Rickets in Healthy Adolescents in Van, the Eastern of Turkey

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ABSTRACT

***Aim**: To investigate the ratio of rickets and vitamin D deficiency in healthy adolescents at Van region.*

***Method**: Totally 126 cases were included in this study. All cases were evaluated for the presence of rickets symptoms, daily sun exposure, and vitamin usage, covering and eating habit. Diagnosis of rickets was made based on biochemical findings. The children whose vitamin D levels were lower than 10 ng/dl were accepted as vitamin 25(OH)D3 deficiency, but whose levels between 10-20 ng/dl were accepted as vitamin D insufficiency.*

***Result**: Sixty girls (47.6%) and 66 boys (52.4%) were included in this study. They were between 9 and 17 years old (11.94 ± 1.9 years). Vitamin D levels in 60 (47.6%) cases were normal, but 48 (38.1%) cases had rickets, 13 (10.3%) cases had vitamin D insufficiency and 5 (4.0%) cases had vitamin D deficiency. There was no statistically significant difference in the incidence of rickets between the cases with or without covered-dress. However, there was a significant difference in the incidence of vitamin D insufficiency ($p<0.05$). All of the cases had less daily calcium, phosphorus, protein and vitamin D intake than recommended daily amount. In the rickets group, alkaline phosphatase levels were significantly higher comparing with the others ($p<0.05$), but there was no difference in plasma intact parathyroid hormone levels.*

***Conclusion**: Our findings revealed that most adolescents who appeared to be healthy (52.4%) could have vitamin D insufficiency. Therefore, we believe that dietary education and/or vitamin D prophylaxis might be given to all adolescents. However, more extensive researches should be done to elucidate of our suggestion's correction*

***Key words**: Rickets, vitamin D deficiency, adolescents.*

INTRODUCTION

Rickets is a metabolic disease of bone, which results from insufficient mineralization of the bone tissue in the growing up organism and shows its signs mainly in the skeletal system (1). Nutritional rickets is still being a public health problem in the developing and undeveloped countries (2-5). A type of rickets that knows as "adolescent rickets" which results from receiving inadequate of vitamin D (25(OH)D3) and insufficiently sun exposure and increased metabolic requirements secondary to rapid growing in pubertal period, could also be encountered (6,7). This type of rickets that is particularly seen in adolescent girls increase possibility of osteoporosis, osteomalacia and risk of developing bone fractures in the early life of adults (4).

It has been shown that an insufficiency of vitamin D is not stipulation to develop rickets since a negative calcium balance formed by insufficient intake of calcium or a lifestyle impairing absorption of calcium (8). A low level of serum 25(OH)D3 is not only a simple biochemical sign of rickets such as increased releasing of parathyroid hormone (PTH), but also is a sign of increased bone turn-over, osteoporosis, mild osteomalacia and increased possibility of fractures of hip or other bones. On the other hand, subclinic vitamin D insufficiency, which does not develop rickets but increases levels of PTH, is being a substantial problem for public health (9).

The objective of this study was to determine the presence of rickets and/or vitamin D insufficiency in adolescents who considered being healthy in our region as called "endemic" for rickets.

MATERIALS AND METHODS

The study was conducted between February 2003 and March 2004. A total of 126 healthy cases, 60 were females and 66 were males, who were between 9 and 17 years and admitted to our pediatric policlinic because of control one month after the upper tract infection, were included in this study. Means times of sun exposure on faces and hands were learnt. It was talked with a dietitian to determine daily intake of energy, calcium, phosphorus, protein and 25(OH)D3 by a 72 hours dietary recall of record method.

The physical examinations of the cases were performed after their detailed histories including their nutritional conditions, intake of vitamin D and socio-cultural factors. Serum levels of calcium, phosphorus, alkaline phosphatase, osteocalcine, 25(OH)D3 were evaluated, as well as the plasma level of intact PTH to investigate pathological conditions related to vitamin D. Radiographies of lumbosacral vertebra and left hand-wrist were performed. Serum levels of alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen and creatinine were evaluated to eliminate liver and kidney diseases.

Rickets was diagnosed on the basis of abnormal biochemical and/or radiological results (raised serum alkaline phosphatase, with or without raised Parathormone concentration, low serum 25(OH)D3 concentration (<20ng/ml) and presence of radiological findings in some cases (6). The children whose serum levels of vitamin 25(OH)D3 were below 10 ng/ml were accepted as vitamin D deficiency, but between 10 to 20 ng/ml were accepted as vitamin D insufficiency (10,11).

Statistical analysis system and Minitab statistical packet programs were used to evaluate the data. A p value less than 0.05 was considered statistically significant throughout the study.

This study was approved by our hospital ethical committee and Ministry of Education, all the parents of patients allowed us performing our study, after informed consent too.

RESULTS

Of 126 cases, 66 (52.4%) were males and 60 (47.6 %) were females. The mean age of cases was 11.9±1.9 years, between 9 and 17 years. The ratio of boy/girl was 1.1. In 60 (47.6%) cases, 25(OH)D3 level was normal, 48 (38.1 %) had rickets, 13 (10.3 %) had vitamin D insufficiency, and five (4.0 %) had vitamin D deficiency (Table 1).

Table I shows the distribution of the cases according to age. There was no significant difference among the groups for ages ($p>0.05$). In our study, the cases were divided into three groups as vitamin D insufficiency, vitamin D deficiency and rickets. Five (16.6%) female cases with rickets were covered-dress (all body was covered except hand and face) (Table I). When vitamin D levels of girls were evaluated whether they were covered or uncovered, 25(OH)D3 levels were found lower in the covered girls than uncovered ($p<0.05$), but no difference was found for the ratios of rickets between these groups ($p>0.05$) (Table 1).

***Table 1**. Distributions of the cases according to gender, ages, settling area and female subjects' clothing style*

	Normal n (%)	*Vitamin D insufficiency n (%)*	*Vitamin D deficiency n (%)*	*Rickets n (%)*	*Total n (%)*
Female	*21 (35%)*	*7 (11.6%)*	*2 (3.4%)*	*30 (50%)*	*60 (100%)*
Male	*39 (59%)*	*6 (9%)*	*3 (4.6%)*	*18(27.4%)*	*66 (100%)*
p	*>0.05*	*>0.05*	*>0.05*	*<0.05*	
Age (years) (M±SD)	*11.9 ± 1.9*	*12.3 ± 1.7*	*11.4 ± 1.9*	*11.8 ± 1.9*	*11.9 ± 1.9*
Distrubution of cases according to settling area					
Rural	*19 (39.6)*	*8 (61.5)*	*2 (40)*	*6 (12.5)*	
Center	*41(68.4)*	*5 (38.5)*	*3 (60)*	*42 (87.5)*	
	X2=13.8 P <0.01				
Distrubution of female subjects according to Clothing Style					
Uncovered	*20 (39.2)*	*5 (9.8)*	*1 (2.0)*	*25 (49.0)*	*51*
Covered	*1 (11.1)*	*2 (22.2)*	*1 (11.1)*	*5 (55.5)*	*9*
Total	*21 (35.0)*	*7 (11.6)*	*2 (3.4)*	*30 (50.0)*	*60*

M±SD: mean±standard deviation

All cases were receiving less than recommended daily amount of calcium, phosphorus, protein and vitamin D (Table 2). There was no difference between the groups for serum calcium levels ($p>0.05$). Serum phosphorus level was mildly higher in rickets group than those of others were ($p>0.05$). Serum alkaline phosphatase level was significantly higher in rickets group than in the other groups ($p<0.05$).

There was no significant difference between the groups for plasma intact PTH level ($p>0.05$). When compared to vitamin D insufficiency and vitamin D deficiency, serum osteocalcine levels were higher in rickets and normal groups ($p<0.05$) (Table 2).

When pubertal development of the cases were evaluated, it was determined that ratios of rickets, vitamin D insufficiency and deficiency were increased by progression of pubertal stages, but this increase was not statistically significant ($p>0.05$) (Table 3). When nourishment conditions of the cases were examined according to pubertal stages it was seen that they were receiving daily calcium, phosphorus, vitamin D and protein less than the recommended daily in all stages (Table 3).

Regarding of settlement of cases, it was seen that 42 (87.5 %) cases were living in centre of Van and six (12.5%) in rural ($p<0.001$) settlement (Table 1). There was no difference between groups of vitamin D insufficiency and deficiency and rickets for settlement (Table 1).

In our study, three (6.25%) cases had mild osteopenia on ulna in a left hand-wrist and on vertebrae in lumbosacral radiography, which were thought to be rickets. In addition to this, 18 (44%) cases had abnormal radiographical signs such as transverse metaphysial lucent band, metaphysial deformation and osteopenia on lumbosacral and hand-wrist radiographies.

DISCUSSION

It has been reported that nutritional rickets is seen with a frequency of 3.2 to 19% in different studies done in different regions of Turkey (12). In a retrospective study performed by Narchi et al (6) in Saudi Arabia, symptomatic rickets' prevalence was found to be 68 per 100.000 children years. El-Hajj Fuleihan et al. (13) was designed a study to investigate vitamin D insufficiency in healthy children. Children ages 10 to 16 years from three private schools in Beirut, Lebanon, with differing socioeconomic status (SES) were included in the study. They found that overall, 52% of the students were vitamin D-insufficient; the proportion of insufficiency was 65% in the winter and 40% at the end of the summer. In our study, while the number of cases with rickets and

Table 2. *The comparison of cases according to receiving daily amounts of nourishment components and biochemical parameters*

Parameters	The status of vitamin D				p
	Normal	Vitamin D insufficiency	Vitamin D deficiency	Rickets	
Receiving daily amounts of nourishment ingredients					
Calcium (mg/day)	270 ± 98.0	296 ± 154.8	300 ±101.9	245 ± 125.7	>0.05
Phosphorus (mg/day)	311 ± 226.9	424 ± 244.7	386 ± 225.0	307 ± 218.1	>0.05
Protein (g/day)	22 ± 10.7	23 ± 9.3	25 ± 6.8	22 ± 11.4	>0.05
Vitamin D (IU/day)	32 ± 28.7	30 ± 21.8	38 ± 20.5	31 ± 22.0	>0.05
Biochemical analysis					
Calcium (mg/dl)	9.5 ± 0.5	9.1 ± 0.8	9.1 ± 0.8	9.8 ± 0.5	>0.05
Phosphorus (mg/dl)	4.7 ± 0.9	4.0 ± 1.1	4.9 ± 1.3	5.1 ± 1.0	>0.05
Alkaline phosphatase (U/L)	485.0 ± 224	*339.0 ± 109.0	*393.0 ± 135.0	*,†,‡724.7 ± 353.0	<0.05
Parathyroid hormone (pg/ml)	52.4 ± 27.0	42.0 ± 17.0	39.4 ± 18.0	67.0 ± 56.0	>0.05
Osteocalcine (ng/ml)	56.2 ± 30.0	*26.5 ± 22.0	*17.4 ± 9.9	†,‡63.0 ± 29.0	<0.05
Vitamin D (ng/ml)	28.2 ± 6.4	*14.9 ± 2.9	*,†7.6 ± 2.3	*,‡13.8 ± 4.3	<0.05

*Post-hoc LSD (lesat significant difference) test results: *: p <0.05 (Comparison with normal), † p <0.05 (Comparison with vitamin D insufficiency), ‡: p <0.05 (Comparison with vitamin D deficiency)*

low vitamin D level was 66 (52.4%), the number of cases with rickets alone was 48 (38.1%).

In our study, 30 (62.5 %) of 48 cases with rickets in adolescent period were female. In similar studies, it has been reported that vitamin D insufficiency occurred in adolescent period and rickets were seen more commonly in girls. Of 21 cases with adolescent rickets diagnosed in Saudi Arabia, 95.2% were females (5). A study which was performed approximately in a period of 2 years in India has shown that 21 adolescents with symptomatic rickets were females (14). The higher rates of female with rickets in these two studies (95-100%) may be explained by a higher rate of veiling seen in Saudi Arabia and India.

In our study, serum 25(OH)D3 level in covered girls was statistically lower than that in uncovered girls (p<0.05). Approximately a half of girls in Turkey are covered and they have a limited activity out of home. It has been established that, not to benefit from sun and covered-clothing style were risk factors for occurring vitamin D deficiency in adolescent girls and in women, in many studies performed in Turkey (15).

Hatun et al (16) designed a study to investigate potential risk factors for vitamin D deficiency. Girls (n = 89) aged 13 to 17 years were enrolled in the study and they found that 39 girls (43.8%) had vitamin D insufficiency and 19 (21.3%) had vitamin D deficiency. They also emphasized that in girls who was living urban and wearing covered dress, the serum 25(OH) D concentrations (28.13 +/- 12.53 nmol/L) were significantly lower than in the other subjects, and within this group, 50% of girls were vitamin D deficient. Finally, they concluded that vitamin D deficiency was an important problem in Turkish adolescent girls, especially in those who follow a religious dress code; therefore, vitamin D supplementation appears to be necessary for adolescent girls (16). It has been described that serum 25(OH)D3 level was lower than reference values in covered-women and with black skins in Australia (17). Since clothes absorb most of the ultraviolet rays, excessive melanin pigmentation reduces the production of vitamin D by skin, so women with covered-clothes or black-skins have a tendency to vitamin D deficiency. It has been determined that an osteoporosis measured by bone densitometer was two and half-folds more common in the Muslim women than in European women (18). A study from France, consisted of volunteer persons, showed that age and sexuality had no any effect on serum level of 25(OH)D3 (19).

In our study, a vitamin D deficiency was determined in five (4%) cases, a vitamin D insufficiency in 18 (10.3%), and a rickets in 48 (38.1%). In a study of Hatun et al (16), with 89 cases, a vitamin D deficiency was found in 21.3 %, and a vitamin D insufficiency in 43.8%. A study

Table III: *Vitamin D and nourishment conditions according to pubertal stages*

Pubertal stage	The status of vitamin D				Amounts (receiving daily)			
	Normal n (%)	Insufficiency n (%)	Deficiency n (%)	Rickets n (%)	Calcium (mg/day)	Phosphorus (mg/day)	Protein (g/day)	Vitamin D (IU/day)
Stage 1	14 (61.0)	1 (4.2)	0 (0.0)	8 (34.8)	240 ± 84	310 ± 208.9	19 ± 10.4	31 ± 25.6
Stage 2	27 (49.0)	7 (12.7)	3 (5.4)	18 (32.9)	286 ± 134	342 ± 235.4	24 ± 10.9	31 ± 22.7
Stage 3	13 (46.4)	2 (7.2)	1 (3.6)	12 (42.8)	269 ± 79.5	368 ± 238.9	25 ± 9.6	40 ± 30.2
Stage 4	6 (30.0)	3 (15.0)	1 (5.0)	10 (50.0)	222 ± 127.5	228 ± 179.4	19 ± 10.3	23 ± 21.4
Recommended daily					1200	1200	50	0-1000

consisted of 272 patients from England, a serum level of 25(OH)D3 was found low (<16 ng/dL) in 13.6% of patients (20).

It has been suggested that there were also other factors (except sun exposure insufficiency) which could play a role on etiology of vitamin D insufficiency, since all the cases we enrolled in this study had a daily sun exposure of one hour and had a low rate of covered (15%).

It has been determined that exposure to natural ultraviolet rays increases a serum level of 25(OH)D3 for 2.5 folds, clearly reduces alkaline phosphatase activity, but no change in serum phosphorus level (3). It has also been shown in the other study that a serum 25(OH)D3 level was directly proportional to sun exposure (21). In our study, it was determined that none of the cases had a vitamin D supplementation and the cases had a diet included low amounts of vitamin D and calcium. Insufficient intake of calcium and vitamin D with nourishments and excessive consumption of carbonated drinks are determined to be risk factors for developing rickets in adolescents with symptomatic rickets (6). An 85% of cases in which a moderate and severe vitamin D insufficiency was determined had an intake of vitamin D less than 200 IU (20).

Recently, it has been reported that a majority of pregnant and prolific women (up to 80%) in Turkey had a vitamin D insufficiency (18). Daily intake of vitamin D and calcium lower than recommended amount were shown to be one of the leading to vitamin D insufficiency (22). In female adolescents from Finnland, although intake of calcium was sufficient, vitamin D insufficiency would lead to a vitamin D deficiency (23).

In our study, it has been found that 48 (38.1%) cases of adolescent rickets had an increased serum alkaline phosphatase level and decreased serum 25(OH)D3 level and a normal serum calcium and phosphorus levels. Narchi et al (6) found increased serum alkaline phosphatase levels and decreased serum 25(OH) D3 levels in all 21 cases of adolescent rickets, but hypocalcaemia in 19 cases, and hypophosphatemia in 9 cases. Al-Jurayyan et al (24) noted decreased serum calcium, normal phosphorus, elevated alkaline phosphatase and decreased of 25(OH)D3 levels. No correlation was found between serum vitamin D and plasma PTH levels in our study. This condition can be explained with serum vitamin D levels, which were not too low in our cases of rickets. Harkness et al (25) found a correlation between low vitamin D level and high PTH level in adolescents with rickets. However, Zeghoud et al (26) found elevated PTH level in 53 adolescents, who had very low serum 25(OH)D3 level (<3 ng/ml), but normal PTH level in others.

In our study, the cases of low serum vitamin D levels and rickets were most commonly in stage 4 puberty (14 out of 20 cases, 70%), in stage 3 puberty (15 out of 28 cases, 53.6%) with a second frequency. Similarly, when a pubertal distribution of cases with rickets was evaluated, the most cases were in stage 4 puberty (10 cases of 20, 10%), and the second commonly in stage 3 (12 out of 28 cases, 42.8%). While Narchi et al (6) have reported that all cases with adolescent rickets were in Tanner pubertal stage 2 to 4, Zeghoud et al (26) have noted that the decreased serum vitamin D level was higher (38%) in adolescent with a stage 4 to 5 Tanner puberty.

In our study, 42 (87.5%) of cases of rickets were living

in city center. It has been found that serum vitamin D levels in children who lived in urban and industrial regions with air pollution was lower than those who lived in rural regions without air population, with a ratio of 50%. In another study, it has been revealed that 81% of cases in adolescent period, with low serum vitamin D level, were presented from city center (26).

In our study, only 3 (6.25%) cases had mild osteopenia on ulna in a left hand-wrist and on vertebrae in lumbosacral radiography, which were thought to be rickets. In addition to this, 18 (44%) cases had abnormal radiographical signs such as transverse metaphysial lucent band, metaphysial deformation and osteopenia on lumbosacral and hand-wrist radiographies. a. Al-Jurayyan et al. (24) determined radiologically a skeleton deformation in five and a fracture in three of 42 cases diagnosed with rickets (a ratio of all cases with a determined radiological sign was 19%). Abdul-Motaal et al. (27) found a weak relationship between low serum vitamin D levels and radiological findings in rickets due to vitamin D deficiency.

In our study, all the patients were from Van, a city located in the eastern Anatolia region of Turkey on the eastern coast of Lake Van. Continental climate reigns in this region as well as other cities located on Eastern Turkey. Continental climate is characterized by winter temperatures cold enough to maintain a fixed period of snow cover each year, and a relatively moderate precipitation occurring mostly in the summer. People who living in this area have generally low socioeconomic status (28). On the other hand, the low literacy rate has been found among people living in Eastern Turkey like Van. (29). Therefore, we summurised that people living in this region have low socioeconomic status, low literacy rate, low attention for hygene and climate in this region is defined as continental climate. In literature, it was shown that these factors were also contribute to rickets' development (30).

In our study, vitamin D insufficiency and rickets rate were found to be similar with other studies in literature. (Vitamin D deficiency rate was found to be 52% by El-Hajj Fuleihan et al. (13), 59.4 by Olmez D et al (30), 43.8 % by Hatun et al. (16). However, our rate could be found high when compared to some other studies in literature. The reason of that high rate can be explained following;

1. Receiving daily calcium, phosphorus, and protein less than the recommended daily

2. Vitamin D intake less than 200 IU that was defined as minimum recommended dose for children and adolescents.

3. Living in city center. Living city center with air pollution is the other reason of that high rate of Vitamin D deficiency and rickets.

4. low socioeconomic status, low literacy rate, low attention for hygene and continental climate are other factors which cause that high rickets rate.

In conclusion, our findings revealed that most adolescents who appeared to be healthy (52.4%) could have vitamin D insufficiency. Therefore, we believe that dietary education and/or vitamin D prophylaxis could be given to all adolescents. However, more extensive researches should be done to elucidate our suggestion's correction.

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