3. Borisov DA, Saidasheva EI, Dautova ZA, et al. [Ocular surface in long terms of ortokeratology lenses's use in adolescents with myopia]. Oftalmolohiia. 2020;17(2):223-8. Russian.
doi: https://doi.org/10.18008/1816-5095-2020-2-223-228

4. Efron N, Pritchard N, Brandon K, et al. A survey of the use of grading scales for contact lens complications in optometric practice. Clinical and Experimental Optometry. 2011;94(2):193-9.
doi: https://doi.org/10.1111/j.1444-0938.2010.00549.x

5. Zha Y, Zhu G, Zhuang J, et al. Axial length and ocular development of premature infants without ROP. Journal of ophthalmology. 2017. ID 6823965.
doi: https://doi.org/10.1155/2017/6823965

6. Lee YC, Wang JH, Chiu CJ Effect of orthokeratology on myopia progression: twelve-year results of a retrospective cohort study. BMC ophthalmology. 2017:17(1):1-8.
doi: https://doi.org/10.1186/s12886-017-0639-4

7. Kang P, Watt K, Chau T, et al. The impact of orthokeratology lens wear on binocular vision and accommodation: A short-term prospective study. Contact Lens and Anterior Eye. 2018;41(6):501-6.
doi: https://doi.org/10.1016/j.clae.2018.08.002

8. Gifford KL, Gifford P, Hendicott L, et al. Zone of clear single binocular vision in myopic orthokeratology. Eye & contact lens. 2020;46(2):82-90.
doi: https://doi.org/10.1097/ICL.0000000000000614

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CHARACTIRESTICS OF VITAMIN D LEVEL IN PATIENTS WITH ATOPIC DERMATITIS

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Key words*: atopic dermatitis, vitamin D*
Ключові слова: *атопічний дерматит, вітамін Д*

Abstract. Charactirestics of vitamin D level in patients with atopic dermatitis. Garibeh E., Bondar S.A., Tokarchuk N.I., Vyzgha Y.V. *The peculiarity of the skin is that it acts not only as a place of synthesis of vitamin D, but also as an organ targeted for its biologically active form. The aim of our study was to analyze the level of vitamin D in*

patients with atopic dermatitis. There were examined 48 people aged between 18 to 55 years; they are residents of Vinnytsia and Vinnytsia region. Serum levels of vitamin D, total IgE and eosinophilic cationic protein (ECP) were determined in the subjects. The average level of vitamin D in the serum of patients with atopic dermatitis was 19.2 [11.3-25.4] ng/ml, which corresponded to a deficiency. Among those surveyed, vitamin D deficiency was found in 68.4±4.7% (n=26) while vitamin D insufficiency in 31.6±4.5% (n=12). The severe course of the disease prevailed among patients aged 18-40 years (63.33±8.79) % more than in the age group of 41 years and older, (36.67±8.8%, p<0.05; OR=2.98, S=0.53, 95% SI:1.04-8.52). The proportion of people with vitamin D deficiency and moderate severity of atopic dermatitis was 62.5% (n=10) with a median level of 14 [8.3–19] ng/ml, and patients with severe atopic dermatitis made up 90.9% (n=20) (χ^2=4.6; p=0.023), in which the median level of vitamin D was 14 [8.3-19] ng/ml. Serum vitamin D levels were in the zone of deficiency in patients with moderate and severe atopic dermatitis. Vitamin D deficiency was significantly more common in the group of patients with elevated levels of allergic inflammation markers. A positive correlation of medium strength between the level of vitamin D and ECP in the serum of patients with atopic dermatitis (rs=0.53, p<0.001), was revealed.

Реферат. Особливості забезпеченості вітаміном D хворих на атопічний дерматит. Гарібех Е., Бондар С.А., Токарчук Н.І., Вижга Ю.В. *Унікальність шкіри полягає в тому, що вона виступає не лише місцем синтезу вітаміну D, а і є органом – мішенню для біологічно активної його форми. Метою нашого дослідження був аналіз забезпеченості вітаміном Д хворих на атопічний дерматит. Методи. Обстежено 48 осіб віком від 18 до 55 років, мешканців м. Вінниці та Вінницької області. В обстежених визначали рівень вітаміну Д в сироватці крові, еозинофільний катіонний білок (ЕКБ). Результати. Середній рівень вітаміну D в сироватці крові хворих на атопічний дерматит становив 19,2 [11,3–25,4] нг/мл, що відповідало дефіциту. Серед обстежених дефіцит було виявлено в 68,4±4,7% (n=26) осіб та недостатність вітаміну D мали 31,6±4,5% (n=12) осіб. У хворих на атопічний дерматит тяжкий перебіг захворювання переважав серед осіб віком 18-40 років (63,33±8,79%), ніж у віковій групі 41 і більше років, (36,67±8,8%, p<0,05; OR=2,98, S=0,53, 95% CI: 1,04-8,52). При середньому ступені тяжкості атопічного дерматиту частка осіб з дефіцитом вітаміну Д становила 62,5% (n=10) з медіаною його рівня 14 [8,3-19] нг/мл, а пацієнти з тяжким перебігом становили 90,9% (n=20) (χ^2=4,6; p=0,023), у яких медіана рівня вітаміну Д набувала значення 14 [8,3-19] нг/мл. Висновки. Рівень вітаміну D в сироватці крові знаходився в зоні дефіциту у хворих на атопічний дерматит при середньотяжкому та тяжкому перебігу захворювання. Дефіцит вітаміну D достовірно частіше мав місце в групі хворих із підвищеними показниками алергологічного запалення. Виявлено позитивний кореляційний зв'язок середньої сили між рівнем вітаміну D та ЕКБ в сироватці крові у хворих на атопічний дерматит (rs=0,53, p<0,001).*

Atopic dermatitis is a chronic or recurrent skin disease caused by a complex interaction between genetic, immunological and environmental factors which is characterized by chronic inflammation, disturbance of the epithelial barrier and elevated serum IgE levels [14].

The skin is one of the largest human organs, it performs a number of important vital functions. The uniqueness of the skin also lies in the fact that it is not only a place of synthesis of vitamin D, but also is an organ that is a target for its biologically active form [2].

Today, researches have been conducted on the relationship between vitamin D deficiency and the development of atopic dermatitis (AD). So, we know that in the dermal layer of the skin vitamin D3 is formed from provitamin. Keratinocytes express high levels of 1α-hydroxylase, so the skin is able to respond to an active metabolite of vitamin D. In turn, vitamin D affects the various functions of the skin such as keratinocyte proliferation and differentiation, their apoptosis and other immunoregulatory processes [13].

The special role of vitamin D is to ensure the barrier function of the skin. Vitamin D modulates the structural proteins of the stratum corneum of the dermis and regulates glyceramides needed for the hydrating protective lipid barrier that supports skin hydration. The importance of vitamin D in stimulating the synthesis of filagrin; which in turn plays a key role in the formation of the skin barrier, has also been proven [9].

In addition to the above, calcitriol enhances antimicrobial protection by stimulating the formation of immune proteins in skin cells – antimicrobial peptides, which are a chemical component of the epidermal barrier and, thus, prevents the appearance of infectious skin lesions. Therefore, since vitamin D has immunomodulatory properties and improves the skin barrier, it most likely plays the role in the development of AD and in the suppression of chronic inflammation of the skin. The role of vitamin D in the regulation of allergic inflammation is being studied. Thus, according to the literature, both 1.25(OH)2D and vitamin D receptor (VDR) have an inhibitory effect on the production of monocytes through Toll-like receptors, reduce the activity of dendritic cells, reduce the release rate of mast cells and interleukin 10 (IL-10), reduce the amount proinflammatory cytokines from Th1 cells and inhibit the release of IgE. According to studies, the active form of vitamin D3 has a direct effect on undifferentiated and inactivated T-helpers, T-regulators, and activated T-cells. Mast cells – are proinflammatory effector

cells that can act as initiators and powerful amplifiers of IgE – dependent inflammatory and allergic reactions. Mast cells express the high-affinity IgE receptor FcεRI, which, upon activation by polyvalent-induced antigen aggregation of FcεRI-bound IgE, stimulates the secretion of vasoactive amines, as well as synthesized de novo proinflammatory lipid mediators, cytokines and chemokines. Under certain conditions, when elimination of infectious agents is required, IgE-mediated activation of mast cells is useful. However, according to the literature, hormone of secosteroids vitamin D3 is a decisive immunoregulatory agent, in has a broad anti-inflammatory effect through nuclear VDR [15].

It is known that VDR activity in mast cells represents important mechanisms by which metabolites of vitamin D3, 25OHD3 and 1α,25(OH)2D3 can inhibit clear IgE activated mast cell activation in vitro and in vivo [4].

Eosinophilic cationic protein (ECP) is one of the major proteins contained in the granules of eosinophils and is a marker of eosinophil-mediated allergic inflammatory process. The basis of modern mechanism of AD is supplemented by association of disease with elevated eosinophil cationic protein. However, data about the diagnostic value of ECP in AD are few and contradictory [8].

Also, Vitamin D has the quality of a protective factor which enhances the properties of skin barrier on one side, yet on the other side it is considered as one of the factors leading to the development of atopic dermatitis.

Nevertheless, there is a vicious circle, disruption of the skin functioning in chronic diseases (increased proliferation and disorder of differentiation of keratinocytes) leads to loss of adequate vitamin D synthesis and subsequent reduction of calcidiol in humans [6].

Therefore, it is assumed that vitamin D deficiency may contribute to the development of AD due to impaired epidermal barrier function and immunological disregulations with subsequent disorder of infectious protection.

Therefore, there are some conflicting reports that indicate or deny the role of vitamin D about the positive association of vitamin D deficiency and its risks in the development of AD.

Thus, in addition to the classic phosphorus-calcium effect of vitamin D, it also plays a role in functioning of many organs and tissues, including the skin. Vitamin D plays a pleiotropic effect in the skin (immunomodulator, anti-proliferative, antiapoptic, etc.).

Despite the large amount of research and published data on the topic of atopic dermatitis, today there are a number of unresolved issues. One of them is the lack of assessment of the relationship between the indicators of allergic inflammation and the level of vitamin D in the serum of patients with AD.

The aim of our study was to analyze the level of vitamin D in patients with AD.

The hypothesis of the study: the possibility of using the determination of the level of vitamin D in the serum of patients with AD to assess the severity of the disease and the relationship with the markers of allergic inflammation.

MATERIALS AND METHODS OF RESEARCH

The study was approved by the Commission on Biomedical Ethics for compliance with moral and legal rules of medical research of the National Pirogov Memorial Medical University (protocol No. 10 from 12.12.2019) prior to the research. It has been established that the studies do not contradict basic bioethical norms and comply with the principles of compliance with the basic provisions of the GCP (1996), the Council of Europe Convention on Human Rights and Biomedicine (04.04.1997), the Helsinki Declaration of the World Medical Association on ethical principles of research with human participation (1964-2008) and the order of the Ministry of Health of Ukraine No. 90 dated 23.09.2009 (as amended in accordance with the order of the Ministry of Health of Ukraine No. 523 dated 12.07.2012).

All patients were informed about the purpose and possible consequences of research procedures. All patients signed an informed written consent to participate in the study before the manipulation.

Subjective, objective data, as well as the results of laboratory research methods were entered into specially designed registration cards.

The protocol and implementation of the study followed the basic principles of good medical practice, namely: respect for the individual, patient awareness, risk and benefit assessment.

The work was carried out at the Department of Skin and Venereal Diseases of the National Pirogov Memorial Medical University. There were examined 48 people aged between 18 to 55; residents of Vinnytsia and Vinnytsia region.

The research methodology was based on the use of a systematic approach to a set of studies for patients who applied to a medical institution with complaints that are characteristic of patients with AD. The primary task was to achieve maximum homogeneity of the studied groups of patients.

The criteria for inclusion in the study: patients diagnosed with AD; the study was conducted over the period from October to May; persons who have not taken vitamin D for 6 months, aged 18-55 years.

The main group consisted of 38 patients with AD. The surveyed main groups were divided by age: subgroup I consisted of 20 people aged 18 to 40 years and subgroup II – 18 people aged 41 to 55 years. The control group consisted of 10 healthy individuals. The

average age of the main group was 41.4±0.1 years and almost healthy individuals – 42.5±0.2 years.

All subjects underwent a clinical examination to identify pathological changes in organs and systems. The sociometric survey was conducted by in-depth history taking and questionnaires of both the main group and the control group. Social, household and other features of the life of the subjects, the presence of bad habits in them were specified.

Serum vitamin D levels, eosinophilic cationic protein (ECP) were determined in all subjects. Quantitative immunochemical with electrochemiluminescent detection (ECLIA) was used to determine the concentration of 25(OH)D in the serum; analyzer and test system: Cobas 6000/Cobas 8000; Roche Diagnostics Switzerland). Quantitative immunochemical with electrochemiluminescent detection (ECLIA) was used to determine ESP; analyzer and test system: Cobas 6000/Cobas 8000; Roche Diagnostics Switzerland) [5].

To determine the status of vitamin D, the classification by the International Institute of Medicine and the Endocrine Practice Guidelines Committee was used [3].

Verification of the diagnosis of AD was carried out in accordance to the Recommendations and the treatment of atopic dermatitis of the European Dermatology Forum, 2019 (European Dermatology Forum) and the Unified Clinical Protocol for Atopic Dermatitis No. 670 from 04.07.2016 of the Ministry of Health of Ukraine.

The data were statistically processed using the software package «Statistica 6.1 for Windows», which belongs to M.I. Pirogov VNMU (license No. BXXR901E245722FA). The general statistical analysis involved the calculation of the median and interquartile intervals of Me [UQ-LQ]. For nominal variables correlation was calculated using the criterion of Pearson and Fisher criterion. Assessment direction, strength and significance of correlation between the studied traits were performed using Spearman correlation analysis. The assessment of the impact of adverse factors was performed by calculating the relative risk (RR) and the odds ratio (OR) for the indicator. The Receiver Operating Characteristic Curve (ROC) was analyzed with the definition of AUROC and "cut-off point" [10].

RESULTS AND DISCUSSION

Among the examined patients, women predominated – 60.5% (n=23), men – 39.5% (n=15) ($p<0.005$). The clinical characteristics of the research are presented in the Table. At the time of admission to the hospital, all patients had pronounced clinical manifestations of AD with severe or moderate severity. The average severity was observed in 16 patients (42.1%) with an average value of the SCORAD index – 44±11.2. Severe AD was diagnosed in 22 (57.9%) subjects with a mean value of the SCORAD index – 76.44±11.3. It should be noted that the severe course of the disease prevailed more among individuals aged 18-40 years (63.33±8.79)% than in the age group of 41 years and older (36.67±8.8%, $p<0.05$; OR=2.98, S=0.53, 95% SI: 1.04-8.52).

Clinical characteristics of the study groups

Marker	Main group	Atopic dermatitis (severe form) (n=22)	Atopic dermatitis (mild-severe form) (n=16)	Deference between groups (p)
SCORAD (points)		**76,44±11,3**	**44±11,2**	**p=0,070**
Age distribution: abs. (% in groups):				
18-40 years old	**20 (63,33)**	**16 (80,0)**	**4 (20,0)**	**p=0,007**
41-55 years old	**18 (36,67)**	**7 (38,89)**	**11 (61,11)**	**p=0,007**
Gender distribution: abs. (% in groups):				
male	**15 (39,5)**	**9 (40,9)**	**6 (37,5)**	**p=0,574**
female	**23 (60,5)**	**13 (59,1)**	**10 (62,5)**	
Status of vit D:				
deficiency	**26 (68,4)**	**16 (72,73)**	**10 (62,5)**	**p=0,023**
insuf	**12 (31,6)**	**6 (27,27)**	**6 (37,5)**	
Level of vit D (ng/ml)	**19,2 [11,3-25,4]**	**14 [8,3-19]**	**16,5 [12,7-22,3]**	**p=0,235**
Level of vit D (ng/ml) Depending on age:				
18-40 years	**17,6 [13,4-24,3]**	**15,4 [11,2-21,6]**	**19,6 [16,1-26,5]**	**p=0,013**
41-55 years	**12,5 [10,1-14,3]**	**10,9 [8,8-12,7]**	**16,7 [14,6- 18,9]**	**p=0,017**
Level of ECP (ng/ml)	**43,4 [25,2-65,4]**	**58,74 [53,3-65,4]**	**30,14 [24,8-36,9]**	**p=0,012**

Note: p – significance difference between groups of patients with severe and moderate-severe atopic dermatitis.

AD was characterized by a long course in all examined patients. The duration of the disease ranged from 3 to 45 years, with a mean of 23.5±10.5 years.

The frequency of exacerbations ranged from 3 to 8 times a year. The average frequency of exacerbations in patients with AD with moderate course of disease was 4.4±1.5, while in patients with severe course – 7.2±1.1 ($p<0,005$).

We observed a decrease in the level of vitamin D in the serum of the vast majority of patients with AD, and the average values were in the area of deficiency. Thus, among those surveyed, deficiency was found in 68.4±4.7% (n=26) and vitamin D insufficiency – in 31.6±4.5% (n=12). However, we did not find optimal level of vitamin D in any case among the examined patients.

Analysis of vitamin D in patients depending on the severity of the disease showed that moderate AD proportion of individuals with vitamin D deficiency was 62.5% (n=10) and patients with severe course – 72.73% (n=16) ($\chi^2=4.6$; p=0.023).

According to our research the average level of vitamin D in the blood serum of AD patients was 19.2 [11.3-25.4] ng/ml, which corresponded to the deficit. In patients with severe course of AD median vitamin D level was 14 [8.3-19] ng/ml, with an moderate severity – 16.5 [12.7-22.3] ng/ml.

It should be noted that patients aged 41 and older had significantly lower blood levels of vitamin D 12.5 [10.1-14.3] ng/ml than patients aged 18-40 years in which vitamin D was 17.6 [13.4-24.3] ng/ml, ($p<0.05$).

To assess the status of vitamin D in the subjects, a ROC analysis was performed to determine AUROC. The diagnostic value of the method for determining serum 25(OH)D in patients with AD was maximum. ROC analysis AUROC for vitamin D in patients of subgroup I was in CI 0.8-0.9. Also noteworthy are the results of the diagnostic value of this method in patients of subgroup II, in which the values of the area under the ROC-curve were in CI 0.9-1.0.

Thus, studying the reliability and validity of the diagnostic method for determining the level of 25(OH)D in serum of patients with AD, we believe that this method is highly sensitive and highly specific.

It should be noted that the average level of vitamin D in the blood serum was not gender dependent. However, in women this indicator was 18.32 [12.3-23.3] ng/ml and in men 20.41 [14.4-25.3] ng/ml, ($p>0.05$).

Subsequently, we conducted a study of vitamin D levels depending on the period of the disease and indicators of the allergic status of patients.

It should be noted that the level of vitamin D in patients in remission remained within deficiency or insufficiency and was 23.66 [10.21-25.48] ng/ml. The above fluctuations in vitamin D were independent of age. Thus, in patients aged 41 years and older, and in patients aged 18-40 years, the period of remission was characterized by vitamin D deficiency in the vast majority of subjects (66.7±10.5% and 60±9.3%, respectively).

In a further study, we analyzed the level of vitamin D depending on the indicators of the allergic status of patients. It should be noted that in 35 (90.2±4.3%) patients with AD with elevated eosinophilic cationic protein the frequency of vitamin D deficiency was 70.7±4.5%, (n=27) examined, vitamin D insufficiency occurred in 29.32±5.3% (n=8) patients, ($p<0.05$). The average level of vitamin D in patients with elevated ECP was 16.8 [11.0 -20.48] ng/ml. In the group of persons with indicators of allergic status, which did not exceed the normal values (9.8±4.7%, n=3 examined), the average level of vitamin D was 23.5 [10.21-25.48] ng/ml, ($p<0.05$). It should be noted that we did not find sufficient levels of vitamin D in any patient.

Therefore, vitamin D deficiency occurred significantly more often in patients with elevated indicators of allergic inflammation ($x^2=4.13$, p=0.004 between the group of patients with high and normal ECP maintenance).

During the analysis of variance, we found a probable moderate positive relationship between the level of ECP and hydroxyvitamin D in the serum of the examined patients of subgroup I ($rs=0.54$, $p<0.01$) and subgroup II ($rs=0.46$, $p<0.01$).

Dispersion analysis showed a probable moderate correlation between SCORAD and vitamin D ($rxy=0.645$; $p<0.05$) in subjects aged 18-41 years. However, it should be noted that the association between SCORAD and hydroxyvitamin D in serum decreased in subjects aged 41 years and older ($rxy=0.304$; $p<0.05$).

The results show that the subjects aged 41 years and older had a milder course of atopic dermatitis in maintainance of vitamin D deficiency, which may indicate the influence of other factors on the level of hydroxyvitamin D in the serum in this age group.

The problem of diagnosing AD among the adult population is extremely relevant. Steady growth of morbidity and the development of a severe course of this chronic inflammation of the skin directs scientists to further in-depth study of the mechanisms of disease formation, as well as the search for additional diagnostic methods. This study is aimed at finding the factors that influence the course of AD. More attention is being paid to the study of vitamin D metabolism disorders in patients with AD as a factor that may contribute to the severe course of the

disease, as the skin plays an important role in the metabolism and pleiotropic functions of vitamin D.

There is growing evidence that vitamin D plays a significant role in allergic diseases.

Our study revealed that determination of vitamin D level in the blood serum is a highly sensitive and specific method of examination for patients with AD. According to our data, patients with AD with moderate or severe course of the disease have severe deficiency or insufficiency of vitamin D, which is consistent with the literature, where more than 90% of patients with AD had vitamin D deficiency [12].

It should be noted that the effect of vitamin D on the prevalence and severity of chronic skin diseases has been the subject of a large number of studies that gave controversial results. Thus, conducted population studies have found an increased likelihood of developing AD in individuals with a deficiency or insufficiency of vitamin D [1].

We found a significant difference in the level of vitamin D between the groups of subjects depending on both age and severity of the disease ($p<0.05$).

It should be noted that most scientific studies have addressed the peculiarities of the disease in childhood. Thus, studies conducted among children with AD found that the mild course of the disease did not depend on the level of vitamin D. However; there is an opposite evidence. A number of studies have shown that vitamin D levels correlated with the severity of the disease, especially in children of the first year of life with AD [11].

However, in the analysis of the obtained results, the authors did not take into account age variations of vitamin D in the body of the subjects to be examined. We noted that the subjects, aged 41 years and older, had a milder course of atopic dermatitis in maintainance of vitamin D deficiency.

Thus, according to the literature, people over the age of 40 have an increased risk of vitamin D deficiency due to reduced exposure to sunlight, use of sunscreen, age-related lactase deficiency, diseases of the gastrointestinal tract, which in turn is accompanied by decreased absorption of vitamin D. In addition, the amount of 7-dehydrocholesterol in the dermal layer of the skin decreases with age. In people over the age of 70, the level of 7-dehydrocholesterol is four times lower than in young people, so in the elderly there is a decrease in the synthesis of cholecalciferol by 75%. Scientific studies show that vitamin D is a protective factor that improves the barrier properties of the skin. On the other hand, deficiency of this vitamin is probably a risk factor for atopic dermatitis. Thus, the role of vitamin D in inhibiting IgE secretion is confirmed, which theoretically reduces chronic inflammation of the skin. According to the results of our study, vitamin D deficiency was significantly more common in the group of patients with elevated levels of allergic inflammation, namely ECP. Most studies have linked vitamin D levels to specific total IgE [7].

Therefore, sufficient research has been conducted on the relationship between vitamin D status and the risk of developing AD. However, the analysis of the effect of vitamin D on the development of chronic skin diseases remains relevant, as there is contradictory, debatable evidence of such a connection, which requires further study.

CONCLUSIONS

1. In patients with atopic dermatitis, the severe course of the disease prevailed among persons aged 18-40 years (63.33±8.79)% more than in the age group of 41 years and older, (36.67±8.8%, $p<0.05$; OR=2.98, S=0.53, 95% SI: 1.04-8.52).
2. In moderate atopic dermatitis, proportion of people with vitamin D deficiency was 62.5% (n=10) with a median of 14 [8,3-19] ng/mL, and patients with severe course amounted to 90,9% (n=20) ($\chi^2=4.6$; $p=0.023$), in which the median level of vitamin D was 14 [8.3-19] ng/ml.
3. Vitamin D deficiency occurred significantly more often in patients with elevated indicators of allergic inflammation. A positive correlation of medium strength between the level of vitamin D and eosinophilic cationic protein in the serum of patients with atopic dermatitis ($rs=0.53$, $p<0.001$).
4. Patients with atopic dermatitis aged 41 years and older had a milder course of the disease in maintainance of vitamin D deficiency, which may indicate the influence of other factors on the level of hydroxyvitamin D in the serum in this age group.

Contributors:
Garibeh E. – methodology;
Bondar S.A. – conceptualization;
Tokarchuk N.I. – project administration;
Vyzgha Y.V. – validation.

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REFERENCES

1. Kang JW, Kim JH, Kim HJ, et al. Association of serum 25-hydroxyvitamin D with serum IgE levels in Korean adults. Auris, Nasus, Larynx. 2015;43(1):84-88. doi: https://doi.org/10.1016/j.anl.2015.06.010

2. Bergqvist C, Ezzedine K. Vitamin D and the skin: what should a dermatologist know? G Ital Dermatol Venereol. 2019;154(6):669-80.
doi: https://doi.org/10.23736/S0392-0488.19.06433-2

3. Ferreira CES, Maeda SS, Batista MC, Lazaretti-Castro M, Vasconcellos LS, Madeira M, et al. Consensus – reference ranges of vitamin D [25(OH) D] from the Brazilian medical societies Brazilian Society of Clinical Pathology/Laboratory Medicine (SBPC/ML) and Brazilian Society of Endocrinology and Metabolism (SBEM). Jurnal Brasileiro de Patologia e Medicina Laboratorial. 2017;53(6):377-81.
doi: http://www.dx.doi.org/10.5935/1676-2444.20170060

4. Galvão AA, Sena FA, Belitardo EM, Santana MB, Costa GN, Cruz BA, et al. Genetic polymorphisms in vitamin D pathway influence 25(OH)D levels and are associated with atopy and asthma. Allergy Asthma Clin Immunol. 2020;16:62-75.
doi: https://doi.org/10.1186/s13223-020-00460-y

5. Han YY, Forno E, Celedón JC. Vitamin D insufficiency and asthma in a U.S. Nationwide study. J Allergy Clin Immunol Pract. 2017;5(3):790-796.
doi: https://doi.org/10.1016/j.jaip.2016.10.013

6. Hemanth KK, Sathisha Upparahalli V, Anil M. Synergy of Interleukin (IL)-5 and IL-18 in eosinophil mediated pathogenesis of allergic diseases. Cytokine Growth Factor Rev. 2019;47:83-98.
doi: https://doi.org/10.1016/j.cytogfr.2019.05.003

7. Thorisdottir D, Gunnarsdottir I, Vidarsdottir AG, Sigurdardottir S, Bryndis EB, Thorsdottir I. Infant Feeding, Vitamin D and IgE Sensitization to Food Allergens at 6 Years in a Longitudinal Icelandic Cohort. Nutrients. 2019;11(7):1690.
doi: https://doi.org/10.3390/nu11071690

8. Amber KT, Chernyavsky A, Agnoletti AF, Cozzani E, Grando SA. Mechanisms of pathogenic effects of eosinophil cationic protein and eosinophil-derived neurotoxin on human keratinocytes. Experimental Dermatology. 2018;27(12):1322-7.
doi: https://doi.org/10.1111/exd.13782

9. Navarro-Triviño FJ, Arias-Santiago S, Gilaberte-Calzada Y. Vitamin D and the Skin: A Review for Dermatologists. Actas Dermosifiliogr. 2019;110(4):262-72.
doi: https://doi.org/10.1016/j.ad.2019.04.001

10. Petrie A, Sabin C. Medical Statistics at a Glance. 4th edition. Wiley-Blackwell; 2019. ISBN: 978-1-119-16783-9.

11. Cheon BR, Shin JE, Kim YJ, Shim JW, Kim DS, Jung HL, Park MS, Shim JY. Relationship between serum 25-hydroxyvitamin D and interleukin-31 levels, and the severity of atopic dermatitis in children. Korean J Pediatr. 2015; 58(3): 96-101.
doi: https://doi.org/10.3345/kjp.2015.58.3.96

12. Amon U, Baier L, Yaguboglu R, Ennis M, Holick MF, Amon J. Serum 25-hydroxy vitamin D levels in patients with skin diseases including psoriasis, infections, and atopic dermatitis. Dermato-Endocrinology. 2018;10(1):e1442159-14.
doi: https://doi.org/10.1080/19381980.2018.1442159

13. Zhang L, Zhang S, He C, Wang X. VDR Gene Polymorphisms and Allergic Diseases: Evidence from a Meta-analysis. Immunol Invest. 2020;49(1-2):166-77.
doi: https://doi.org/10.1080/08820139.2019.1674325

14. Umar M, Sastry KS, Ali FA, Al-Khulaifi M, Wang E, Chouchane AI. Vitamin D and the Pathophysiology of Inflammatory Skin Diseases. Skin Pharmacology and Physiology. 2018;31(2):74-86.
doi: https://doi.org/10.1159/000485132

15. Yuan K, Madu CO, Lu Y. Immunological Role of Vitamin D in Skin Diseases and Carcinoma. Oncomedicine. 2017;2:52-60.
doi: https://doi.org/10.7150/oncm.19262

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