Prevalence and Predictors of Vitamin D Insufficiency in Adolescents Living at an Intermediate Altitude

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ABSTRACT

Although vitamin D insufficiency is very common health problem in the world, its prevalence and predictors in adolescents are controversial. We planned to evaluate prevalenve and predictors of vitamin D insufficiency in adolescents living at an intermediate altitude. We also want to give optimal serum 25(OH) vitamin D levels in relation to serum PTH levels.

This study was conducted at 343 primary and high school children aged between 13-17 years living in Erzurum city center. These children were selected using stratified random sampling in the spring (April-May), and were invited to our department for participation in this research study. Of 343 children, 246 could be evaluated again in the autumn (September-October). Subjects with vit D level < 10 ng/ml were considered as vitamin D deficiency, and with 10 - 20 ng/ml as vitamin D insufficiency. If vitamin D level is > 20 ng/ml, it's considered as adequate. In spring, vitamin D deficiency was detected in 17.7 % and vitamin D insufficiency was detected in 72 % of subjects. At the end of summer these rates were 1.6 % and 41.1 % respectively. Serum 25(OH)vitamin D levels at which plasma PTH concentrations begin to form a plateau is 22 ng/mL. Values below estimated lower normal level (22 ng/mL) were detected in 94.2 % of subjects.

Key words: adolescent rickets, altitude, parathyroid hormone, risk factors, prevalence

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We believe that vitamin D prophylaxis could be given to all adolescents as well as regulation of lifestyle. Our results will increase awareness for vitamin D deficiency and insufficiency in adolescents and inform future public health preventative strategies.

INTRODUCTION

Vitamin D, a fat-soluble vitamin is essential for normal calcium metabolism. Vitamin D deficiency has been linked to osteoporosis, hypertension, cardiovascular diseases, multiple sclerosis, diabetes mellitus, infectious diseases, autoimmune diseases and several cancers (1). The vitamin D status is usually evaluated by measuring the level of 25(OH) vitamin D in serum.

Although vitamin D insufficiency is very common health problem in the world, its prevalence and predictors in adolescents are controversial. This discrepency is associated with the absence of consensus on the optimal concentrations of serum 25(OH) vitamin D. The major sources of vitamin D in humans are sun exposure to ultraviolet B radiation, and small amounts (<10%) obtained from diet and supplementation (2). The annual fluence of UVB is very effective in the low latitude and high altitude areas. There is less filtration of UVB by the atmosphere as compared with sea level. Our region (Erzurum, Turkey) is located 39 degrees north of the aquator (borderline latitude) and 1900 m above sea level (intermediate altitude). Sun exposure and clothing habits and geographic properties (differences in fluence rates of UVB from place to place) are likely major determinants on vitamin D status. We planned to evaluate prevalenve and predictors of vitamin D insufficiency in adolescents living at an intermediate altitude. We also recommend optimal serum 25(OH) vitamin D levels in relation to serum PTH levels. So, these will form the basis for recommendations for preventing vitamin D insufficiency in Turkey.

MATERİALS AND METHODS

Informed consent was obtained from parents. This study was approved by the Ethics Committee of the Faculty of Medicine, Atatürk University.

Study site and participants

This study was conducted at 397 primary and high school children aged between 13-17 years living in Erzurum city center. These children were selected using stratified random sampling in the spring (April-May), and were invited to our department for research. Of 397 children, 369 (92,9 %) accepted to participate in the study. During evaluation 23 children were excluded from the study. Of 343 children, 246 could be evaluated during follow-up visit in the autumn (September-October). Subjects were excluded from the study if they had used any relevant medications during the last six months (calcium, vitamin D and drugs known to affect calcium and vitamin D metabolism (anticonvulsant, heparin, corticosteroid etc)) or the last 1 year (antiresorptive or anabolic) prior to the study. Other exclusion criteria were the presence of diseases that affected calcium and vitamin D metabolism such as metabolic diseases (diabetes mellitus, hypo-hyperthyroidism), renal and gastrointestinal disorders. Children with recent fracture, illness that required bed rest or inhibited outdoor play were excluded. All children included in the study were not given any vitamin D supplement during the duration of study and they were healthy. The participants were white.

Demography and sampling

Firstly, questionnaire was administered to the child and physical examination was performed. After that a fasting venous blood sample withdrawn for biochemical analysis at the first visit in the spring. Physical examination and biochemical evaluation were repeated again in the autumn.

On questionnaire child’s age, parent’s education, income, clothing habits, and whether multivitamin use were documented. Dietary, physical activity and outdoor stay time records were evaluated using questionnaire. The nutritionist helped to evaluate the mean calcium intake daily (mg/day) according to the seven-day dietary recall data because low dietary caicium intakes might play a role in the pathogenesis of rickets in this age group. The information for physical activity (min/day) and outdoor stay time (min/day) was also assessed from a seven-day diary data.

Weight and height measurements, and Tanner staging were performed using the same equipment and by the same observer. All of them were in Tanner stage IV and V. Subjects were naked when weight. BMI (body mass index) was calculated as [kg/m^2].

Overnight fasting blood samples were taken from all subjects for determinations of serum 25(OH) vitamin D and plasma intact PTH levels. Serum 25(OH) vitamin D levels were measure by chemiluminescent assay (Roche Diagnostic GmbH Mainheim/Germany). Serum intact PTH levels were determined by 2-step chemiluminescent assay (Beckman Coulter Access Intact PTH (iPTH), Galway, Ireland).

Although there is no consensus regarding the different ranges of sufficiency and insufficiency levels of 25(OH) vitamin D in the serum, in the present study we defined vitamin D deficiency as level of 25(OH) vitamin D below 10ng/mL and vitamin D insufficiency was defined as levels below 20 ng/mL (1,2).

Statistical analysis was conducted with the SPSS/PC program, version 15.0 statistics were calculated for each variable. Categorical data were summarized with percentages and frequencies. Continous data were presented as means $\pm$ SD. Variables were evaluated by student *t* test, Mann-Whitney U test, Chi-square and Kruskal Wallis, Fisher test and Spearman test. Two-tailed tests were used throughout. A p value of <0.05 was considered significant.

RESULTS

The mean age of all children was 15.44 + 1.28 years (13-17 years). Of all children, 198 (57.7 %) were male, 145 (42.3 %) were female in the spring. Frequency and mean values of vitamin D deficiency and sufficiency according to sex and season were given in Table 1 and Table 2, respectively. Serum 25(OH) vitamin D level in females was normal in just 2 cases (1.4 %) in spring. Of males, 16.7 % were normal. Frequencies of vitamin D deficiency and sufficiency were quite high for both sexes in spring after winter. In males, both mean serum 25(OH) vitamin D levels and frequency of normal vitamin D levels were significantly higher in fall than those in spring ($p < 0.05$) (Table 1). Although no child took oral vitamin D, after summer, mean serum 25(OH)vitamin D levels significantly increased while frequency of insufficienciencies or deficiencies decreased in fall.

Sociodemographic properties of children according to vitamin D status at the admission were shown in Table 2. Income, parent’s education level, number of family members, use vitamin D in the first year of life did not significantly affect frequency vitamin D deficiency and insuffiency.

Height, weight, BMI measurements of adolescents did not correlate with serum vitamin D levels. Mean oral calcium intake, outdoor stay time and physical activity time of adolescents were given in Table 3. Mean oral Ca intakes of groups were similar ($p>0.05$). Mean outdoor time and physical activity times were lower in females than males in both spring and autumn.

When clothing habit of females was evaluated, mean vitamin D levels were not different between groups (Table 4). Frequency of normal vitamin D level increased to 46.7 % in adolescents who did not wear islamic style after summer. On the other hand, it was just 19.2 % in adolescents wearing islamic style.

Complaints of adolescents regarding muscle pain or bone or joint pain were given in Table 5. Muscle pain in vitamin D deficient and sufficient adolescents was significantly frequent complaint compared to controls ($p<0.05$). There was an inverse linear correlation between serum 25(OH) vitamin D and PTH levels in both spring and autumn ($p<0.05$) (Figure 1). Serum 25(OH)vitamin D levels at which plasma PTH concentrations begin to form a plateau is 22 ng/mL (Figure 2). Values below estimated lower normal level (22 ng/mL) were detected in 94.2 % of subjects.

DİSCUSSİON

Vitamin D insufficiency in adolescents results from insufficiently sun exposure and receiving inadequate vitamin D and increased requirements secondary to rapid growing in pubertal period (3,4). To our knowledge, our study is the most extensive epidermiological study to report the prevalence of vitamin D insufficiency in adolescents.

Absoud et al (5) found that 35.1 % of children aged 4-18 in Great Britain were vitamin D insufficient (vitamin D levels: < 20ng/ml) and there was no significant gender difference. ln sunny environment of Israil (latitude 30-33° N) mean serum vitamin D levels were 22.9 + 10.1 ng/ml and percentage of insufficient vitamin D was 78 % (6). Liang et al (7) also found that 28.3 % had vitamin D levels in infants in San Diego (latitude 38 degrees) . Szalay et al (8) also demonstrated that 14% of children living in a sunny climate had vitamin D levels < 20 ng/mL. According to these studies a sunny climate does not assure vitamin D sufficiency. There were different frequencies in literature, so vitamin D levels relate to many factors. In our country, in different city, Van, 25(OH)D3 levels was normal in 47.6 % of adolescents (9). Frequency of adolescent rickets was higher in females and 25(OH)D3 levels were lower in the covered girls (9). Our high prevalence can be related to clothing habits and lifestyle such as less exposure to sunlight due to shorter outdoor stay time and physical activity. Nowadays, the time that children play outside is diminishing. A study in Minnesota reported that 40% of children regularly watch television by age 3 months, and that found 90% by age 2 (10). Children from 2 to 17 years of age spend almost 6 hours per day with electronic media (11). Another study also reported that <18% children aged 9 to 15 years walk to school even 1 day per week (12). Children who spent more time doing outdoor exercise (at least an hour/day/week) and less time waching TV per day (<2.5 hours) also higher vitamin D levels (5). Both from the literature and from our study, it is apparent that the major effect on vitamin D levels seems to come from vitamin D supplementation and outdoor lifestyle and physical activity. This modern lifestyle may result in lower vitamin D levels that threaten bone health for a lifetime.

Classically, vitamin D insufficiency is associated with high latitude and high altitude. Latitude is attributed to reduced ultraviolet radiation exposure in areas far from the equator (1). However, several studies like our study showed that this problem is not limited to sun-deprivated regions of the world. So, other risk factors causing vitamin D insufficiency must be demonstrated quite well for maintenance of optimal health. At higher altitudes, a thinner atmosphere filters less UV radiation. With every 1000 metres increase in altitude, UV levels increase by 10 to %12 % (13). Recently, Holick et al (14) reported the effects of altitude on previtamin D3 synthesis. Norsang et al (15) found that the average vitamin D status was similar although the annual dose of vitamin D-generating UVB is about five times larger in Lhasa (in Tibet, lalitude: 29°, altitude: 3670 m) than in Oslo. In Guatemalan, at 2333 m above sea level, 46.3 % had values below 20 ng/ml (16). These and our results suggested that altitude is probably not major factor, as people exposure only face and hands, and they don’t stay enough time outdoor.

Different studies showed that vitamin D levels declined and insufficiency rates rose as the age increased (5,6). We did not find correlation between age and vitamin D levels. It might be related to the narrow age range in our study.

The 25(OH)vitamin D level has not been standardized. There was no consensus what cutoff criteria define deficient, low, or adequate/optimal 25(OH) vitamin D level. Vitamin D insufficiency is defined by most experts as a serum 25(OH)vitamin D level < 20 ng/ml (1,2,6,14,17). It is suggested that optimal range of 25(OH)vitamin D for skeletal health is level that reduces PTH levels to a minimum (18). Vitamin D deficiency is accepted to contribute to bone loss by stimulating PTH secretion. In 2009, Bacon et al (19) found that vitamin D supplementation was only able to suppress parathyroid hormone levels in older individuals with baseline vitamin D levels less than 20 ng/m. Data in adults demonstrates evidence of impaired calcium absorption and lower bone density at levels < 32 ng/mL (20). Optimal level of 25(OH) vitamin D have been based on estimates of the level of 25(OH) vitamin D required to minimize PTH levels. Increased PTH levels are usually seen with 25(OH)vitamin D levels < 40ng/mL (14). Singhellakis et al (21) researched the lower normal levels of 25(OH)vitamin D by using a vitamin D loading test in a normal adults, and found that basal serum 25(OH)vitamin D levels >22 ng/mL should be considered as a vitamin D sufficient. In that study it was reported 57.7 % of adults had vitamin D insufficient (< 22 ng/mL) (21). In another study, Bacon et al (19) reported that PTH and P1NP (procollagen type 1 amino-terminal propeptide) were only suppressed by vitamin D treatment in those with baseline 25(OH)vitamin D levels <50 and <30 nmol/L, respectively. It should be underlined that low levels of 25(OH)vitamin D (<22 ng/mL) were observed in most of the all studied children (94.2 %) in our study. The minimum value for vitamin D insufficiency definition is quite close, namely 20 vs 22 ng/mL in our study. However, 5.8 % or 10.3 % of adolescents had normal vitamin D levels if lower normal serum 25(OH)vitamin D level was accepted as

20 ng/mL or 22 ng/mL, respectively. So, we recommend that cutt-of value for serum 25(OH)vitamin D must be 22 ng/mL according to these results. Further corroboration of these results is needed.

Although Saliba et al (22) found the threshold 46.2 nmol/L (≈18.6 ng/mL), Thomas et al (23) suggested 15 ng/mL to define vitamin D sufficiency for PTH stabilization.

In the literature, musculoskeletal pain has been reported (24). The distinction vitamin D sufficient adolescents is not easy because most vitamin D deficient children have no symptom and signs.

This study's results confirm the high prevalence of vitamin D deficiency and insufficiency among adolescents living at the intermediate altitude and sunny city. Our findings also showed that females had an increasing risk of vitamin D insufficiency. The percentage of abnormally low serum 25(OH)vitamin D levels in our group is unexpectedly high for a region with a temperate climate and at a relatively low northern lalitude (39°N).

This study also suggests that a sunny climate and high altitude does not quarantee adequate vitamin D levels. Vitamin D supplemantation should be routine during adolecence. We believe that vitamin D prophylaxis could be given to all adolescents as well as regulation of lifestyle. Our results will increase awareness for vitamin D deficiency and insufficiency in adolescents and inform future public health preventative strategies one more time.

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Table 1. Frequency and mean of serum vitamin D levels in vitamin D deficiency and sufficiency according to sex and season

		Spring									**Autumn**									
	Sex	**Deficiency**		**Sufficiency**		**Normal**		**Total**		**p**	**Deficiency**		**Sufficiency**		**Normal**		**Total**		**p**
		n	**%**	**n**	**%**	**n**	**%**	**n**	**%**		**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	
Frequency	Female	53	36.5	90	62.1	2	1.4	145	42.3	**<0.05**	4	4.2	70	73.6	21	22.2	95	38.6	**<0.05**
	Male	8	4.0	157	79.3	33	16.7	198	57.7	**<0.05**	0	-	31	20.5	120	79.5	151	61.4	**<0.05**
	Total	61	17.7	247	72.0	35	10.3	343	100	**<0.05**	4	1.6	101	41.0	141	57.4	246	100	**<0.05**
Vitamin D level	Female	8.4±1.2		13.1±2.3		23.8±3.2		11.6±3.3		**<0.05**	8.7±0.9		14.8±2.6		23.4±2.7		16.1±4.5		**<0.05**
	Male	8.7±1.7		15.8±2.8		23.3±2.7		16.7±4.2		**<0.05**	-		17.1±2.3		25.1±3.6		23.3±4.8		**<0.05**
	Total	8.5±1.2		14.8±2.9		23.3±2.9		14.5±4.6		**<0.05**	8.7±0.9		15.5±2.7		24.9±3.6		20.5±5.8		**<0.05**

Kruskal Wallis test

Table 2. Sociodemographic properties of children according to vitamin D status at the admission

	Deficiency		Sufficiency		Normal		
Property	**n:61**	**%**	**n:247**	**%**	**n:35**	**%**	**p**
Age (year)	15.8±1.2		15.3±1.3		15.6±1.4		**0.06**
Sex							
Female	53	36.5	90	62.1	2	1.4	
Male	8	4.0	157	79.3	33	16.7	**0.00**
Father's education							
Illiterate	1	9.1	9	81.8	1	9.1	
Primary school	57	20.3	194	69.0	30	10.7	0.83
High school	3	5.9	44	86.3	4	7.8	
Mother's education							
Illiterate	13	20.3	44	68.7	7	10.9	
Primary school	47	8.2	497	87.1	27	4.7	0.13
High school	1	12.5	6	75.0	1	12.5	
Mother's job							
Housewife	61	18.3	238	71.5	34	10.2	
Business women	0	0	9	90.0	1	10.0	0.91
No of family member							
3-4	10	17.8	40	71.4	6	10.7	
5-6	33	16.3	148	73.3	21	10.4	0.58
7 and up	18	21.2	59	69.4	8	9.4	
Region of city							
Rural	48	19.9	166	68.8	27	11.3	0.24
Urban	42	18.2	168	72.7	21	9.1	
Montly income							
<500 TL*	13	21.3	42	68.8	6	9.8	
500-1000 TL	31	21.7	99	69.2	13	9.1	0.28
>1000 TL	17	12.2	106	76.3	16	11.5	
Use vitamin D in first year of life							
Yes	32	23.5	91	66.9	13	9.5	
No	29	14.0	156	75.4	22	10.6	0.17

Kruskal Wallis H

*TL: Turkish lira

Table 3. Mean oral calcium intake, outdoor time and physical activity time of adolescents

	Spring				Autumn			
	Female	**Male**	**Total**	**p**	**Female**	**Male**	**Total**	**p**
Oral Ca intake(mg/day)	381±113	391±128	387±122	>0.05	378±115	394±129	387±131	>0.05
Outdoor time (min/day)	46.9±9.5	76.2±18.3	66.5±30.6	**<0.05**	87±17.9	8±16.4	100±29	**<0.05**
Physical activity (min/day)	22.9±11.5	37.2±17	31.2±16.5	**<0.05**	37.2±17.2	52.3±14	5.9±17.2	**<0.05**

Mann-Whitney U

Table4. Distribution of clothing habit (islamic style) and vitamin D status in females

	Season													
	Spring							Autumn						
	No islamic		**Islamic**		**Total**		**p**	**No islamic**		**Islamic**		**Total**		**p**
	n	%	n	%	n	%		n	%	n	%	n	%	
Vitamin D level (ng/ml)	12.5±4		11.4±3.1		11.6±3.3		0.15	19.1±6.4		15.8±4.1		16.3±4.5		0.11
Deficiency	8	32	46	37.4	54	36.4		0	0	4	4.8	4	4.2	
Insufficiency	17	68	75	61.0	92	62.2	1*	8	53.3	63	75.9	71	72.4	**0.04***
Normal	0	0	2	1.6	2	1.3		7	46.7	16	19.2	23	23.4	

Mann-Whitney U and Chi-Square Test
* Fisher test

Table 5. Complaints of adolescents

		Vitamin D (ng/ml)								
Complaints		**Deficiency**		**Insufficiency**		**Normal**		**Total**		
		n	**%**	**n**	**%**	**n**	**%**	**n**	**(%)**	**p**
Bone pain	No	50	81.9	224	90.7	32	91.4	306	89.2	
	Yes	11	18.1	23	9.3	3	8.6	37	10.8	0.13
Muscle pain	No	48	78.7	222	89.9	33	94.3	303	88.4	
	Yes	13	21.3	25	10.1	2	5.7	40	11.6	**0.02**
Joint pain	No	52	85.3	220	89.1	34	97.1	306	89.2	
	Yes	9	14.7	27	10.9	1	2.8	37	10.8	0.19
Tremor	No	60	98.7	247	100.0	35	100.0	342	99.9	
	Yes	1	1.6	0		0		1	0.1	0.09

Spearman test

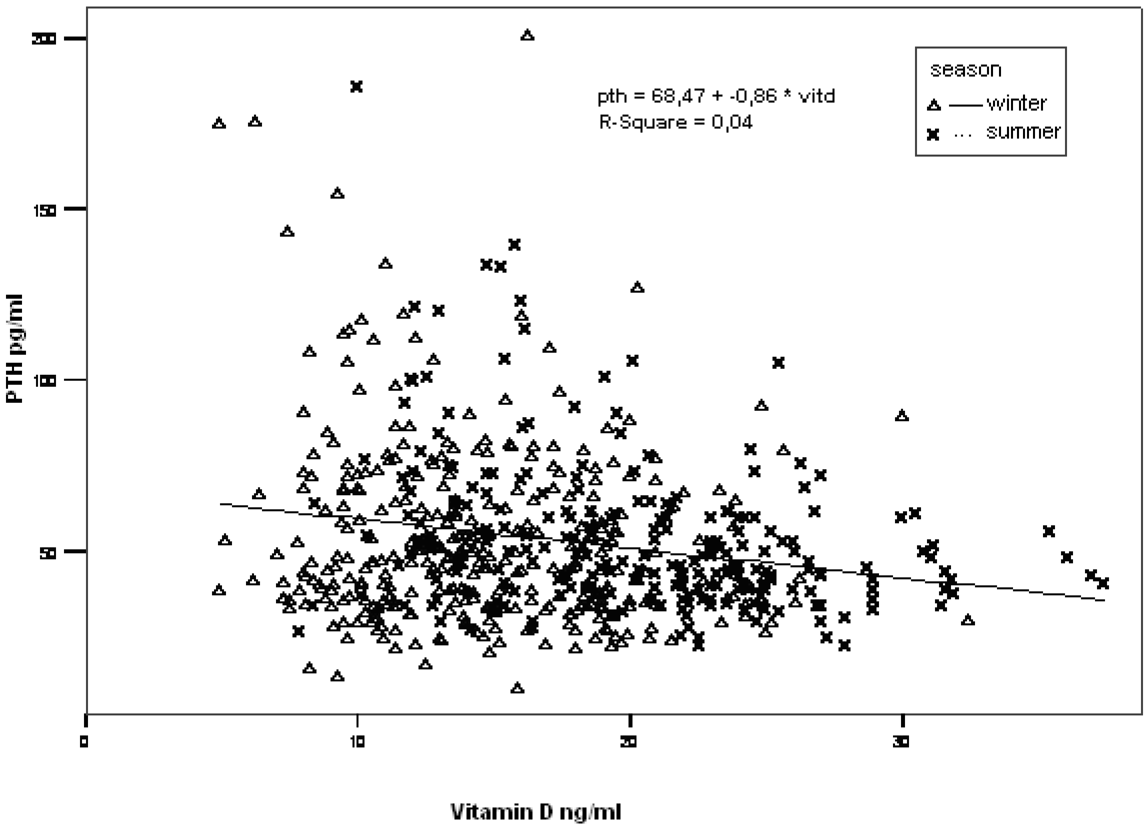

Figure 1. Significant negative linear correlation between serum intact PTH and 25(OH)vitamin D levels

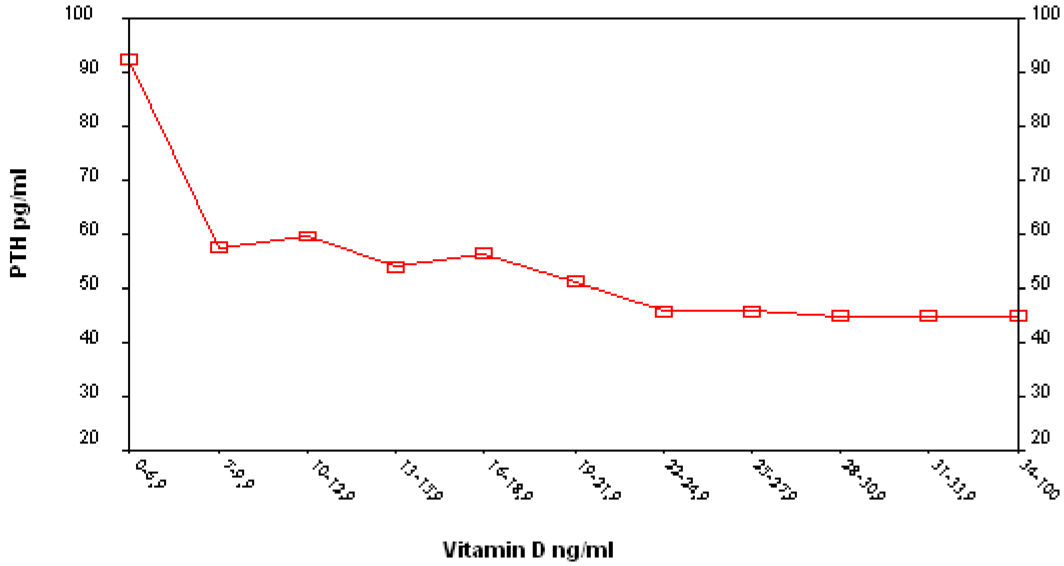

Figure 2. Serum 25(OH)vitamin D levels at which plasma PTH concentrations begin to form a plateau

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Short title: Prevalence and Predictors of Vitamin D insufficiency in Adolescents

Brief synopsis: We evaluate vitamin D insufficiency in adolescents living at an intermediate altitude; and optimal serum 25(OH) vitamin D levels in relation to serum PTH levels. In spring, vitamin D deficiency was detected in 17.7 % and vitamin D insufficiency was detected in 72 % of subjects. At the end of summer these rates were 1.6 % and 41.1 % respectively. Serum 25(OH)vitamin D levels at which plasma PTH concentrations begin to form a plateau is 22 ng/mL.