

Potential Role of Vitamin D in Pathogenesis of Acute Rheumatic Fever

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OBJECTIVES

Acute rheumatic fever (ARF) is a non-suppurative complication of group A beta-hemolytic streptococcus (GAS) pharyngitis which underlying pathologic mechanisms have not been fully elucidated yet. It usually develops following GAS pharyngitis in children between 5 and 15 years-old. Vitamin D, involves in the calcium homeostasis and bone mineralization. Some immune-modulator and anti-inflammatory effects on various infectious and autoimmune diseases have also been reported. Incidences of GAS infections and ARF make a overlaped seasonal peak at winter and spring months when the 25(OH)D levels is expected to be lowest due to lack of sun exposure. To the best of our knowledge, vitamin D status has not been assessed in ARF patients so far. In present study, we evaluated the 25(OH)D levels in children with ARF in comparison with age-matched healthy controls in order to investigate the relationship between vitamin D deficiency and disease phenotype.

PATIENTS&METHODS

Participants: 30 patients admitted to our Pediatric Cardiology Clinic and diagnosed with ARF and 16 age- and sex-matched healthy controls evaluated for innocent murmur between December 2011 and March 2013 were prospectively recruited. The patients with any other systemic disease and taking any medication that can affect the calcium and vitamin D metabolism were excluded.

Ethics: Study was approved by ethics committee of Dicle University and an informed consent was obtained from legal guardians of all participants.

Laboratory measurements: Serum calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), magnesium (Mg), parathormon (PTH), and plasma 25(OH)D levels were measured both in patients with ARF and controls. Serum anti-streptolysin O (ASO), erythrocyte sedimentation rates (ESR), C-reactive protein (CRP) levels were measured only in patient group. A plasma 25(OH)D level ≥ 30.0 ng/mL was considered as sufficient. A level < 20.0 ng/mL was considered as deficient, while a value between 20.0-29.9 ng/mL was considered as insufficient. The diagnosis of ARF was considered according to the modified Jones criteria.

Echocardiography: Echocardiographic findings of ARF cases was assessed as absence of valvulitis, presence of mild, moderate and severe regurgitation either in mitral or aortic valve. The severity of valvular dysfunction was evaluated according to previously described methods. Carditis was defined as mild, moderate, and severe.

Statistical analysis: Data was analyzed using the SPSS software (version 16.0, SPSS Inc., Chicago, IL). Data were presented as mean \pm standard deviation or median (min-max). Student's t-test was used for comparison of variables with normal distribution, while abnormally distributed variables were compared using Mann-Whitney U test. Statistical significance was considered at a p value of < 0.05 .

Table 1: The characteristics of patients with the diagnosis of ARF and control group*

	Study group (n=30)	Control group (n=16)	P value
Age (year)	12 \pm 2.94	11 \pm 2.96	0.628
Sex (female/male)	12/18	7/9	0.806
Height (cm)	139.0 \pm 3.0	141 \pm 1.4	0.997
Weight (kg)	44.8 \pm 2.3	35.1 \pm 1.3	0.221
BMI (kg/m ²)	27.1 \pm 6.1	24.3 \pm 6.6	0.168
ESR (mm/h)	90 \pm 3 (27-122)	NA	NA
CRP (mg/dl)	69.8 \pm 5 (14.5-190)	NA	NA
ASO (IU/L)	760 \pm 3 (240-1760)	NA	NA
Serum 25(OH)D (ng/ml)	25.41\pm1.38	14.56\pm8.31	0.002
Calcium (mg/dl)	9.46 \pm 0.62	9.53 \pm 0.38	0.679
Phosphorus (mg/dl)	4.46 \pm 0.66	4.80 \pm 0.75	0.124
Magnesium (mg/dl)	2.17\pm0.28	1.95\pm0.09	0.001
Serum ALP (IU/L)	168 (89-389)	225 (79-368)	0.269
Serum PTH (pg/ml)	37.83 \pm 2.63	47.91 \pm 2.32	0.205

*Variables were shown as means \pm standard deviations or median (min-max). ALP: alkaline phosphatase, ASO: anti-streptolysin O, BMI: body mass index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, NA: not applicable, PTH: parathormon

RESULTS

Anthropometric and biochemical characteristics of study group and controls are shown in Table 1. Serum 25(OH)D levels in study group were significantly lower than those of controls (25.41 \pm 1.38 ng/ml vs. 14.56 \pm 8.31ng/ml, p=0.002) (Figure 1). Although, were within normal limits in both groups, serum Mg levels in patient group were significantly higher than in control group (2.17 \pm 0.28 mg/dl vs. 1.95 \pm 0.09 mg/dl, p=0.001). 23 out of 30 patients with ARF (77%) and 8 out of 16 controls (50%) had vitamin D deficiency (p=0.066).

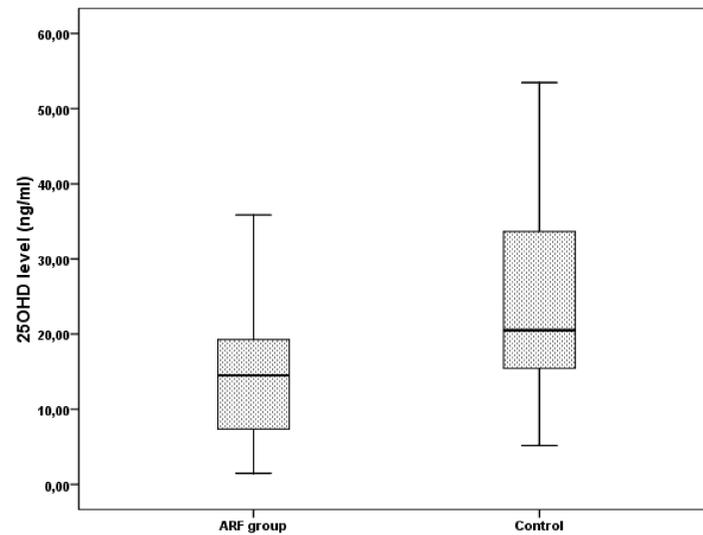


Figure 1: Serum 25(OH) D levels in study group were significantly lower than those of controls

Evaluation of ARF patients for cardiac involvement revealed that 29 out of 30 patients had carditis (Figure 2). Thirteen of 29 patients with carditis (44.8%) had single valve involvement (mitral valve in 11, aortic valve in 2), 16 (55.2%) had both mitral and aortic valve involvement.

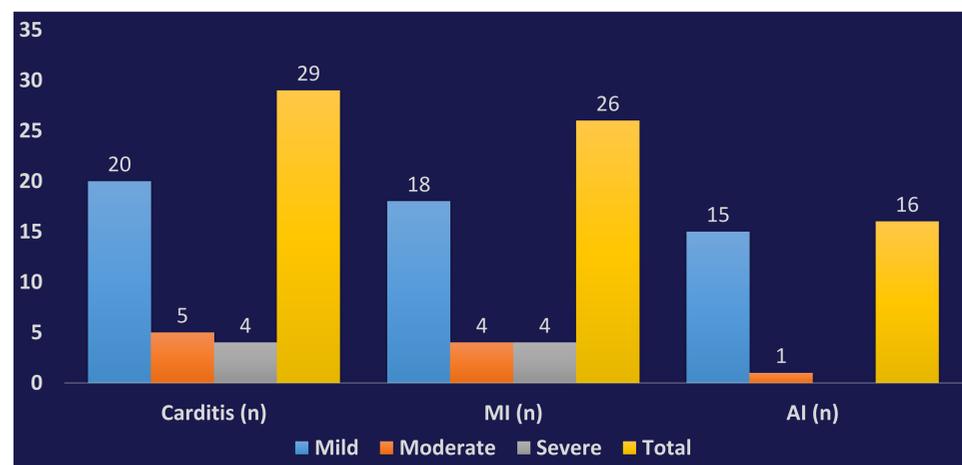


Figure 2: Presence of carditis and valvular involvement (MI: mitral insufficiency, AI: Aortic insufficiency)

CONCLUSIONS

In conclusion, in this to the best of our knowledge the first study evaluating the relationship between vitamin D deficiency and ARF we detected 25(OH)D levels lower in cases with ARF compared to the healthy controls. Vitamin D deficiency and resultant decrease in its immune-modulator effect may activate immune response and predisposes developing ARF. Studies evaluating larger number of ARF patients with and without carditis are warranted to further elucidate the role of vitamin D deficiency in the pathogenesis of ARF and its impact on disease phenotype.