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HYPOVITAMINOSIS D;
IN CHILDREN IN THE ABSENCE OF SIGNIFICANT CLINICAL SYMPTOMS AND SIGNS

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ABSTRACT… Objectives: To determine the frequency of vitamin D deficiency in children under 12 years of age in the absence of significant clinical signs and symptoms in an ambulatory care settings. **Study Design**: Descriptive study. **Settings and duration**: This study was conducted in Pediatric Out Patient Department of KAUH from June 2013 to June 2014. **Materials and methods**: Patients attending the pediatric clinic in KAUH Riyadh, KSA, from June2013 to June 2014, in which 287 healthy children under 12 years were enrolled. Serum calcium, phosphorus, alkaline phosphatase and 25-hydroxyvitamin D [25(OH) D] were measured .X ray wrists were taken for radiological evidence of rickets. 25(OH) D levels <50 ng/mL and <25 ng/mL were defined as insufficiency and severe vitamin D deficiency, respectively. **Results**: A high prevalence of vitamin D deficiency is observed in healthy children even in absence of clinical signs and symptoms. The problem should be highlighted and there is a need to create awareness among people about the etiology of vitamin D deficiency and its prevention.There is a strong need for long term planning including populationscreening, dietary supplementation with vitamin D and food fortification.

Key words: 25(OH) D, rickets, vitamin D deficiency, insufficiency, calcium.

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INTRODUCTION

Vitamin D is an essential nutrient for bone health. Severe deficiency of vitamin D can cause rickets or low body calcium in children and osteomalacia in adults. Vitamin D is serving the body in many different ways.[1] It has been found that vitamin D receptor (VDR) is present in many issues of human body along with the bones and endocrine system, and according to a research conducted recently, it acts upon more than 200 genes in the whole body. Vitamin D deficiency plays a major role in a variety of diseases including rickets, obesity, diabetes, asthma, autoimmune disorders, and psychiatric illnesses.[2-3] Malnourished and children with chronic illnesses have the highest frequency of these illnesses.[4] Rickets is also found in children of developed nations due to lack of food fortification ,dietary intake or supplements along with limited sun exposure.[5] Human diet has less than 10 percent of vitamin D in the absence of dietary supplement and food fortification. Mild vitamin D deficiency has less evident side effects however, severe and chronic vitamin D deficiency leads to reduced bone mineral density and poor bone health, even in the absence of clinical evidence of osteomalacia or rickets.[6-7]

Vitamin D functions like a prohormone which is synthesized in skin after exposure to sunlight. After being exposed to ultraviolet rays the prohormone vitamin D in skin is converted to the active form of vitamin D in liver and kidneys. Vitamin D is a fat soluble vitamin and converted to two metabolites of clinical importance in the body: 25-hydroxyvitamin D and 1-25-dihydroxyvitamin D. 25-hydroxyvitamin D in serum represents vitamin D stores and is commonly used in laboratory to determine vitamin D level in blood.1-25-dihydroxyvitamin D is the active form, but it doesn't not reflect vitamin D stores.[8]

It is found that serum 25-hydroxyvitamin D levels should be above 50 nmol/L in children to prevent rickets. Severe vitamin D deficiency (25-hydroxyvitamin D level < 30 nmol/L) can lead to rickets, bowing of the long bones, widening of

wrists, frontal bossing, dental anomalies, deformity of the joints along with long term implications for skeletal growth. It is a well-established fact that people are at risk of deficiency when serum 25OHD falls below < 30 nmol/L. A serum 25OHD level of 30–50 nmol/Lis termed as 'vitamin D insufficiency' and it puts people at risk of having vitamin d deficiency.[9]

According to an estimate over one billion people suffer from vitamin D deficiency or insufficiency all over the globe. Despite the abundance of sunshine vitamin D deficiency is a major health issue all over the gulf countries in all ages especially children, pregnant females and elderly people. Multiple factors are considered to be responsible for that including lack of sun exposure, use of sun blocks, darkly pigmented skin and dietary deficiencies.[6-7]

OBJECTIVES AND HYPOTHESIS

The objective of this study is to observe the frequency of vitamin D deficiency. Our hypothesis is that there are significantly low blood levels of vitamin D in absence of clinical signs and symptoms and there is a need for population screening for vitamin D deficiency.

PATIENTS AND METHODS

Children of both genders under 12 years of age following in pediatric clinic for scheduled visit for various reasons were enrolled in the study after informed consent from the parents. Children with mal absorption syndromes, hepatic and renal diseases and all other causes of rickets other than vitamin D deficiency were excluded from the study. After informed consent and collection of properly filled pro forma, base line investigations were performed with additional test including 25OH vitamin D levels, Parathyroid hormone, Urea, Electrolytes, Bone profile, phosphorus and Alkaline Phosphatase from the venous samples. Samples were sent to biochemical laboratory in King Abdul Aziz University Hospital Riyadh for interpretation. Serum calcium, phosphorus and ALP were measured using photometric methods and vitamin D levels were measured using ELISA technique.

X-ray wrists were done for each patient and assessed by expert radiologist for signs of rickets. Data was collected including age, gender, anthropometry, and nutritional history, exposure to sunlight, multivitamin intake, parents' ethnicity and educational level. Patients were divided into three groups according to their vitamin D levels .Group 1 with normal levels (50nm/l), group 2 with insufficiency having levels between 30-50nm/land third groups with vitamin D deficiency having levels below 30nm/l.

A child's weight status is determined using an age- and sex-specific percentile for BMI rather than the BMI categories used for adults because children's body composition varies as they age and varies between boys and girls. CDC Growth Charts were used to determine the corresponding BMI-for-age and sex percentile. For children and adolescents: **Overweight** is defined as a BMI at or above the 85th percentile and lower than the 95th percentile for children of the same age and gender. **Obesity** is defined as a BMI at or above the 95th percentile for children of the same age and gender. Underweight is defined as weight below 5th centile for age.

Baseline characteristics were summarized by appropriate descriptive statistics. Statistical analysis was performed using SPSS version 21. For quantitative data mean and standard deviation were calculated. The t-test was applied to compare both groups. For qualitative data, frequency and percentage was calculated and chi square test applied. P-value ≤ 0.05 was considered as level of significance.

RESULTS

A total of 287 patients were studied. Mean age in our sample population was 7.3+-2.2 months. 89.54% were Saudis and other nationalities included Sudanese (4.52%), Egyptians (3.48%) Indians (1.39%) and Pakistanis (1.04%).

Group 1 had 46 subjects (16%) with sufficient vitamin D levels(above 50nm/l) of which 10.3%were less than 5 years and 5.22 % were above 5 years showing a significant number of children below 5

years with normal vitamin D levels (p value 0.004). Male to female ratio was almost 1: 0.84 (p value of 0 .2) which is not a significant difference.
Group 2 included 162 subjects (56.44%) having vitamin D insufficiency (levels between 30-50nm/l). Children below 5 years were 45(15.67%)and above 5 years included 117 (40.76%) showing a significant number of children above 5 years having low vitamin D levels(p value= 0.0001) Male to female ratio was 1:1.3 being not significant as p value = 0.03
Group 3 included 79 subjects (27.52%) having vitamin D deficiency (levels below 30nmol/l). Children below 5 years were 15(6.27%) and above 5 years were 61(21%) showing a significant difference as vitamin D levels decrease with age (p value < than 0.001). Vitamin D deficiency was more frequently observed in females as male to female ratio was 1:4.2 (p value< 0.05)

The most common symptom was leg pain 246 patients (88%) p value < 0.001.Other features included back ache (14.28%) p value>0.05, delayed walking (8%) widened wrist (4.5%). X-ray evidence of rickets was found in only (2.09%) p value> 0.05.

Mean Serum calcium was 2.2mm/l (reference range was 2.1to 2.5mm/l).Total 7 patients had low Calcium (2.43%). Out of which 5 were those having low vitamin D levels and only 2 from the group with normal vitamin D levels which does not show any significant difference. (P value>0.5).

Mean level of alkaline phosphate was 321.42IU. Reference range was 0-200IU.Of the total patients 136 (47.3%) had raised alkaline phosphatase which included 119 patients from the group with low vitamin D levels accounting for 77 %and 17 patients (36.9%)from group with normal vitamin D levels. (p value= 0.06) which is not significant making alkaline phosphatase as a poor predictor of vitamin D deficiency.

Mean parathyroid hormone level was 43.21pg/l. Reference range was 15-65pg/l. Total 54(18% of total patients) had high parathyroid hormone. It included 21% of those with low vitamin D levels and only 2.17%of those in the group with normal vitamin D levels (p value= 0.001) which shows parathyroid hormone level as a good predictor of low vitamin D levels.

Parents of 254 (88%) patients were aware of the vitamin D deficiency prevalent in gulf.

Children with vitamin supplements were 91 (31%) which included 18(39%) from group with normal vitamin D and 73(30.29%) from group with low vitamin D levels (p value= 0.11) which is not significant.

Another finding of interest was that only 6.27% of patients from the group with normal vitamin D levels were overweight as compared to 23% of children who were overweight as well as vitamin D deficient which is a significant difference.

level	Range
25OHD, ng/mL	27.07±5.41
PTH, pg/L	43.21±7.21
Alkaline phosphatase, U/L	321.42±2.40
Calcium, mm/L	2.2±1.2

Table-I. Biochemical markers of 287 children in KAUH Riyadh Ambulatory care settings between June2013-June 2014

variables	Cases n=287	percentage
Age	7.3±2.2	
Males	126	44.12%
Females	157	55.70%
Nationality		
Saudi Sudanese Egyptian Indian Pakistanis	256 13 10 4 3	89.54% 4.52% 3.48% 1.39% 1.04%
Obese	66	23%
Under weight	94	33%
Normal vitamin D levels	46	16%
Insufficiency	162	56.44%
deficiency	79	27.52%

Table-II. Characteristics and 25(OH) vitamin D status in 287 children in KAUH Riyadh Ambulatory care settings between June 2013-June 2014

DISCUSSION

Vitamin D deficiency in children is a major health problem all over the globe especially the Middle Eastern and African countries despite adequate sunshine, Hypovitaminosis D is not uncommon among pediatric population especially young females.[12]

However, the prevalence varies with countries and populations because of various risk factors which include dark skin, lack of sun exposures due to various reasons, exclusively breast-fed infants, elderly and pregnant ladies.[13]

In our study low levels of vitamin D were present in total 241 out of 287(83.9%) patients showing high percentage of children including males and females being vitamin D deficient .It raises a concern that a major part of study population was deprived of the health benefits of vitamin D in the body .This overall figure of 83.9% having low vitamin D levels below 50nmol/l is comparable to other studies conducted in Jeddah and Qatar in children.[14-15] The prevalence of vitamin D deficiency among the Qatari children was (68.8%), mostly in the age group (11-16) years and (61.6%) in Jeddah. This was evident from other studies around the world[1-3].

Overall, 9% of the pediatric population, representing 7.6 million US children and adolescents, were 25(OH) D deficient and 61%, representing 50.8 million US children and adolescents, were vitamin D insufficient.[16-17]

Mean age in our study was 7.3 years and is comparable to the study (Jeddah)and showing relationship of low vitamin D with increasing age which is in contrast to study in Qatar who studied vitamin D in less than 5 years of age.[14]

We found that children were having low vitamin D inspite of the multivitamin supplementation. 35% of children took multivitamin supplements including vitamin D. Out of these 4.87% were those with normal vitamin D levels and 30% had low vitamin D levels .It was quite evident from the number that even with oral vitamin supplements children had vitamin D in suboptimal range .This can be explained by the genetic predisposition, lack of sun exposure, dietary deficiencies and inadequate intake of vitamin D.

We found a high proportion of kids above five years to be vitamin D deficient and only few of them were below 5 years of age which could be explained by the protective effect of milk intake by the kids below 3 years. It raises the serious concern of subclinical vitamin D deficiency with serious consequences as patients are not routinely screened for vitamin D levels without symptoms. Out of these only 8% presented with delayed walking and 4.5% had widened wrist X ray evidence of rickets was found in only (2.09%)p value more than 0.05.This signifies the importance of screening by x rays and vitamin D levels in children living in high risk regions. In a study in China the highest mean level of serum 25(OH)D was found in the 0-1y stage (99 nmol/L) and the lowest one was found in 12-16y stage (52 nmol/L) in China.[18]

Another interesting fact noticed in our study was marked low vitamin D levels in females as compared to males. 47.38% females were vitamin D deficient in contrast to 29.26%males who were deficient in vitamin D. This could be explained by the fact that females have conservative dress codes, use of sun screens and avoiding the sun in summer. This is evident from studies done in Asia and Middle East.[19-21]

Vitamin D deficiency was higher in overweight children in our study which is similar to other studies. This can be explained by the fact that adipose tissue decreases the bioavailability of fat soluble vitamins including vitamin D.[22]

We found an inverse relationship between parathyroid hormone and vitamin D levels as it was high in 21.99%of children with low vitamin D levels in contrast to 2.17%of those with normal vitamin D levels. Calcium and phosphorus and alkaline phosphatase were found to be poor predictors of low vitamin D in the body.[23]

To our knowledge it was the first study in Riyadh to see the frequency of vitamin D deficiency in children and its various variables. There were some limitations of our study as being descriptive study it could not assess the causative factors for low vitamin D in the body. The subjects were not sampled from the whole paediatric population in Riyadh, and other possible relating factors of vitamin D status including intake of daily total vitamin d, children's BMI, duration of sun exposure, calculation of total body surface area exposed under sun, use of sun screens, dietary deficiencies and the time of physical activities were not calculated. A further study based on subjects sampled on a population basis should be carried out and the possible relating factors of vitamin D status should be investigated. Furthermore, the optimal vitamin D level among children to avoid vitamin D deficiency should be calculated.

CONCLUSION

Vitamin D is a major health issue in gulf region including Saudi Arabia. It is common in children as well as adolescents. Its association with obesity and female gender raises the serious concern regarding the health of nation. Studies should be done at a large scale and effort should be made to identify the causes and create awareness among the people. Routine screening for Vitamin D deficiency and food fortification with Vitamin D should be implemented.

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"Don't raise your voice,
improve your argument."

Anonymous

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