002	.006	.757	1.002	.990	1.014
PTH	.014	.013	.283	1.014	.989	1.040
Cr	.314	.385	.415	1.368	.644	2.909

BMI: Body mass index, Ca: Calcium, PO4: Phosphate, Alk.PO4: Alkaline phosphatase, PTH: Parathyroid hormone, Cr: Creatinine, HbA1c: Glycated haemoglobin, IGT: Impaired glucose tolerance.

serum 25(OH)D and vitamin D reserves may directly correlate with the quantity of subcutaneous body fat.[20] Studies indicate that regardless of the cutaneous vitamin D precursor present, obese individuals experience a 53% lower increase in serum 25(OH)D levels compared to their normal-weight counterparts following exposure to sunlight.[19]

In keeping with the previously recorded association,[21,22]the current study also found a statistically meaningful correlation of T2DM and IGT with VDD. Moreover, the study found a significant association between vitamin D levels with dyslipidaemia. Several studies have investigated the relationship between vitamin D levels and serum lipids, and most have found that low levels of vitamin D were related to deranged lipid profiles.[23,24] Large-scale studies are required to determine the role of VDD in the development as well as prognosis of chronic non-communicable diseases.

The current study uncovered a noteworthy correlation between vitamin D levels and autoimmune diseases, an association extensively explored given the recognition of vitamin D as a natural immune modulator and regulator of various immune-mediated processes.[25] A comprehensive literature review, encompassing 130 studies, revealed a consistent inverse relationship between vitamin D levels and the onset of numerous autoimmune conditions, including systemic lupus erythematosus (SLE), thyrotoxicosis, type 1 diabetes mellitus (T1DM), multiple sclerosis (MS), iridocyclitis, Crohn's disease, ulcerative colitis, psoriasis vulgaris, seropositive rheumatoid arthritis (RA) and polymyalgia rheumatic disease.[26]

The current study has its strengths as it provides valuable insight regarding the burden and distribution of VDD among patients suffering from various metabolic and endocrine disorders in Karachi. The study used standard cut-off values for diagnosing and stratifying VDD, which makes it easier to compare study findings with other reported studies.

Nevertheless, the study has a few inherent limitations as it was a retrospective analysis of medical records of the patients attending a private facility offering specialist endocrine services. The findings, as such, may not accurately reflect the characteristics of the broader population or the community at large. Moreover, the study is not representative of VDD patient not seeking healthcare services for any reason. Due to the limited sample size, multivariable analysis was conducted on dichotomous outcome variables; vitamin D level either normal or deficient. In addition, the data available through medical records was deficient in the information

regarding many important potential confounders, which could have affected VDD, such as ethnicity, level of physical activity, total time spent outdoors, use of sunblock, and occupations. Hence, large-scale community-based studies are required to determine the association between VDD and chronic or non-communicable diseases prevalent in urban and rural populations of Pakistan.

Conclusion

The burden of VDD was found to be alarmingly high among those who presented at a private endocrine and medicine clinic serving a middle and upper socioeconomic class population. In a relatively young cohort, VDD was significantly associated with age <40 years. VDD was found significantly associated with increasing BMI, T2DM, IGT, dyslipidaemia, and autoimmune disorders.

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Authors' Contribution:

TA: Concept, design, revision, final approval and agreement to be accountable for all aspects of the work.

SG: Concept, design, data analysis, drafting, final approval and agreement to be accountable for all aspects of the work.

ES: Concept, design, data analysis, interpretation, drafting, final approval and agreement to be accountable for all aspects of the work.

WA, UE, SAJ: Data analysis, drafting, final approval and agreement to be accountable for all aspects of the work.