LEVEL OF 25-HYDROXYVITAMIN D IN PEDIATRIC ARTHRITIS PATIENTS

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Vitamin D deficiency is common and widespread globally. Vitamin D has an immunomodulatory effect, but it is still unclear whether its deficiency is associated with higher disease activity. The aim of this retrospective study was to determine the serum concentration of vitamin D in children with paediatric arthritis (juvenile idiopathic arthritis and reactive arthritis). Prevalence of hypovitaminosis D among 98 children with juvenile idiopathic arthritis and reactive arthritis was determined and association between serum concentration of vitamin D and disease activity markers was found. Prevalence of vitamin D deficiency among children included in this study was 69.07%. Children with juvenile idiopathic arthritis had a significantly lower vitamin D level than children with reactive arthritis. There was a statistically significant moderate negative correlation between serum concentration of vitamin D and patient age, as well as a weak negative correlation between vitamin D level and patient body mass index. The significant correlations found between vitamin D level and inflammatory markers indicate that further research on the role of vitamin D in disease activity is needed.

Key words: vitamin D, juvenile idiopathic arthritis, reactive arthritis.

INTRODUCTION

Vitamin D deficiency is common and widespread globally. On average, 13% of Europeans have a vitamin D level below 30 ng/ml, which is considered as a deficit (Cashman *et al.*, 2016). Vitamin D has traditionally been important in the metabolism of calcium and phosphorus, but in recent years new evidence has shown that vitamin D plays a major role in the regulation of immunity and that its deficiency is associated with a more severe course of rheumatic diseases. For several years, vitamin D has been known to have an immunomodulatory effect (Myszka *et al.*, 2014), but it is still unclear whether its deficiency is associated with higher disease activity in rheumatologic patients.

Vitamin D is capable of binding to the vitamin D receptor (VDR), which is found in many target tissues such as bones, intestines, kidneys and brain (Christakos *et al.*, 2003; Pike and Meyer, 2012). Vitamin D receptor (VDR) plays an im-

portant role in achieving the biological effects of vitamin D. It is a hormonal receptor found in the cell nucleus and is specifically activated by 1,25(OH)₂D₃ (Yasmin *et al.*, 2005; Pike *et al.*, 2012). VDR binds to 1,25(OH)₂D₃, and regulation of gene transcription is carried out, which results in production of specific proteins that implement vitamin D₃ functions.

Many tissues and immune cells express VDR and enzymes required for local 1,25(OH)₂D₃ production. The activity of these enzymes is induced by other unknown factors. By discovering these factors, it could be easier to understand the role of vitamin D in pathogenesis of autoimmune diseases (Raman *et al.*, 2011).

More than 200 single nucleotide polymorphisms (SNPs) that determine the activity of this receptor have been detected in the VDR gene. VDR polymorphic alleles are risk factors for diseases such as celiac disease, SLE, autism

spectrum disorders and many others (Booth *et al.*, 2016; Cieřlińska *et al.*, 2017). Studies are ongoing to investigate the effects of VDR polymorphisms on the risk of developing rheumatoid arthritis (RA). Kalthoum and Kamel (2015), in a meta-analysis of 12 studies, concluded that the VDR gene *TaqI* and *FokI* polymorphisms have an impact on the risk of RA development.

1,25(OH)₂D acts on the immunity through VDR located in most of the cells in immune system, especially antigen presenting cells — monocytes, macrophages and dendritic cells. Further, 1,25(OH)₂D induces hereditary immunity and inhibits the acquired immunity. Thus, vitamin D plays a role in both infections and autoimmune diseases (Mangin *et al.*, 2014).

Vitamin D can modulate cytokine response and reduce Toll-like receptor (TLR) activation, thereby reducing both local and systemic inflammation (Jeng *et al.*, 2009). 1,25(OH)₂D₃ acting on monocyte VDR induces the expression of antimicrobial peptide (antimicrobial peptide (AMPs), such as cathelicidin and beta defensin (Mangin *et al.*, 2014). As VDR are found in many different cells of the immune system, including dendritic cells and activated T-lymphocytes, the effect of vitamin D on acquired immunity can be realised directly by action on T-lymphocytes and indirectly by modulating the response of dendritic cells. *In vitro* vitamin D can inhibit monocyte differentiation into dendritic cells and stimulate the development of dendritic cells with tolerogenic properties, i.e. the ability to be immunolabeled (Penna and Adorini, 2000). Vitamin D has also been reported to inhibit the production of CD4 + T-lymphocyte interferon γ (Staeva-Vieira and Freedman, 2002) and interleukin 17 (IL-17) (Ikeda *et al.*, 2010).

Tumour necrosis factor-alpha (TNF- α) is a cell signalling protein. It is one of the cytokines that creates the acute phase reaction. TNF- α is mainly produced by activated macrophages, although it can also be secreted by many other cell types, such as CD4 + lymphocytes, NK cells, neutrophils, white cells, eosinophilic leukocytes, adipocytes, fibroblasts, and neurons (Popa *et al.*, 2007). Many TNF- α -producing cell nuclei contain VDR (Cantoma, 2000; Cantorna *et al.*, 2004), making it difficult to distinguish specific mechanisms by which 25(OH) vitamin D can affect circulating TNF- α concentrations. Experimental results show that vitamin D can suppress TNF- α production. Studies with humans show a positive effect of vitamin D on TNF- α concentration. For example, in patients with chronic heart failure serum TNF- α levels gradually increased during a period of nine months, whereas in patients with the same diagnosis, supplemented with vitamin D therapy (2000 IU/day), serum TNF- α remained constant (Schleithoff *et al.*, 2006). Similarly, treatment with calcitriol (1,25(OH)₂D₃) for six months in postmenopausal women with osteoporosis resulted in a significant decrease in serum TNF- α concentration (Inanir *et al.*, 2004).

Recently, evidence has come to light that the risk of developing various diseases depends on the birth season. A retro-

spective study conducted in 2015 analysed the levels of serum 25-hydroxyvitamin D in 1,145 adult patients who were stratified according to year of birth. Serum vitamin D levels were significantly lower in patients born in winter than those born in spring and summer. Specifically, the winter season was associated with an 11% higher risk of developing vitamin D deficiency later in life compared to springtime when there is a longer period of daylight (Lippi *et al.*, 2015). However, in a similar study conducted in Norway in 2016, in which 10 203 patients were studied, no relationship was found between the month of birth and the level of vitamin D in later life (Zostautiene *et al.*, 2016).

The aim of our study was to determine the level of vitamin D in patients with juvenile idiopathic arthritis and reactive arthritis. In Latvia, vitamin D levels in children with arthritis have not been analysed.

MATERIALS AND METHODS

In a retrospective study conducted from 2016 to 2017, 98 patients at the Children's Clinical University Hospital "Gaiēzers" were analysed. Patient age was from 1 to 18 years (average 12.28 $\pm$ 4.26 years). The group consisted of 59 girls and 35 boys diagnosed with juvenile idiopathic arthritis (JIA) and reactive arthritis (ReA).

The patients were divided into two groups according to diagnosis — patients with JIA (n = 55) and patients with post-viral ReA (n = 40). We analysed separately the JIA patient group with severe disease — high disease activity, persistent high disease activity, polyarthritis and frequent flares (n = 22).

The following parameters were collected from patient medical records — date of birth, age, sex, height, weight, calculated body mass index (BMI), total 25(OH) vitamin D in serum, rheumatoid factor (RF), antinuclear antibodies (ANA), anti-DNA antibodies (anti-dsDNA), TNF-alpha (TNF α), leukocytes count (WBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), haemoglobin level (Hb), and HLA-B27. The serum concentration of 25(OH) D was determined by immune chemiluminescence (Roche).

The average vitamin D levels were determined for children born each month. We also calculated the average UV index of each month in 2017, based on data of the Latvian Environment, Geology and Meteorology Agency (www.meteo.lv).

Statistical analysis was performed using IBM SPSS 22.0.

RESULTS

The determined values of vitamin D, body mass index (BMI) and laboratory markers of autoimmunity are shown in Table 1. The average level of vitamin D among patients was low: 25.26 $\pm$ 9.02 ng/ml with range from 8.17 to 52.71 ng/ml (Fig. 1). Vitamin D levels in girls were significantly

Table 1

MINIMUM, MAXIMUM, AND MEAN VALUES FOR VITAMIN D, INFLAMMATORY MARKERS AND BMI IN THE JIA AND REA PATIENT GROUPS

Patient groups		25(OH)D, ng/ml	RF, IU/ml	ANA, IU/ml	BMI, kg/m ²
ReA	n	39	34	28	31
	Min	11.84	3.1	Neg	14.05
	Max	45.81	8.6	Neg	24.69
	Mean	27.44	6.93	Neg : pos = 23:5	17.85
<i>p</i> *		0.036	0.028	0.029	
JIA	n	59	52	43	40
	Min	8.17	4.8	Neg	14.95
	Max	52.71	121.4	Pos	29.38
	Mean	24.12	10.21	Neg : pos = 27:16	19.83

*p** – comparing JIA and ReA patient groups; data are statistically significant if *p* < 0.05.

Fig. 1. Normal distribution of serum vitamin D levels among all patients included in the study (red marked 30 ng/ml; the lower level being considered as vitamin D deficiency).

lower than in boys (24.05 ng/ml and 28.09 ng/ml, respectively; *p* = 0.022). In children with juvenile idiopathic arthritis, the average vitamin D level (24.12 ng/ml, range 8.17–52.71 ng/ml) was significantly lower (*p* = 0.036) than in children with reactive arthropathy (27.44 ng/ml; range 11.84–45.81 ng/ml).

We tested for differences in laboratory data for patient groups depending on vitamin D levels (Table 2). Vitamin D deficiency (25(OH) D below 30 ng/ml) was found in a total of 69.07% of children (*n* = 67). A statistically significant difference (*p* = 0.008) was observed between RF levels in patients with vitamin D deficiency (25(OH) D below 30 ng/ml) and normal vitamin D levels (25(OH) D below 30 ng/ml) (see Table 2). A statistically significant difference between these groups was also observed for the level of

Table 2

MEAN VALUES OF AGE, BMI AND INFLAMMATORY MARKERS IN PATIENTS WITH AND WITHOUT VITAMIN D DEFICIENCY

Parameters	25(OH)D below 30ng/ml (n = 67)	25(OH)D higher than 30ng/ml (n = 32)	<i>p</i> *
25(OH)D, ng/ml	20.58 ± 5.29	36.97 ± 5.69	0.000*
Age, years	13.32 ± 3.66	9.9 ± 4.79	0.491
RF, IU/ml	7.47 ± 3.50	11.48 ± 21.59	0.008*
anti-DNA, IU/ml	8.15 ± 5.87	8.61 ± 6.61	0.033*
TNF-α, pg/ml	6.82 ± 2.68	8.11 ± 3.70	0.688
CRP, mg/l	1.86 ± 7.55	2.74 ± 7.04	0.013*
ESR, mm/h	6.81 ± 7.03	13.29 ± 17.43	0.620
WBC, ×10 ³ /ul	7.67 ± 2.48	8.84 ± 3.37	0.997
Hb, g/dl	13.56 ± 1.27	13.02 ± 0.93	0.130
BMI, kg/m ²	19.71 ± 3.43	17.01 ± 2.30	0.001*

*p** – data statistically significant if *p* < 0.05.

anti-DNA antibodies (*p* = 0.033), CRP (*p* = 0.013) and BMI (*p* = 0.001).

The 25 (OH) D level was significantly correlated with TNF-alpha and ESR both in the JIA group and in the overall patient population (Table 3). There is a statistically significant moderate negative correlation between vitamin D level and patient age (*r* = 0.443; *p* = 0). This correlation is also seen in JIA patients (*r* = 0.481; *p* = 0). There is a weak negative correlation between vitamin D level and BMI, which was statistically significant (*r* = 0.372, *p* = 0.002). There was also a moderate correlation between anti-DNA antibody and vitamin D level (*r* = -0.401, *p* = 0.017, *n* = 36) in the arthropathy group.

There was a weak negative correlation between the mean monthly value of vitamin D for children and the average monthly UV index, which was not statistically significant (*r* = 0.395, *p* = 0.204) (Fig. 2).

The average total leukocyte count (WBC) in both JIA and ReA patients was 8.08 ± 2.89 (4–20.2) thousands per 1 mm³ of peripheral blood. There was no statistically significant difference in leukocyte count between JIA and ReA patients (*p* = 0.153). There was also no statistically significant correlation between vitamin D level and leukocyte count.

DISCUSSION

The results of literature on the level of vitamin D in children with arthritis are contradictory. The average vitamin D level among patients included in our study was 25.26 ± 9.02 (8.17–52.71) ng/ml. In a comparative study of 50 JIA patients living in Brazil, the average vitamin D level was 31.6 ± 10.0 ng/ml, which was higher than in the control group of 30.4 ± 5.7 ng/ml (*p* > 0.05) (De Sousa Studart *et al.*, 2015). However, Stagi *et al.* (2014) reported a significantly lower

Table 3

CORRELATIONS BETWEEN SERUM 25 (OH) D LEVELS AND INFLAMMATORY MARKERS, AGE AND BMI

Patient groups		RF, IU/ml	anti-DNA, IU/ml	TNF- α , pg/ml	CRP, mg/l	ESR, mm/h	WBC, $\times 10^3/\mu\text{l}$	Hb, g/dl	Age, years	BMI, kg/cm^2
Reactive arthritis	<i>R</i>	0.18	-0.401	0.39	-0.01	-0.036	0.164	-0.247	-0.31	-0.39*
	<i>p</i> *	0.919	0.017*	0.081	0.941	0.852	0.338	0.153	0.055	0.031
JIA (with severe JIA)	<i>R</i>	-0.042	0.03	0.698	0.2	0.769	0.499	-0.107	-0.69	-0.434
	<i>p</i> *	0.869	0.898	0.008*	0.425	0.001*	0.042*	0.672	0.001*	0.121
JIA (patients with moderate and self-limiting course)	<i>R</i>	0.154	0.142	0.381	0.092	0.446	0.19	0.032	-0.481	-0.305
	<i>p</i> *	0.284	0.306	0.024*	0.521	0.002*	0.165	0.803	0.000*	0.059
All patients	<i>R</i>	0.107	-0.029	0.347	0.024	0.303	0.145	-0.041	-0.443	-0.372
	<i>p</i> *	0.331	0.79	0.009*	0.874	0.007*	0.17	0.701	0.000*	0.002*

*p** data statistically significant if $p < 0.05$. BMI, body mass index; JIA, idiopathic arthritis.

Fig. 2. Average vitamin D concentration in patients depending on their birth month average UV Index.

Data of Latvian Environment, Geology and Meteorology Centre, 2017

level of 25(OH)D in patients with JIA than in the control group ($p < 0.001$). In JIA patients in Turkey, an average vitamin D level of 17.7 ± 11.6 ng/ml was observed (Çomak *et al.*, 2014). In Latvia, the vitamin D level has also been studied in the adult population. Semjonova and Rasa (2012) analysed data of 3868 people and determined that the average vitamin D level was 21.1 ng/ml, which was lower than in our study — 25.26 ± 9.02 (8.17–52.71) ng/ml. In a similar study using 4809 patient data from the Latvian Central Laboratory database, the average level of 25(OH) vitamin D was 20.1 ng/ml (Mukane *et al.*, 2015).

In JIA patients in Turkey, an average vitamin D level of 17.7 ± 11.6 ng/ml was observed, of whom in 53.2% of patients the serum 25 (OH) vitamin D was below 15 ng/ml (Çomak *et al.*, 2014). Similar data were obtained in our study — a 25(OH) vitamin D level below 30 ng/ml was found in 72.41% JIA patients, and a level below 15 ng/ml only in 12.07%.

In literature, female gender is often referred to as a risk factor for hypovitaminosis D (Mithal *et al.*, 2009; Verdoia *et al.*, 2015). For example, Verdoia *et al.* (2015) reported that women had not only lower vitamin D levels than men (14.5 ± 10.9 vs. 15.9 ± 9.5 ng/ml; $p = 0.007$), but also more frequent severe vitamin D deficiency (41.9% vs. 30.4%, $p < 0.001$). Also, in our study 25 (OH) vitamin D serum levels in girls were on average lower than in boys, 24.05 ng/ml and 28.09 ng/ml, respectively ($p = 0.022$). The low level of vitamin D in women compared to men is explained by the

fact that vitamin D is deposited in adipose tissue and women have a higher percentage of body fat (Gharaibeh *et al.*, 2009).

Many literature sources have reported a negative association between vitamin D level and age (Mithal *et al.*, 2009; Anonymous, 2014; Hajjaj-Hassouni *et al.*, 2017). This trend might be explained by vitamin D replacement therapy given often to infants and toddlers, which is discontinued as the child grows. Also, older children and adolescents tend to spend more time indoors.

A negative correlation between vitamin D level and body mass index (BMI) has been described in literature (O'Dell *et al.*, 2002; Rovner et O'Brien, 2008; Anonymous, 2014; Bani-issa *et al.*, 2017; Elizondo-Montemayor *et al.*, 2017; Hajjaj-Hassoun *et al.*, 2017; Kumaratne *et al.*, 2017). For example, Bani-issa *et al.* (2017) found that in patients with BMI of $30 \text{ kg}/\text{m}^2$ or more, there was a risk of more than five times for vitamin D deficiency than for patients with BMI below $25 \text{ kg}/\text{m}^2$. A negative association between the patient's BMI and serum vitamin D levels was also observed in our study ($r = -0.372$; $p = 0.002$), which is similar to the results of Sadiya *et al.* (2014) ($r = 0.15$; $p = 0.01$). Wortsman *et al.* (2010) reported a correlation $r = -0.55$ ($p = 0.003$) in study groups with adipose and normal body mass, and suggested that adipose persons have reduced bioavailability of vitamin D from skin and dietary sources, because vitamin D tends to deposit in adipose tissue. Other authors consider that vitamin D hypovitaminosis in adipose

patients is explained by the synthesised and absorbed volumetric dilution of vitamin D, rather than sequestration in increased fat tissue (Drincic *et al.*, 2012). It is also possible that adipose patients have less exposure to direct sunlight due to reduced physical activity (Cheng *et al.*, 2010; Ahmadi *et al.*, 2013). In some studies, no correlation was found between vitamin D levels and BMI (De Sousa Studart *et al.*, 2015).

In children with juvenile idiopathic arthritis, vitamin D levels were significantly ($p = 0.036$) lower (23.71 (8.17–52.71) ng/ml) than in children with reactive arthritis — 27.44 (11.84–45.81) ng/ml. The available literature does not report any difference in vitamin D levels between JIA and ReA patients. De Sousa Studart *et al.* (2015) found that vitamin D levels were higher in JIA patients than in a control group, which might be due to vitamin D substitution in the JIA patient group. In another study, patients with JIA showed statistically significant lower levels of 25 (OH) vitamin D compared to a control group ($p < 0.001$), which was also observed for different forms of JIA (oligoarticular form — $p < 0.05$; polyarticular form — $p < 0.005$; systemic form — $p < 0.001$; enthesitis associated form — $p < 0.005$) (Stagi *et al.* 2014).

In our study, positive correlation between ESR and vitamin D was found ($r = 0.303$; $p = 0.007$), which was also found in the severe form JIA patient group ($r = 0.769$; $p = 0.001$). These correlations contradict previous studies that found negative correlations, which are currently explained by the potential properties of vitamin D to reduce autoimmune disease activity. For example, Kavellou-Athanassiou *et al.* (2012) found a negative correlation between ESR and vitamin D levels ($r = -0.18$) in a study on effect of vitamin D effect on RA disease activity. In a study on 294 patients with type 2 diabetes mellitus (Kaya *et al.* 2018), ESR was higher in patients with vitamin D deficiency ($p < 0.001$) and there was a negative correlation between ESR and vitamin D level ($r = 0.256$; $p < 0.001$). However, there are studies where no association between vitamin D levels and ESR was found (Yildirim *et al.*, 2013).

Positive correlations have also been found between vitamin D and TNF-alpha levels ($r = 0.347$; $p = 0.009$), which is contrary to current literature, where a negative correlation is described (Peterson *et al.*, 2008; Bellia *et al.*, 2013; de Souza *et al.*, 2016; Elizondo-Montemayor *et al.*, 2017). Rodriguez *et al.* (2018) in a meta-analysis showed that patients given vitamin D had lower levels of TNF-alpha compared to control groups ($n = 0.380$; $p = 0.04$). Azizieh *et al.* (2016) found that there was no statistically significant difference between TNF- α levels in women with vitamin D deficiency (in this case below 25 nmol/l) compared to those with levels higher than 25 nmol/l ($p = 0.724$), although the mean level of TNF- α was slightly higher in the vitamin D deficiency group (9.90 vs. 9.75 pg/ml). In our study, patients with vitamin D levels below 30 ng/ml had, on average, a lower TNF- α level (6.82 ± 2.68 pg/ml) compared to patients with levels higher than 30 ng/ml (8.11 ± 3.70 pg/ml), but this difference was not significant ($p = 0.688$).

The statistically significant positive correlations found between vitamin D levels and ESR ($r = 0.303$; $p = 0.007$) and TNF-alpha levels ($r = 0.347$; $p = 0.009$) require further study.

Several studies have found a negative correlation between vitamin D level and CRP: for example, Kavellou-Athanassiou *et al.* (2012) — $r = 0.115$, Eleftheriadis *et al.* (2012) — $r = -0.360$; $p = 0.04$, Ashraf *et al.* (2012) — $r = -0.25$; $p = 0.049$, Wang *et al.* (2018) — $r = 0.231$; $p = 0.004$. Some studies did not find such correlation (Petersen *et al.*, 2008; Michos *et al.*, 2009; Yildirim *et al.*, 2013). Also, our data showed no statistically significant correlation in any group of patients: neither in all included patients ($r = 0.044$; $p = 0.687$) nor in the JIA group ($r = 0.092$; $p = 0.521$), nor in patients with ReA ($r = -0.013$; $p = 0.941$).

JIA patients in our study were significantly more likely to have positive antinuclear antibodies (ANA) compared to ReA patients ($p = 0.029$). Comparison of vitamin D levels in ANA positive patients and ANA negative patients suggests that D vitamin is significantly lower in ANA positive patients (17.4 versus 29.4 ng/ml; $p < 0.01$). Also, Ritterhouse *et al.* (2011) reported that ANA positive SLE patients were more likely to have vitamin D deficiency (below 20 ng/ml) compared to ANA negative SLE patients ($p = 0.011$).

Literature provides data on negative correlation between vitamin D and anti-DNA antibody levels (Bonakdar *et al.*, 2011; Szodoray *et al.*, 2011; Mok *et al.*, 2012; AlSaleeme *et al.*, 2015). For example, Mok *et al.* (2012) reported a weak negative correlation ($r = -0.13$; $p = 0.02$). Our study also found significant negative correlation between vitamin D and anti-DNA antibody levels in patients with reactive arthritis ($r = 0.401$; $p = 0.017$). On the other hand, Thudi *et al.* (2008) found a higher anti-dsDNA titre in a small systemic lupus erythematosus (SLE) patient cohort with vitamin D levels higher than 47.7 nmol/l, compared to patients with 25 (OH) D lower than 47.7 nmol/l ($p = 0.0069$) ($n = 37$). Our study also found a significant difference between anti-DNA antibody levels in patients with and without vitamin D deficiency (8.15 ± 5.86 versus 8.61 ± 6.61 IU/ml; $p = 0.013$).

There was no association between vitamin D and haemoglobin level ($r = -0.041$; $p = 0.701$). Also, Ernst *et al.*, 2016) observed that vitamin D therapy had no effect on anaemia patients. In a study of 50 children diagnosed with sickle cell anaemia (Busse *et al.* 2013), a negative association occurred between vitamin D and haemoglobin levels ($p = 0.017$).

The effect of vitamin D on the number of leukocytes is contradictory in the literature. De Oliveira *et al.* (2017) describe a negative correlation between these parameters. In contrast, Soliman *et al.* (2012) found no relationship between vitamin D level and red blood cell count, nor between vitamin D and white blood cell count. In our study, total number of leukocytes (WBC) in both JIA and ReA patients was on average 8.08 ± 2.89 (4–20.2) thousands per 1 mm³ of peripheral blood. There were no significant differences in the

number of leukocytes between JIA and ReA patients ($p = 0.153$)

Similar to Zostautiene *et al.* (2016), we also did not find a statistically significant correlation between vitamin D levels and the birth season ($r = 0.395$, $p = 0.204$). However, it should be noted that the patients included in the study were generally born during the “dark” months of the year (57:43), which suggest that children born in these months have a tendency to rheumatic diseases. This phenomenon could not be explained by a general increase in birth rates during the “dark” months of the year, as more children are born in the summer months, according to information published on the Central Statistical Bureau of Latvia website. It is possible that a child's birth season affects the risk of developing rheumatologic diseases, because the mothers of these children have had a vitamin D deficiency during their pregnancy. For example, Molla *et al.* (2005) show that 40% of mothers and 60% of newborns have vitamin D deficiency on their birthday and these values were closely correlated ($r = 0.790$, $p < 0.001$). Also, Nesby-O'Dell *et al.* (2002) pointed out that one of the main risk factors for infant vitamin D deficiency is deficiency in mothers during pregnancy.

Since individual authors have discovered that neither the oral administration of vitamin D to patients nor exposure to sunlight has a significant effect on 25-(OH) D levels (Elizondo-Montemayor *et al.*, 2017), apparently there are still unknown factors determining level of vitamin D.

CONCLUSIONS

Vitamin D deficiency is common among both JIA and reactive arthritis patients. Overall, average the vitamin D level among all patients included in the study was 25.26 ± 9.02 ng/ml. In children with JIA, vitamin D levels were significantly lower compared to children with reactive arthritis ($p = 0.036$).

The vitamin D levels in girls were lower than in boys ($p = 0.022$). There was a significant moderate negative correlation between vitamin D level and patient age ($r = 0.443$; $p = 0$). There was a weak negative correlation between vitamin D level and BMI, which was statistically significant ($r = 0.372$, $p = 0.002$).

Detected positive correlations between vitamin D levels and ESR ($r = 0.303$; $p = 0.007$) and TNF-alpha levels ($r = 0.347$; $p = 0.009$) require further study.

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25 – HIDROKSIVITAMĪNA D LĪMENIS PACIENTIEM AR JUVENĪLU IDIOPĀTISKU ARTRĪTU UN REAKTĪVU ARTRĪTU

D vitamīna deficīts ir plaši izplatīts un sastopams visā pasaulē. Lai gan jau vairākus gadus ir zināms, ka D vitamīnam piemīt imūnmodulators efekts, joprojām nav skaidrs, vai tā deficīts ir asociēts ar augstāku slimības aktivitāti reimatoģiskajiem pacientiem. Šī retrospektīvā pētījuma mērķis bija noskaidrot D vitamīna līmeni bērniem ar juvenīlu artrītu un reaktīvu artrītu. Pētījumā tika noskaidrota D hipovitaminozes prevalence 98 bērniem ar juvenīlu idiopātisku artrītu (JIA) un reaktīvo artrītu (ReA), kā arī meklētas asociācijas starp seruma D vitamīna koncentrāciju un slimību aktivitātes marķieriem. Pētījumā iesaistītajiem pacientiem D vitamīna deficīts bija novērojams 69,07% gadījumu. Bērniem ar JIA D vitamīna līmenis bija statistiski ticami zemāks, salīdzinot ar bērniem, kuriem bija reaktīvs artrīts. Tika konstatēta arī statistiski ticama vidēji cieša negatīva korelācija starp D vitamīna līmeni un pacienta vecumu, kā arī vāja negatīva korelācija starp D vitamīna līmeni un ķermeņa masas indeksu. Noskaidrotās atsevišķās korelācijas ar iekaisuma marķieriem parāda, ka nepieciešama turpmāka D vitamīna un slimības aktivitātes asociāciju izpēte.