Vitamin D Level in Healthy Bangladeshi Adults- A Pilot Study

Anil Yadav[1*], Shahjada Selim[2], Tahniyah Haq[2], Anil Kumar Shah[3], Md. Shahed-Morshed[4], Md. Habibul Ghani[5], Ibrahim Faisal[6], Murshed Ahamed khan[2], Marufa Mustari[2], Mostafa Hasan Rajib[2], Md. Firoj Hossain[7], M A Hasanat[2], Md. Fariduddin[2]

Abstract

Background: *Vitamin D level has profound clinical implications but there is dilemma of optimal vitamin D cut-off level among Bangladeshi population as well in many parts of the world. This study aimed to determine the sufficient level of vitamin D [25 hydroxyvitamin D, 25(OH)D] in relation to intact parathormone (iPTH) in apparently healthy adult volunteers.*

Materials and Methods: *This cross-sectional study was carried out among 130 apparently healthy adult participants [age (years): 37.57±12.23, mean±SD; m/f: 67/63] in Bangabandhu Sheikh Mujib Medical University, Dhaka. Demographic profile, sunlight exposure and dietary history were taken, physical examinations were done and fasting blood was taken to measure 25(OH)D, iPTH, calcium, albumin and phosphate. Serum 25(OH)D was measured by high performance liquid chromatography whereas iPTH, serum calcium, albumin and phosphate were measured by chemiluminescent method.*

Results: *The mean serum 25(OH)D of apparently healthy Bangladeshi adults was 15.44 – 18.44 ng/ml. Vitamin D level was significantly affected by age group [p=0.002], sunlight exposure time [p=0.013] and body surface area [p=0.023] along with sunscreen use [p=0.026]. Serum 25(OH)D had negative predictive association with iPTH [β=-0.220, p=0.012] and positive predictive association with daily sunlight exposure time [β=0.235, p=0.007]. Serum 25(OH)D level above 30 ng/ml was sufficient to keep maximum suppression of iPTH at 54.56 pg/ml by using the quadratic model.*

Conclusion: *The optimal level of 25(OH)D for apparently healthy adults in Bangladesh is above 30.0 ng/ml.*

Key words: *healthy adults, intact parathormone; vitamin D, 25(OH)D*

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Introduction

Vitamin D deficiency is currently recognized as a worldwide epidemic and its potential health implications are currently the subject of significant interest and controversy.[1] The major circulating form of vitamin D is 25- hydroxyvitamin D {25(OH)D}. It is widely considered as the best indicator of vitamin D status because of its stability, better co-relation with clinical features, and accurate reflection of body storage.[2] However, there is no absolute consensus as to what a normal range for 25(OH) D should be. Many studies used inverse relationship between serum 25(OH) D and intact parathormone (iPTH) levels to determine normal serum 25(OH)D levels. With the maximum efficiency of intestinal calcium absorption and adequate bone mineral density, iPTH concentrations began to plateau at their nadir.[3,4] Different guidelines have set different cut-off of optimal vitamin D status such as the Endocrine Society and many experts recommend ≥30 ng/ml and Institute of Medicine recommend ≥20 ng/ml.[3,5,6] Bangladeshi patients are being treated by the guidelines applicable for other population, which may or may not be appropriate for our population. This study is aimed to determine the sufficient level of serum 25(OH)D in healthy Bangladeshi adults by analyzing the dynamic relationship between 25(OH)D and iPTH.

Materials and Methods

This observational cross-sectional study was conducted in the Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. The study was conducted from January 2018 to July 2019. The ethical approval was taken from the Institutional Review Board of

1. Department of Medicine (Endocrinology Division), Birat Medical College Teaching Hospital, Biratnagar, Nepal
2. Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, 3Department of Medicine (Endocrine Division), Chitwan Medical College, Chitwan, Nepal. 4Department of Emergency, Kurmitola general hospital, Dhaka, Bangladesh
5. Department of Internal Medicine, Jinjira 20 Beded Hospital, Dhaka Bangladesh
6. Department of Endocrinology, Indira Gandhi Memorial Hospital, Kanbaa Aisa Rani Higun, Male, Republic of Maldives,
7. Department of Endocrinology Mugda Medical College, Dhaka, Bangladesh

***Corresponding author:** Dr. Anil Yadav; Department of Medicine (Endocrinology Division), Birat Medical College Teaching Hospital, Biratnagar, Nepal. Email: cool.dewup@gmail.com, Cell# +977-9812395912.

BSMMU (No. BSMMU/2018/6572). Informed written consent was taken from the participants.

The sample size was calculated by using the following formula,

Total sample size, $N=\left[\frac{(Z_\alpha)+Z_\beta}{C}\right]^2+3$; whereas, $C=0.5\times 1\text{ n}\left[\frac{(1+r)}{(1-r)}\right]$

Alpha (a) is the probability of rejecting a true null hypothesis. The standard normal deviate for a, Za = 1.96. Beta (b) is the probability of accepting a false null hypothesis. The standard normal deviate for b, Z_b = 0.85. r is the sample correlation (relationship between vitamin D and iPTH), r= -0.25.[7] Applying r value in the above equation, C = 0.2534. Conferring to the total sample size formula, the minimum required sample size was 125.

Adult attendants of patients of BSMMU were requested to participate in the study. Initially, 144 apparently healthy adults were consecutively recruited by purposive sampling to screen with clinical features and biochemical tests [serum alanine amino transferase (ALT) and creatinine]. Participants who were taking or had received vitamin D or calcium supplements within last 120 days of sample collection, or took medications that might affect calcium, vitamin D metabolism, and bone, or who had any known diseases (chronic heart failure, renal failure, cancer, etc.) along with pregnant or lactating mothers were excluded from study. Prior to enrollment, it was established that all of the participants had normal liver (serum ALT £40 U/L) and kidney function (eGFR ³60 ml/minute/1.73 m^2 body surface area). After exclusion, a total of 130 apparently healthy adults were enrolled in the study (Figure 1).

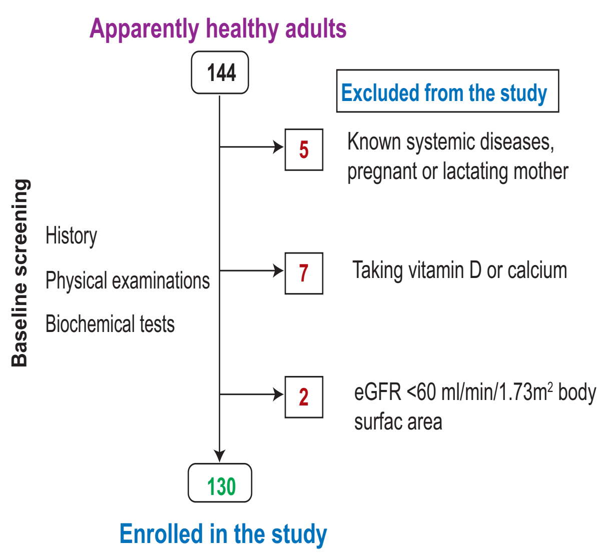

Figure 1. *Flow chart of study participants' selection*

Demographic profile along with sunlight exposure and dietary history were taken. Sunlight exposure of more than one hour between 11 am to 2 pm at least three days a week with exposure of at least 18% body surface area without use of sunscreen (sun protecting factor ³8) was considered as adequate.[8] Food frequency questionnaire was used to collect dietary history.[9] Height, weight, waist circumference (WC) and blood pressure were measured by standard procedures. Body mass index (BMI= weight in kg ÷ height in meter^2) ³25 kg/m^2, WC ³90 cm for male and ³80 cm for female and blood pressure ³140/90 mm-Hg were considered as general obesity, central obesity and hypertension respectively.[10,11] About 10 ml of venous blood was drawn from each participant in the fasting state. Serum was separated by centrifugation and stored in -20^0 C until assay. Assay of the collected samples were done for 25(OH)D by high performance liquid chromatography method (HPLC) in SIL 20 series prominence HPLC analyzer with a coefficient of variability 2.6 – 4.9%. Serum iPTH, calcium, albumin along with phosphate were analyzed by chemiluminescent enzyme-labeled immunometric assay with Immulite 2000 systems Siemens, USA analyzer. Corrected calcium was calculated from fasting calcium and albumin by using correction formula {corrected calcium (mg/dl) = measured calcium (mg/dl) + 0.8 × (4 – measured albumin in gm/ dl)}.

All data were processed by the SPSS program (version 22.0). Data were expressed in frequencies or percentages for qualitative values and mean (±SD) or median (interquartile range) for quantitative values. To compare the mean value of subgroups, independent-samples T test, one way ANOVA were used as appropriate. Spearman's correlation test was used to correlate between vitamin D, iPTH and other variables. The association between 25(OH)D and iPTH concentrations was studied both by linear and non-linear regression models. A quadratic model with plateau was fitted to see the relationship between serum iPTH and serum 25(OH)D levels to objectively identify the 25(OH)D level where the iPTH reaches a plateau. P values <0.05 were considered as statistically significant.

Results

Table 1 is showing serum vitamin D level with different characteristics of the study population [age (years): 37.57±12.23; BMI (kg/m^2): 23.87±3.01, mean±SD]. Patients with age e"60 years had significantly higher vitamin D level than other age groups [post hoc Tukey test: vs. 20 – 39 years: p=0.013; vs. 40 – 59 years: p=0.001]. Vitamin D levels among categories of other different characteristics were statistically similar [p=NS for all].

Table 1. *The characteristics of the study population (N= 130)*

Variables	Categories	Number (%)	25(OH)D (ng/ml) mean±SD	p value
Age group	20 – 39 years	88 (67.7)	16.82±7.86	0.002
	40 – 59 years	31 (23.8)	14.00±8.29	
	≥60 years	11 (8.5)	24.31±9.83	
Sex	Male	67 (51.5)	16.27±8.20	0.482
	Female	63 (48.5)	17.32±8.78	
Residence	Urban	97 (74.6)	16.33±8.44	0.307
	Rural	33 (25.4)	18.08±8.55	
Occupation	House wife	31 (23.8)	16.85±8.80	0.064
	Service holder	38 (29.2)	18.72±8.17	
	Student	34 (26.2)	13.63±7.90	
	Others	27 (20.7)	17.92±8.51	
Educational status	Primary	38 (29.2)	19.43±8.15	0.068
	Higher secondary	47 (36.2)	15.43±8.22	
	Graduate and above	45 (34.6)	15.96±8.68	
Socio-economic status	Lower	53 (40.8)	16.91±8.46	0.966
	Middle	62 (47.7)	16.59±8.55	
	Higher	15 (11.5)	17.13±8.77	
Physical activity level	Low	17 (13.1)	18.55±10.95	0.136
	Moderate	83 (63.8)	15.66±8.04	
	High	30 (23.1)	18.86±8.47	
Smoking status	Smoker	40 (30.8)	15.89±5.87	0.267
	Nonsmoker	90 (69.2)	17.41±8.55	
Blood pressure	Hypertensive	22 (16.9)	19.69±6.65	0.079
	Normotensive	108 (83.1)	16.38±8.81	
BMI category(kg/m^2)	Underweight (<18.5)	3 (2.3)	14.21±3.33	0.644
	Normal (18.5 – 22.9)	54 (41.5)	16.40±9.32	
	Overweight (23 – 24.9)	31 (23.8)	18.40±7.68	
	Obese (≥25)	42 (32.3)	16.25±8.17	
WC category	Centrally obese	74 (56.9)	16.29±7.71	0.445
	Nonobese	56 (43.1)	17.44±9.42	

Within parentheses are percentages over column total
Independent-Samples T test/ One-way ANOVA was done

Patients with inadequate sunlight exposure time [15.64±8.55 vs. 19.76±7.61, p=0.013], exposure of inadequate body surface area to sunlight [15.98±8.80 vs. 20.32±5.80, p=0.023] and use of sunscreen [9.28±5.93 vs. 17.14±8.43, p=0.026] had significantly lower vitamin D level (ng/ml) than adequate sunlight exposure time, body surface area and without history of use of sunscreen respectively. Considering all the three factors, participants with adequate sunlight exposure had significantly higher vitamin D (ng/ml) than inadequate sunlight exposure [20.32±5.80 vs. 15.98±8.80, p=0.005]. Vitamin D levels had no significant associations with consumption of different amount of milk, egg and large fish [p=NS for all] (Table II).

Table II. *Dietary and sunlight exposure history in the study population (N= 130)*

Variables	Category	No. (%)	Vitamin D (ng/ml) mean±SD	p
Number of cups of milk consumption/ week	None	48 (36.9)	17.83 ±7.89	0.100
	1 to 3	74 (56.9)	15.47±8.45	
	4 to 6	7 (5.4)	22.43±10.56	
	7 and above	1 (0.8)	23.35	
Number of egg consumption/ week	None	12 (9.2)	19.21±8.37	0.378
	1 to 3	24 (18.5)	15.00±6.95	
	4 to 6	34 (26.2)	18.11±8.66	
	7 to 10	60 (46.2)	16.25±8.90	
Number of pieces of large fish consumption/ week	None	20 (15.4)	17.85±8.04	0.749
	1 to 5	7 (5.4)	15.23±6.20	
	6 to 10	64 (49.2)	17.03±8.68	
	11 to 15	6 (4.6)	19.40±6.65	
	15 and above	33 (25.4)	15.48±9.16	
Sunlight exposure time	Adequate	36 (27.7)	19.76±7.61	**0.013**
	Inadequate	94 (72.3)	15.64±8.55	
Sunlight exposure of body surface	Adequate	24 (18.5)	20.32±5.80	**0.023**
	Inadequate	106 (81.5)	15.98±8.80	
Sunscreen use	Yes	6 (4.6)	9.28±5.93	**0.026**
	No	124 (95.4)	17.14±8.43	
Overall sunlight exposure	Adequate	24 (18.5)	20.32±5.80	**0.005**
	Inadequate	106 (81.5)	15.98±8.80	

Within parentheses are percentages over column total
Independent-Samples T test/ One-way ANOVA was done

The descriptive statistics of serum 25(OH)D are shown in Figure 2. The mean vitamin D in Bangladeshi healthy adults was (mean±2×standard error of mean) 16.94±1.50 ng/ml. Most of the participants had vitamin D level of only 2.00 ng/ml. The median (interquartile range) corrected serum calcium was 9.20 (8.70, 9.50) mg/dl, inorganic phosphate was 3.70 (3.40, 4.00) mg/dl and intact parathormone was 60.25 (41.80, 78.08) pg/ml. Vitamin D was significantly and positively correlated with daily sunlight exposure time in minutes [r=0.254, p=0.004] and negatively correlated with iPTH [r=-0.259, p=0.003] but was not significantly correlated with corrected calcium and phosphate and other variables [p=NS for all]. On linear regression analysis, one ng/ml increase of vitamin D was associated with 0.22 pg/ml reduction of iPTH [p=0.012]. Similarly daily one minute increase of sunlight exposure between 11 am to 2 pm was associated with 0.235 ng/ml increase of serum vitamin D [p=0.007].

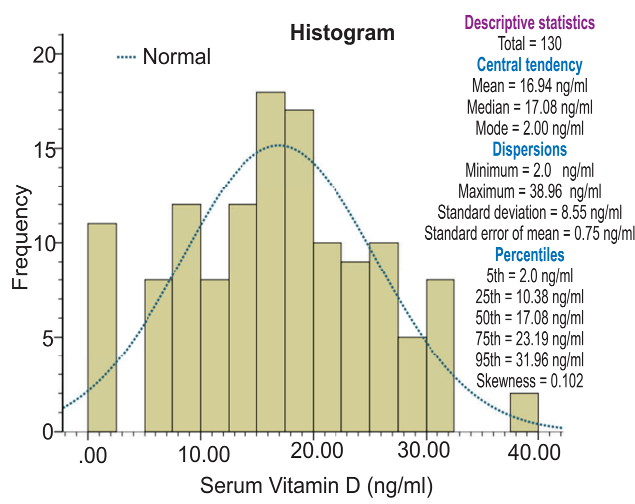

Table 2. *Distribution of serum 25(OH)D with its descriptive statistics*

The quadratic correlationship between vitamin D and iPTH is shown in Figure 3. At vitamin D level from 30.1 ng/ml to 31.2 ng/ml, iPTH level reaches its plateau at 54.56 pg/ml. Considering 30.1 ng/ml, 10 (7.7%) participants had sufficient vitamin D level which was 44 (33.8%) with IOM criteria (cut-off of 20 ng/ml).

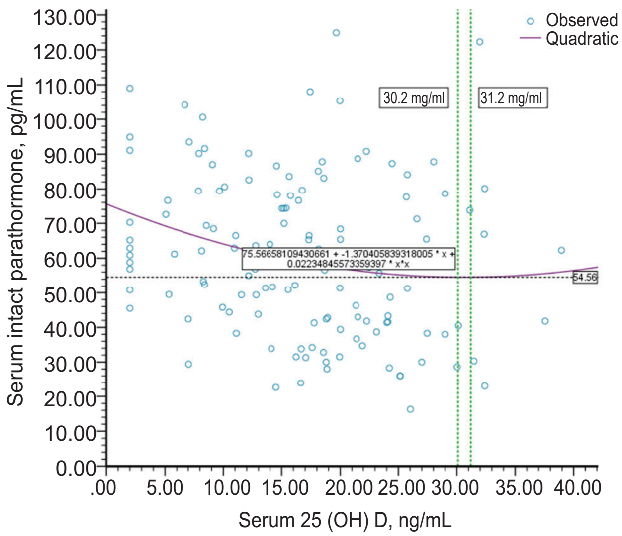

Figure 3. *Quadratic relationship of serum 25(OH)D with iPTH in the study population*

Discussion

This study found that the mean serum 25(OH)D of apparently healthy Bangladeshi adults was 15.44 – 18.44 ng/ml. Vitamin D level was significantly affected by age group, sunlight exposure time and body surface area along with sunscreen use. Serum 25(OH)D level had negative predictive association with iPTH and positive predictive association with daily sunlight exposure time. Vitamin D level above 30 ng/ml was sufficient to keep maximum suppression of iPTH at 54.56 pg/ml.

The mean vitamin D level of Bangladeshi healthy adults was in the deficiency group according to Endocrine Society's criteria (<20 ng/ml), 2011 and insufficient according to Institute of Medicine criteria, 2011. A systematic review consisting of 40 studies conducted among 19,761 apparently healthy Indians found a population mean of vitamin D of 14.16±0.89 (13.27 – 15.05) ng/ml. The level is lower than our study result.[12] This may be due to use of predominantly older methods (radioimmunoassay, chemiluminescent immuno-assay, enzyme-linked immunosorbent assay etc.) in most studies rather than HPLC method. Only 7.7% of the study population had vitamin D sufficiency with vitamin D level >30 ng/ml in our study. A previous study conducted among 189 Bangladeshi adults attending out-patient department (without mentioning disease status) found 12.2% of participants with vitamin D sufficiency (30 – 100 ng/ml).[13] So, vitamin D insufficiency is very common among Bangladeshi adults.

Vitamin D status also allies to age. A study in Canada found that vitamin D status among the 60"79 age group was higher comparing the 20 – 30 age group. In our study, also the result showed that mean serum 25(OH)D concentrations in age 60 and above was higher than 20 – 39 and 40 – 59 age group. However, this study revealed 40 – 59 age group had the lowest 25(OH)D level.[14] A tenable explanation could be that most of them were working in the indoor setting. As a result, they spent less time outside, hence less sunlight exposure.

Exposure to the sunlight is essential to obtain adequate vitamin D, as it is mainly produced in skin by exposure to UVB radiation from the sunlight.[1] The timing and proper skin exposures are also important for vitamin D photosynthesis.[15] In this study, only 18.5 % gave history of proper sunlight exposure whereas 81.5% study population had inadequate sun exposure as most of them spent a major part of daytime in office building as service holder and housewife 29.2% and 23.8% respectively. The people with overall adequate sunlight exposure had significantly higher vitamin D level than those without adequate sunlight exposure. We presume and agree with the authors who indicated that low intensity of the sun in the morning, shaded sun shines, shadows of tall buildings and trees, upright position of the subjects, high pollution in the air, covered-up-dressing style as well as the dark skin necessitate the need for prolonged exposure for adequate synthesis of vitamin D in the skin.[16] We also found a positive association between sunlight exposure times with serum vitamin D level. This finding is consistent with a study conducted in India.[8]

In this study, the intake of selected vitamin D containing food did not show significant correlation with Vitamin D. Similarly, few studies suggested that about 10% of vitamin D is derived from dietary sources indicating dietary intake of vitamin D is a relatively poor predictor of overall vitamin D status.[17,18] Insignificant affiliation between dietary vitamin D intake and serum level of 25(OH)D has been shown in studies performed in Europe.[19,20,21] Fortification of food with vitamin D is limited in Bangladesh.[22]

We found an inverse association between vitamin D and iPTH. Other studies also found similar finding.[23,24] Based on the relationship between serum 25(OH)D and iPTH concentration, this study found that the plateau for the iPTH concentration by quadratic model was reached at 54.56 pg/ml. However, due to heterogeneous and small population the plateau level was not consistent. We observed that 25(OH)D concentrations higher than 30.0 ng/ml were required to keep iPTH at its lowest concentration. A previous study conducted among adult female garment workers from Bangladesh found only vitamin D level of 15.2 ng/ml was required to keep iPTH suppressed with a plateau at 21.4 pg/ml.[7] The iPTH level depends on several factors including age and body composition. Our study population was relatively older with higher BMI than that of the study population. Besides, the study population and method of vitamin D estimation was different.[25] The optimal level of 25(OH)D (30.1 ng/ml) of the participant was almost similar to the Endocrine Society (≥30 ng/ml) based on elevated iPTH that was consistently lowered to a plateau when serum 25(OH)D was at 30 ng/ml or higher.[5] However, the IOM defined optimal level of 25(OH)D (≥20 ng/ml) based on human requirement of vitamin D for the general population in context of its relevance to bone accretion, bone maintenance and bone loss.[6] Substantial studies found that 25(OH)D concentrations from 12 – 50 ng/ml (30 – 125 nmol/L) were required to maintain a normal iPTH level.[26,27] In the Israeli population, serum 25(OH)D levels <20 ng/ml were associated with a steep increase in iPTH levels, which lessen with increasing 25(OH)D levels and reached a plateau at 25(OH)D levels of 30 to 34 ng/ml. It was appraised that iPTH began to increase when serum 25(OH)D level was < 31.56 ng/ml. This point corresponded to a serum iPTH level of 62.5 pg/ml in all cases tested.[23] In French population, iPTH levels began to plateau at their nadir when 25(OH)D levels were between 30 and 40 ng/ml.[28] Healthy individuals in Australia and Riga, serum 25(OH)D of 38 ng/ml was sufficient to avoid rise in iPTH.[24,29]Among young Lebanese people iPTH reached a plateau was maximally suppressed when 25(OH)D was 10 ng/ml or less.[30] However, in few studies no plateau or no relationship was found between serum 25(OH)D and serum iPTH.[25]

Estimation of vitamin D by HPLC method is the main strength and small sample size is the main limitation of our study. We were also unable to correlate vitamin D level with bone mineral density (BMD), biochemical bone markers and maximal efficiency of intestinal calcium absorption.

Conclusion

The optimal level of serum 25(OH)D for apparently healthy Bangladeshi adults is above 30 ng/ml. Large scale study encompassing people from different regions of our country and measuring serum vitamin D round the year, may yield more robust level of serum vitamin D. Simultaneous measurement of BMD, biochemical markers (osteocalcin, N-telopeptides etc.) and calcium absorption will further help us to precise the optimal level of vitamin D in general population of Bangladesh.

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Conflict of interest

None of the authors has any conflict of interests to declare.

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