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REPORT

ABOUT RESEARCH WORK

# CLINICAL AND GENETIC MARKERS OF D-VITAMIN STATUS IN CHILDREN UNDER ONE YEAR OLD IN THE KAZAKH POPULATION

(final)

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Aktobe 2021

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## ESSAY

Report 41c., 8 tables, 12 figures, 22 sources, 4 ann.

CHILDREN UNDER ONE YEAR OF AGE, PHYSICAL DEVELOPMENT, COMPREHENSIVE HEALTH ASSESSMENT, BONE METABOLISM, D-VITAMIN STATUS.

The object of the study is children under 1 year of the Kazakh population

Key words: children under one year old, physical development, comprehensive assessment of health status, bone metabolism, D vitamin status. The object of the study was children under one year old of the Kazakh population.

Objective of the study: To study the D-vitamin status in children under one year old and to assess the impact of vitamin D deficiency in correlation with genetic factors and methods of correction.

Research methods: In accordance with the goal and objectives of the project, 100 children under one year old who are in maternity hospitals and children's clinics in Aktobe were examined using the following methods: Clinical and anamnestic research, determination of vitamin D in blood serum, research for genetic markers.

In the course of the research work, the following scientific results were obtained: deviations in the state of health were revealed in 80.2% of the mothers of the surveyed group. It has been proven that the presence of infectious and inflammatory diseases in mothers before and during pregnancy, as well as the absence of D-vitamin prophylaxis, increases the risk of vitamin D deficiency and D deficiency in their children, respectively, by 2.5 (OR = 2.4 CI95% [ 1.1 ÷ 4.8]); 4 (OR = 4.2 CI95% [1.9 ÷ 9.1]) times.

Osteopenia is caused by unfavorable factors of the antenatal and postnatal period: complicated course of the present pregnancy (AR = 34.9%; p = 0.01); early irrational artificial feeding (AR = 42.3%; p = 0.03); rickets transferred in the first year of life (AR = 38.1%; p = 0.02).

Prenatal use of VMC (vitamin and mineral complex) in 24 women (18.5%) was completely absent during pregnancy. The mean time to discontinue vitamin D prophylaxis was 12.4 ± 1.7 months.

The average level of vitamin D supply in children corresponded to vitamin D deficiency and averaged 20.16 ± 1.7 ng / ml. The introduction of complementary foods increased the chances of normalizing vitamin D levels by 5 times. It was revealed that the nature of the relationship between the T / T and T / C genotypes of the VDR gene and changes in the concentration of vitamin D below the normal value is relatively strong, which proves the presence of a direct relationship between the level of vitamin D and the risk of developing pathology of the skeletal system in children (F> 0.05 units).

Scope of the results: pediatrics, neonatology.

Recommended: For children with antenatal calcium deficiency, it is advisable to study mineral metabolism and markers of bone remodeling in the first year of life - bone strength during the neonatal period. For children of mothers at risk of calcium deficiency, prevention of mineral metabolism disorders, linear growth, bone strength, skeletal deformities and the development of rickets should be carried out with vitamin D in conjunction with calcium preparations. To revise the prophylactic and therapeutic dose of vitamin D in children under one year old of the Kazakh population.

Practical significance of the work: the mother's intake of calcium and vitamin D preparations from the first trimester of pregnancy has a positive effect on the bone strength of the child's skeleton, reduces the severity of rickets symptoms and the risk of mineral metabolism disorders in infants. Taking calcium (1000 mg) and vitamin D (400 IU) preparations, starting from the first trimester, has a positive effect on the bone quality of the mother and child.

The presence of a direct relationship between the level of vitamin D and the risk of developing pathology of the skeletal system in children (F> 0.05 units) has been proven. The use of the obtained results of the work helps to reduce the risk of developing bone pathology in children.

**CONTENT**

## LIST OF ABBREVIATIONS AND DESIGNATIONS

The following abbreviations and designations are used in this research report:

FD - physical development

CCT - calcitonin

BMI - body mass index

BMD - bone mineral density (bone tissue)

BW - body weight

PCR - polymerase chain reaction

EDTA - ethylenediaminetetraacetic acid

RCF- Relative Centrifugal Force

VMP - vitamin and mineral complex

BF - breastfeeding

AF - artificial feeding

CMV - cytomegalovirus

HSV - herpes simplex virus

## INTRODUCTION

Recently, more and more attention is paid to the problems of mineral metabolism, osteopenia. It is believed that the state of bone tissue is an indicator that reflects the general development of the child, his functional status, as well as the level of health in general. The dynamics of human bone mass is characterized by its growth in childhood, reaching a maximum by the age of twenty, then by its stabilization and progressive loss after 35 years, which ultimately leads to the development of osteoporosis [1,2,3]. The prevalence of the disease is high, for example, in the United States about 10 million people suffer from osteoporosis, and a decrease in bone mass is observed in another 18 million [4], according to the Children's Health Center (Moscow) with densitometry performed in 1000 children aged 7-15 years , in 40% of the surveyed, a decrease in bone mineral density (BMD) was found [5]. According to a study in Western Kazakhstan, among 396 apparently healthy children aged 12-17 years, osteopenia was detected in 70% of cases [6,7]. Critical periods of development are distinguished when the high activity of biological processes against the background of linear growth and differentiation of bone tissue is accompanied in children by accelerated remodeling (resorption and bone formation).

Critical periods are characterized by high growth rates of skeletal bones and are typical for children in the first year of life, for children aged 5-7 years and during puberty. [eight]. In this regard, great importance is attached to assessing the state of bone health depending on age, especially during critical periods of growth, one of which is the first year of life, which includes the neonatal period [9, 10]. The high frequency of osteopenia conditions in children determines the relevance of studying bone metabolism. The role of genetic factors modulating the risks of developing disorders of phosphorus-calcium metabolism is discussed. Studies by foreign authors on twins have shown that the level of 25 (OH) D in blood serum has a direct impact on genetic factors [11]. The contribution of the genotype to fluctuations in serum values of 25 (OH) D ranges from 23-43% to 77-80%. [12]. The genes GC fBP, CYP24A1, CYP2R1, CYP27B1, VDR, NADSYN1 / DHCR7 were identified as the main candidate genes, mutations in which affect the concentration of 25 (OH) D [13,14,15,16].

We put forward a hypothesis to assess the possible relationship between genetic factors and the content of bone metabolism indicators, which may be of practical importance for identifying children at risk of vitamin D deficiency, changes in bone metabolism and individualization of treatment and prophylactic measures. Considering that such studies have not been carried out in children in the Kazakh population, it is promising to study the dependence of the processes of bone remodeling and genotype in them. In this regard, this study is relevant from the point of view of molecular genetic testing - VDR (rs1544410, rs2228570), RANKL

(rs9594738, rs9594759), with the study of the frequency distribution of alleles and genotypes by polymorphisms, analysis of the relationship of molecular genetic markers with indicators bone metabolism and the development of a diagnostic algorithm.

Objective: To study the D- vitamin status and features of allelic gene polymorphism - VDR (rs1544410, rs2228570), RANKL (rs 9594738, rs9594759) in children of the Kazakh population

Tasks:

1) Conduct comprehensive studies of vitamin D status in children under one year old in the Kazakh population.

2) Determine the frequency of allelic variants of the VDR genes (rs1544410, rs2228570), RANKL (rs9594738, rs9594759,) in children under one year of the Kazakh population.

3) To study the relationship between the presence of allelic polymorphism of the VDR genes (rs1544410, rs2228570), RANKL (rs 9594738, rs9594759,) and the degree of vitamin D deficiency and deficiency in children under one year of the Kazakh population.

4) To assess the role of determining the polymorphism of the VDR genes (rs1544410, rs2228570), RANKL (rs 9594738, rs9594759,) in the diagnosis of bone health in children under one year old of the Kazakh population

## THE MAIN PART OF THE RESEARCH REPORT

### 1. General characteristics of the study

**Materials and methods:** In accordance with the purpose of the study, 100 children in the Kazakh population, born and living in Aktobe, were examined.

Design: Descriptive cross-sectional study.

The analytical part of the study was carried out on the basis of the Department of Pediatric Diseases No. 1 with neonatology "WKMU" named after Marat Ospanov.

Inclusion criteria: "practically" healthy children from 0 - 12 months;

(1, 2 health groups) [Order No. 145 dated March 16, 2011] in a satisfactory condition at the time of the study, without genetic syndromes, subject to informed consent signed by the parents or legal representatives.

Exclusion criteria: children taking vitamin D in a therapeutic dose, the presence of hereditary diseases, severe chronic somatic diseases, disability for other diseases, prematurity, age over 1 year.

Clinical-anamnestic research included: analysis of children's anamnestic data, questionnaires of parents, assessment of the initial state of health of the child (Annexes B).

An individual registration card was entered for each child included in the study.

To determine the child's belonging to the Kazakh population, the parents filled out a questionnaire approved by the termination committee of the Marat Ospanov WKMU. When using the questionnaire, there was no conflict of interest (Annexes A).

Biochemical blood test was carried out in the laboratory "OLIMP" at 57 Aliya Moldagulova Avenue, in Aktobe. Blood serum was taken in a treatment room, in compliance with the generally accepted rules for taking blood from a vein for its biochemical analysis. The rooms were equipped with everything necessary, according to the orders, for this procedure - sterile disposable syringes with needles; sterile trays with cotton balls and tweezers; tourniquet, rubber pad and disinfectant wipes, sterile tubes, tray for used material.

The blood sample will be taken on an empty stomach. VACUETTE® vacuum systems with yellow lid were used. Their volume is 5 ml. They contain a coagulation activator at the factory to reduce the likelihood of hemolysis and foaming of the sample.

After taking blood, according to the official instructions for vacuum systems, the nurse turned the tube upside down 5-6 times, mixed the collected serum with the activator gel. Next, the medical staff places the tubes in a centrifuge at 1800 g (GCS) for 10 minutes at room temperature. Further, samples with less than 0.5 ml of serum were subjected to freezing at a

temperature of -20 ° C. Further, observing the temperature regime, the test tubes with the biomaterial were sent to the centralized laboratory.

Methods: D vitamin-electrochemiluminescence immunoassay (ECLIA) according to the criteria of the International Society of Endocrinologists, vitamin D supply (recommended level) is diagnosed at a value of 25 (OH) D 30-80 ng / ml, deficiency - at 20-30 ng / ml, deficiency - at 10–19 ng / ml, severe deficiency - at a value less than 10 ng / ml [19].

Research for genetic markers will be carried out for 4 VDR polymorphisms (rs1544410, rs2228570), RANKL (rs 9594738, rs9594759)

Biomaterial for research: whole blood (2 ml) taken with EDTA(ethylenediaminetetraacetic acid).

Determination method: PCR and restriction analysis. It will be determined using the "real-time" PCR method using adjoining fluorescently labeled samples (kissingprobes) by measuring the melting temperature of the samples after amplification (meltingcurveanalysis), will be carried out using the detecting amplifier "DT Prime" (Scientific and Practical Center of WKMU named after Marat Ospanov ).

The statistical processing methods used in the work to assess the reliability of the results were carried out in Microsoft Excel using pivot tables and descriptive statistics from the Statistika 10.0 plug-in analysis package for a personal computer.

Descriptive analysis included the determination of the arithmetic mean, standard deviation, error of the mean (m) when calculating the Student's test. We used well-known graphic techniques to express statistical data. The critical level of significance (p) when testing statistical hypotheses in the study was taken equal to 0.05. To assess categorical features, the values of associative indicators - absolute risk (AR), relative risk (RR), odds ratio (OR).

Were examined 100 children under the age of 1 year, of which 60 boys and 40 girls.

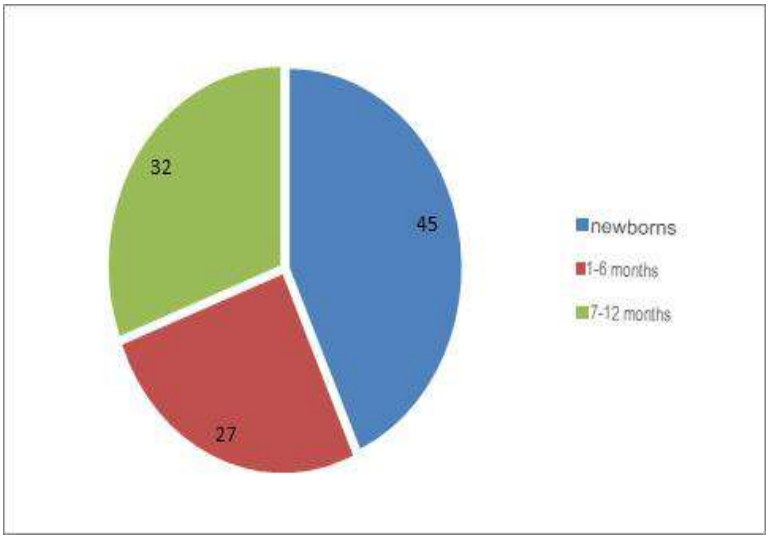


Figure 1 - Age structure of the examined children

All examined children were divided into groups, in accordance with which group 1 was represented by children from 0 to 28 days (newborns), group 2 consisted of children aged 1 to 6 months, group 3 included children over 6 months. The age groups of the examined children were formed taking into account the peculiarities of the exogenous intake of vitamin D (figure 1).

In particular, in the 1st group of children, it is assumed that there is a direct dependence of the vitamin D content on the same maternal indicator. The quantitative content of vitamin D in the second group of the examined does not depend on exogenous receipts, because children of this age group do not receive complementary foods. In group 3, represented by children older than 6 months, additional intake of vitamin D with complementary foods is expected, in accordance with the content of the National Program for Optimizing Feeding of Children of the First Year of Life.

## 2. Research results and their discussion

The study of the anamnesis showed that the majority (80.2%) of the mothers of the surveyed group had deviations in the state of health. Infectious and inflammatory diseases predominated in the structure of maternal pathology (50%, n = 30): chronic adnexitis, intrauterine infections (mycoplasmosis, chlamydia), carriage of herpes infection (CMV, HSV type 1, during this pregnancy - gestational pyelonephritis, acute respiratory infections (sinusitis) , sore throats, pharyngitis) Most women (70.8%) were in active reproductive age: every second (49.2%) child was born from 1 pregnancy; 76.2% of children - from full-term pregnancy. 68.9%; accompanied by acute respiratory infections - in 30.6%. 20.2% (n = 14) women received only calcium supplements; in 35.7% (n = 25) - a combination of VMC with calcium supplements; in 25.6% (n = 32) - only IUD. Prenatal prophylaxis was performed with VMC and calcium preparations in 81.5% of cases. D stopped after 1 year; The mean time to discontinue vitamin D prophylaxis was 12.4 ± 1.7 months. In 86.2% of cases, the prophylactic dose of vitamin D was 500 IU, in 13.8% of children - 1000 IU.

Analysis of the development and health of children revealed that FD corresponded to the passport age in the majority (63.8%) of the surveyed; lag in FD was most often recorded in the 2nd half of life in 13.8%. FD was harmonious in 62.3%, disharmonious - in 29.2%, sharply disharmonious - in 8.5%. One third of children (31.5%; n = 22) had late teething.

Vitamin D supply in children

The average vitamin D content in the blood serum in the study group in the examined children was 20.16 ± 1.7 ng / ml, which corresponded to vitamin D deficiency (Table 1, figure 2).

Table 1 - The content of vitamin D in the blood serum of the examined children

| 25 (OH) D Ng / ml | All children | Up to 1 month | 2-6 months | 7-12 months | P |
|---|---|---|---|---|---|
| M±m | 20,16±1.7 | 17,5±1.45 | 12,3±2,7 | 43.54±1,7 | * |

Note * P1-3, 1-4 <0.001

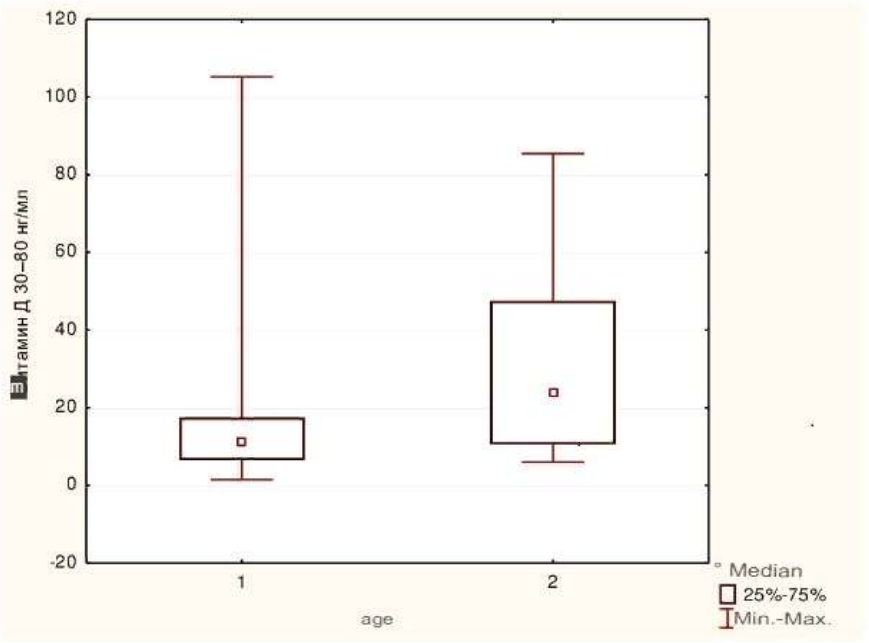


Figure 2 - Vitamin D content depending on age

The analysis of the frequency distribution of the provision revealed a normal level of vitamin D only in 21.8%, deficiency - in 59.2% and insufficiency - in 19% of children. A high frequency of vitamin D deficiency was revealed in children from 2 months to 6 months and up to 1 month (41.8% each, respectively).

In the 1st year, 18.6% of children had a normal supply of vitamin D (table 2).

Table 2 - Frequency of occurrence of normal supply, insufficiency and deficiency of vitamin D in the examined children

| 25 (OH) D<br>Ng / ml | Allchildren<br>70 children | Upto 0-6 months<br>35 children | 7-12 months<br>35 children | P |
|---|---|---|---|---|
| | | 1 | 2 | |
| Norm | 21,8 % (15) | 9,1 % (3) | 77,8%(27) | * |
| Failure | 19 % (14) | - | 22,2 % (8) | |
| Deficit | 59,2 % (41) | 90,9% (32) | | |

P*1-2 <0,001

Vitamin D supply depending on the type of feeding.

Depending on the type of feeding, the children were divided into 4 groups: Group 1 - BF - n = 38 (54.3%); Group 2 - AF - n = 10 (14.3%); Group 3 - B + C - n = 16 (22.8%); Group 4 - A +C - n = 5 (7.14%) (Figure 3).

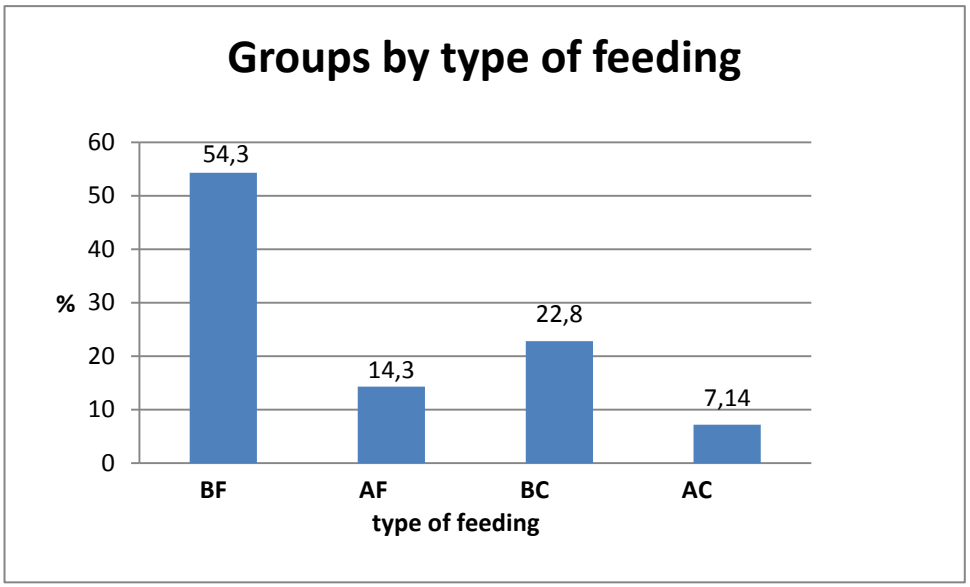


Figure 3 - Provision from the type of feeding

The content of vitamin D in the blood serum of children in the groups BF, B + C, was normal and did not have significant differences, respectively 35.20 ± 11.7; 42.7 ± 3.05 ng / ml; in children, those on artificial feeding, corresponded to deficiency - 21.9 ± 2.744 ng / ml. There was revealed a high frequency of normal vitamin D supply in the groups receiving complementary foods, depending on the type of feeding - B + C (42.7 ± 3.05 ng / ml); but low A + C - (15.34 ± 1.096 ng / ml). The incidence of vitamin D deficiency was highest in groups of children without complementary foods and in the group A + C (Figure 4).

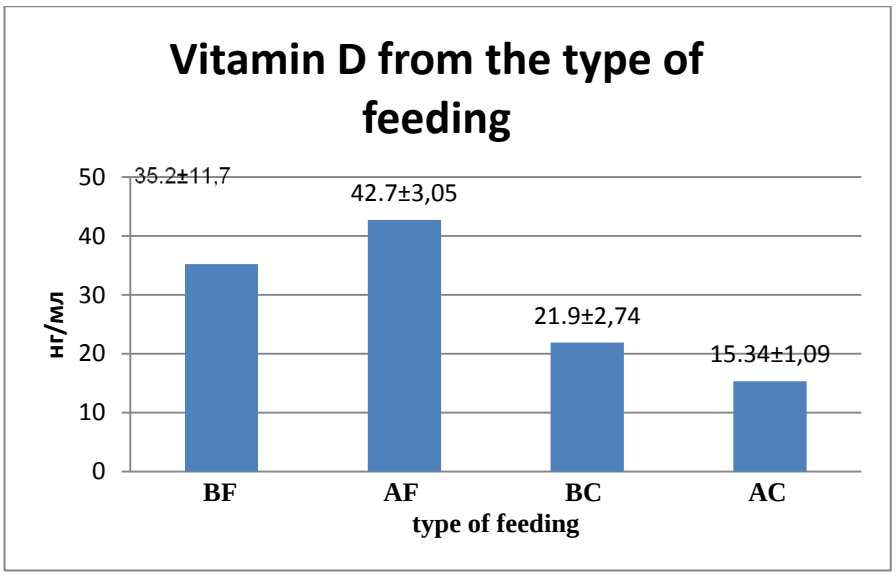


Figure 4 - The content of vitamin D from the type of feeding

Thus, the introduction of complementary foods increased the chances of normalizing vitamin D levels by 5 times. With BF +BC (OR = 5.6; CI 95% [2.46 ÷ 12.8]) and with AF +AC- 4 times (OR = 4.0; CI 95% [0.87 ÷ 18, 25])

Vitamin D provision depending on the presence / absence of D vitamin prophylaxis.

Low vitamin D supply was detected more often in children without D-vitamin prophylaxis compared with children with prophylaxis at the 1st year of life (n = 37), respectively 52.8% and 41.4%; p <0.01; Thus, in the absence of D-vitamin prophylaxis in the first 6 months, there is a risk of developing a low supply of vitamin D (20.38 ± 0.784 ng / ml) than during prophylaxis (35.70 ± 1.700 ng / ml) p <0 , 01 (table 3).

Table 3 - Provision with vitamin D depending on vitamin D prophylaxis

| 25 (OH) D Ng / ml | Prophylactic dose of vitamin D | | | P |
|---|---|---|---|---|
| | 500 IU ,n=23 | 1000IU,n=10 | Didnotreceive | |
| | 1 | 2 | 3 | |
| M±m | 35,70±1,700 | 33,169±4,37 | 20,38±0,784 | P 1-3<0,001<br>P1-2<0,001 |

Vitamin D supply of children and maternal health.

Among children born to mothers with deviations in health, 57.1% (n = 40) had a low supply of vitamin D. Among children born to mothers who did not have infectious-

inflammatory diseases, D-vitamin deficiency was found in 42, 9% of cases (n = 35).

Thus, the probability of a child's low vitamin D supply increased 1.6 times if the mother had infectious and inflammatory diseases during and before pregnancy (OR = 1.6 CI 95% [1.8–7.3]). The calculation of the etiological fraction showed that if infectious and inflammatory diseases of a woman before and during pregnancy are a causally significant factor in the low supply of vitamin D in children in the postnatal period, then in 1.3% (AR% = 1.3%) of these children, D-vitamin insufficiency is in isolation associated with pathology in the mother (table 4).

Table 4 - Relationship between the level of vitamin D supply in children and the presence of an infectious history in the mother

| Pathology Pregnant women | Decreased vitamin D | | AR CI 95% | Standard error S | RR CI 95% | OR CI 95% | AR% |
|---|---|---|---|---|---|---|---|
| | n | % | | | | | |
| Low vitamin D supply (deficiency + deficiency, n = 70) | | | | | | | |
| Yes, n = 65 | 40 | 61,5 | 21,5 5,3÷37,7 | 0.345 | [1,8÷7,3] | 1,6 | 1,3 |
| No, n = 5 | 35 | 40 | | | | | |

Vitamin D supply and health status of children

Analysis of the incidence of symptoms "traditional" for the rickets process - baldness of the occipital region, late teething - with different levels of vitamin D supply revealed no connection between the presence of these symptoms and vitamin D deficiency. D in blood serum than with low (66.7% and 33.3%, respectively), late teething - significantly more often with normal supply than with deficiency or low supply of vitamin D (78% and 12.2%; $p < 0.01$; 78% and 21.9%; $p < 0.01$)

A molecular genetic study was carried out in 100 children with the determination of the following gene polymorphisms: VDR rs1544410, VDR rs2228570, RANKL rs 9594738, RANKL rs9594759

VDR rs1544410, also known as BsmI (A <G) polymorphism, plays a role in metabolic disturbances and decreased sensitivity to vitamin D. VDR plays a key role in osteogenesis and mineral metabolism. A number of studies have shown the association of VDR polymorphism

with the occurrence of fractures. The VDR gene encodes the nuclear hormone receptor for vitamin D3. This receptor also functions as receptors for a secondary bile acid, lithocholic acid. The receptor belongs to the family of trans active regulatory transcription factors and has sequence similarities with steroid and thyroid hormone receptors. Subsequent targets of this nuclear hormone receptor are primarily involved in mineral metabolism, although the receptor regulates a variety of other metabolic pathways, such as those involved in the immune response and cancer. Mutations in this gene are associated with type II vitamin D-resistant rickets. Single nucleotide polymorphism in the start codon leads to a shift of the initiation codon by three codons from the beginning. As a result of alternative splicing, several variants of transcripts encoding various proteins are formed. Vitamin D receptors are expressed in the intestines, thyroid gland and kidneys and play a vital function in calcium homeostasis. Hereditary mutations in the VDR gene lead to rickets, which is characterized by muscle weakness, stunting, bone deformity, and secondary hyperparathyroidism. The human gene encoding the vitamin D receptor is located on chromosome 12q12-q14. Mutation inheritance type: autosomal dominant (occurs in men and women with the same frequency, for the development of the disease it is enough to inherit 1 mutant variant of the genefrom one of the parents, the probability of the disease in children is 50%). Carriers of variant A of this polymorphism have an increased risk of disorders in low bone mineral density, which leads to a deterioration in its mechanical properties. G- Reducing the risk of disorders of low bone mineral density.In 17% of children, the VDR rs1544410 mutation gene was identified (Figure 3).

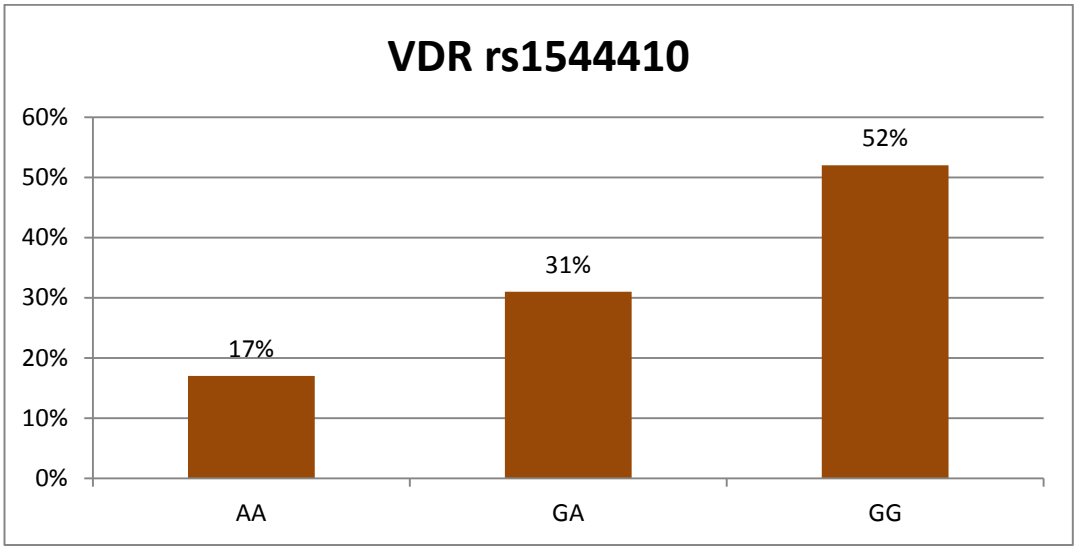


Figure 5 - Distribution of the allelic variant of the VDR rs1544410 gene polymorphism among the examined children

VDR rs2228570 C <T is located in the VDR gene and is a single nucleotide substitution "C" for "T" at position 47,879,112 in chromosome 12. Carriers of variant T have an increased risk of

abnormalities in low bone mineral density.C - reduced risk of disorders of low bone mineral density.4% had a VDR rs2228570 defective gene (Figure 6).

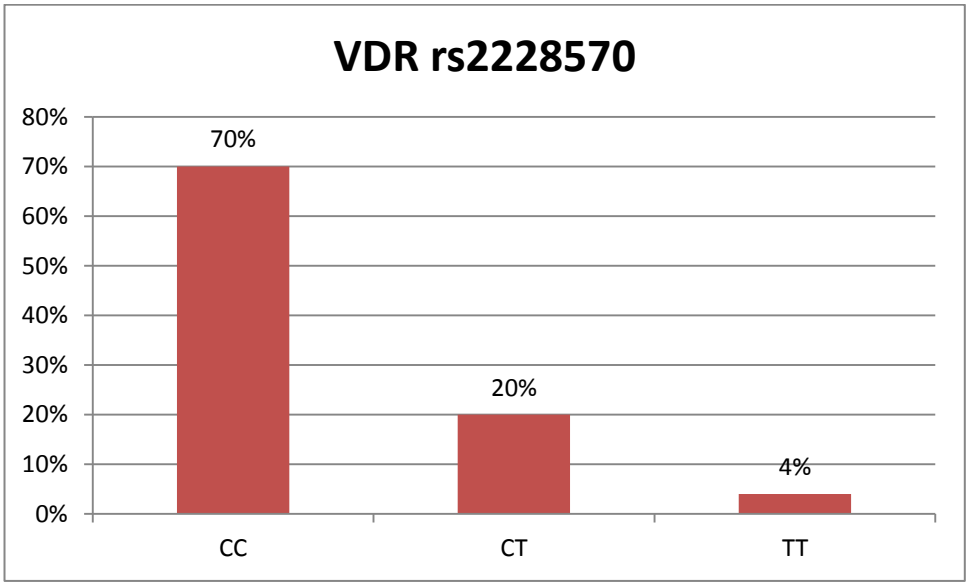


Figure 6 - Distribution of the allelic variant of the VDR rs2228570 gene polymorphism among the examined children

RANKL rs 9594738 C> T. Nuclear factor kappa-B receptor activator ligand

Its main function is to stimulate cells that destroy bone tissue (osteoclasts) and inhibit their apoptosis.Carriers of variant T of this polymorphism have an increased susceptibility to changes in bone mineral density,carriers of variant C of this polymorphism are not at risk.

RANKL rs 9594738 was detected in 28% (Figure 7).

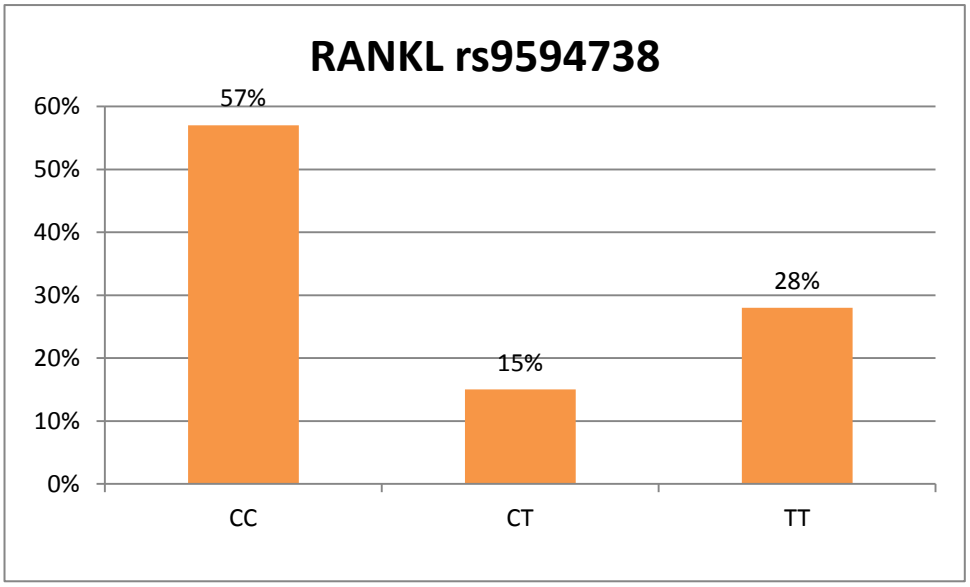


Figure 7 - Distribution of the RANKL rs 9594738 allelic variant of gene polymorphism among the examined children

RANKL rs9594759 C> T. Its main function is to disrupt bone remodeling. Associated with osteoporosis; in carriers of variant T, it increases susceptibility to changes in bone mineral density.

Carriers of variant C of this polymorphism are not at risk.RANKL rs9594759 TT genotype was detected in 28% (figure 8).

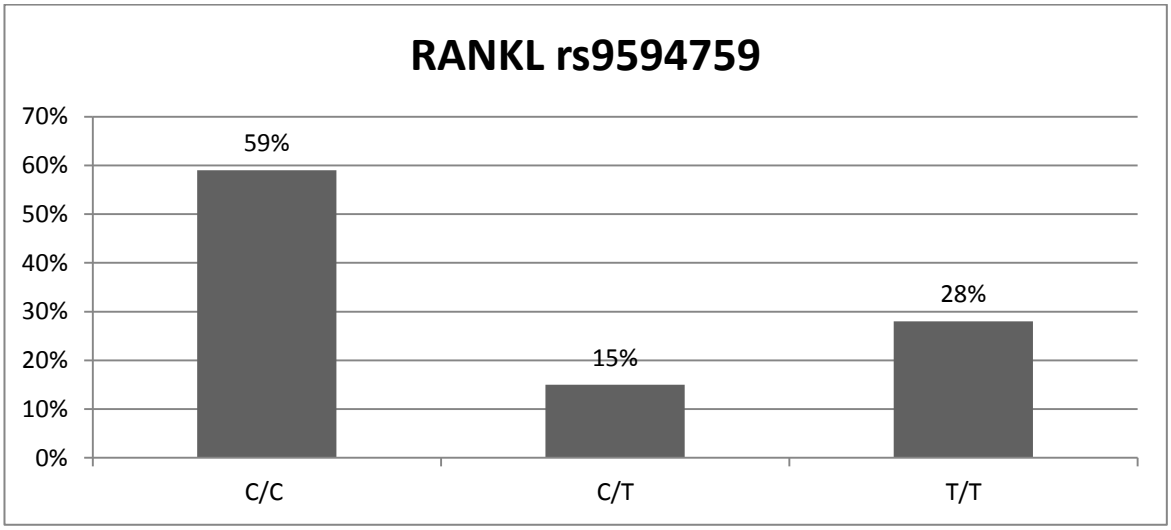


Figure 8 - Distribution of the allelic variant of RANKL rs9594759 gene polymorphism among the examined children

When examining 100 children, it was recorded that (78%) of the child had a decrease in the level of vitamin D (in accordance with the reference values) [18], among which 69 (85.1%) had a deficiency, and 12 (14, 8%), vitamin D deficiency was stated.

According to the concentration of vitamin D, the children were divided into 3 groups. 1 norm from 30.0 to 75.0, group 2 - with vitamin D deficiency, group 3 - children with vitamin D deficiency

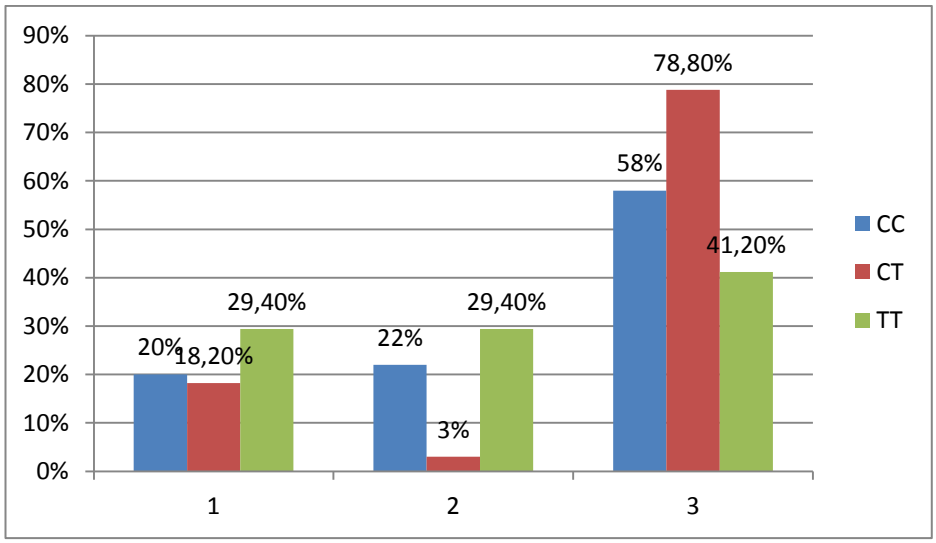


Figure 9 - Vitamin D content depending on RANKL rs9594759

In children with RANKL rs9594759 with the C / C genotype, normal vitamin D levels were observed in 20% of cases, deficiency - in 22%, deficiency - in 58% of cases. With the C / T genotype: the norm of vitamin D is 18.2%, insufficiency - in 3.0%, deficiency - in 78.8% of cases. T / T: norm - in 29.4%, insufficiency - in 29.4%, deficit - in 41.2% of cases (figure 9).

RANKL rs9594738 with C / C genotype normal vitamin D levels were noted in 22.8%, deficiency - in 19.2%, deficiency - in 57.8% of cases.C / T: norm - in 25.0%, insufficiency - in 21.4%, deficit - in 53.5% of cases.T / T: norm - in 6.6%, deficit - in 93.3% of cases (figure 10)

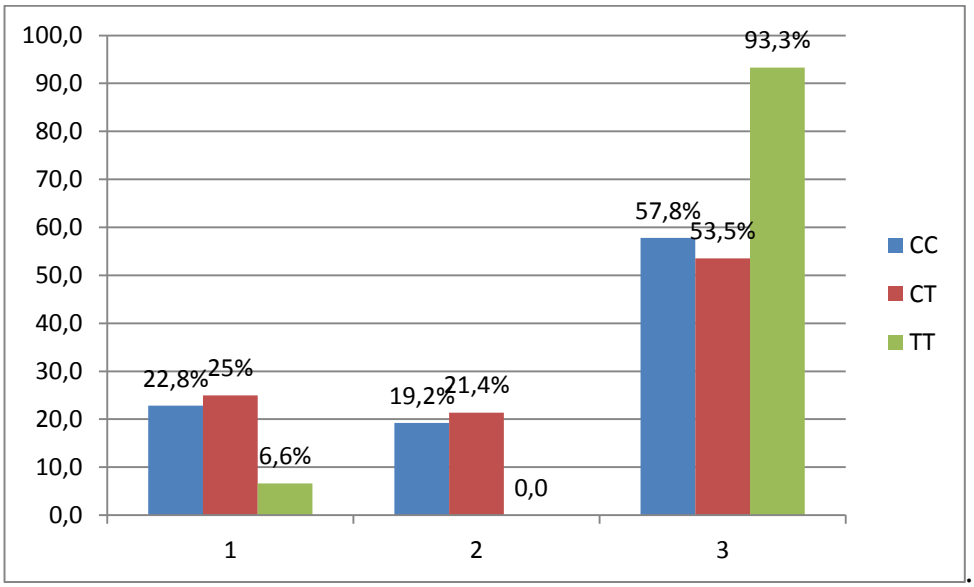


Figure 10 - Vitamin D content depending on RANKL rs9594738

VDR rs2228570 with the C / C genotype normal vitamin D values - in 13.4%, deficiency - in 21.1%, deficiency - in 65.3 cases. C / T: norm - in 29.0%, insufficiency - in 6.4%, deficit - in 64.5% of cases. T / T: norm - in 29.4%, insufficiency - in 23.5%, deficit - in 47.0% of cases (figure 11).

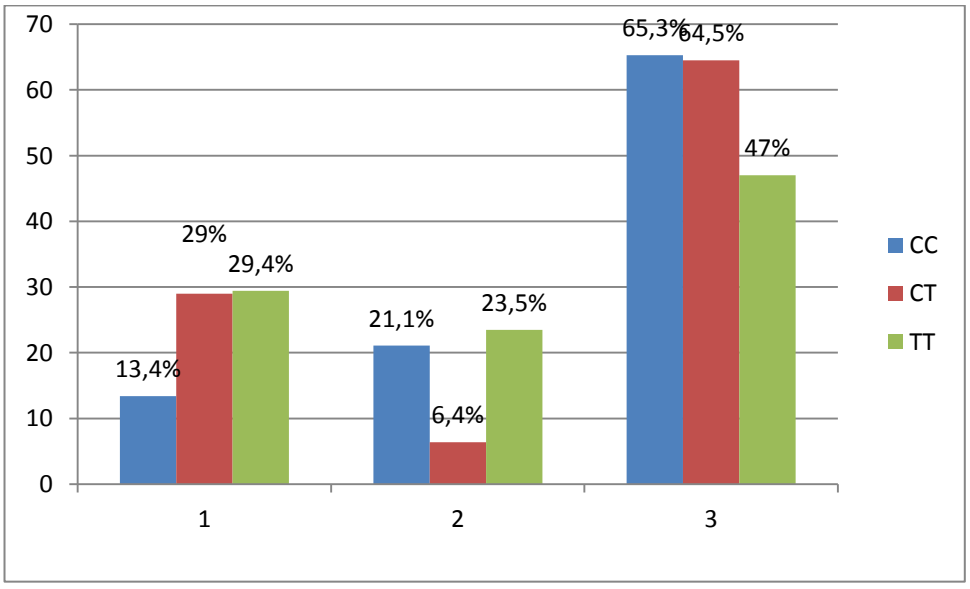


Figure 11 - Vitamin D content depending on VDR rs2228570

VDR rs1544410 with the G / G genotype normal vitamin D levels - in 40%, deficiency - in 15%, deficiency - in 45% of cases.G / A: norm - in 17.0%, failure - in 18.0%, deficit - in 64.0% of cases. A / A: deficit - in 100% of cases(figure 12).

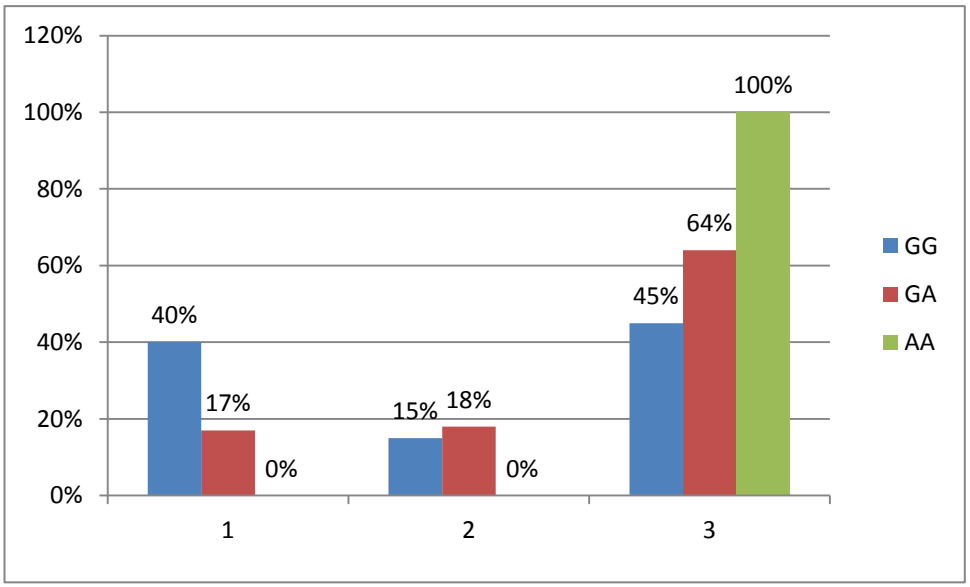


Figure 12 - Vitamin D content depending on VDR rs1544410

The relationship between the indicators of vitamin D concentration in children and the distribution according to genotypes was calculated using 2 methods of Fisher's exact test and the Krammer V test.

As a null hypothesis, we accepted the statement that the risk of developing pathology of the skeletal system does not depend on the concentration of vitamin D. The critical level of significance was taken as 0.05. When the calculated Fisher's criterion was exceeded, its critical value was assumed to be the null hypothesis.

When studying the effect of the level of vitamin D concentration on the risk of developing pathology of the skeletal system in children, depending on the genotype, it was found that the nature of the relationship between the T / T and T / C genotypes of the VDR gene and changes in the concentration of vitamin D below the normal value is relatively strong, since the value Fisher's criterion (F) was less than the critical level of significance (F> 0.05 units), respectively, at a significance level of 0.05 (Table 5).

This means that in this case, an alternative hypothesis is accepted and a conclusion is made that there is a direct relationship between the level of vitamin D and the risk of developing bone pathology in children.

Table 5 - Relationship between indicators of vitamin D concentration in children and RANKL rs9594738

| RANKLrs 9594738 | Vitamin D | | p |
|---|---|---|---|
| | Fisher'scriterion / KrammerV | The nature of the connection | |
| CC и CT | 0,275 | average | 0,043 |
| CC и TT | 0,147 | weak | 0,481 |
| CT и TT | 0,437 | Relatively strong | 0,008 |

Table 5 revealed an average association between the CC, CT and vitamin D genotypes and a relatively strong association between CT, TT and vitamin D

Table 6 - Relationship between indicators of vitamin D concentration in children and RANKL rs9594759

| RANKL rs9594759 | Vitamin D | | p |
|---|---|---|---|
| | Fisher's criterion / KrammerV | The nature of the connection | |
| CC и CT | 0,306 | average | 0,033 |
| CC и TT | 0,041 | insignificant | 0,93 |
| CT и TT | 0,411 | Relatively strong | 0,026 |

As can be seen from table 6, the relationship between the indicators of the concentration of vitamin D in children and RANKL rs9594759 is visible. Revealed an average relationship between the CC, CT genotypes and a relatively strong relationship between CT, TT and vitamin D

Table 7 - Relationship between indicators of vitamin D concentration in children and VDR rs2228570

| VDR rs2228570 | Vitamin D | | p |
|---|---|---|---|
| | Fisher's criterion / KrammerV | The nature of the connection | |
| CC и CT | 0,248 | average | 0,047 |
| CC и TT | 0,194 | weak | 0,27 |
| CT и TT | 0,255 | average | 0,208 |

Table 7 shows the relationship between indicators of vitamin D concentration in children and VDR rs2228570. Revealed the average relationship between genotypes CC, CT and vitamin D

Table 8 - Relationship between indicators of vitamin D concentration in children and VDRrs1544410

| VDRrs1544410 | Vitamin D | | p |
|---|---|---|---|
| | Fisher'scriterion / KrammerV | The nature of the connection | |
| GGGA | 0,225 | average | 0,086 |
| GG и AA | 0,163 | weak | 0,342 |
| GA и AA | 0,411 | average | 0,131 |

Table 8 shows that there is no association between genotypes GG, GA, AA and vitamin D. The level of evidence is not significant.

We see that all genotypes have a relationship with the carriage of heterozygous and homozygous damaged alleles.

The pathology of the musculoskeletal system in adolescents is the result of the interaction of many hereditary (genetic) factors and adverse environmental factors. The main role in the pathogenesis of the disease is assigned to more than 30 genetic factors, which are dispersed along various gene networks of both local and integral order [2, 3]. Significant progress in the early diagnosis and prevention of pathology of the skeletal system has been achieved due to the introduction of precise methods of quantitative densitometry into laboratory practice and the development of clear quantitative criteria for assessing the state of the skeletal system. Despite a certain contradiction in the data on the genetics of osteoporosis, the results of meta-analyzes of population studies made it possible to establish the presence of allelic variants that are reliably associated with low bone mineral density. These include the VDR and RANKL genes [10]. Testing of allelic variants of these genes opens up wide opportunities for the prevention of pathology of the skeletal system, since it allows to effectively identify persons with a high risk of the disease long before the onset of diseases of the musculoskeletal system. These methods belong to the field of preventive medicine. The identification of heterozygotes and, moreover, homozygotes of the genotype for pathological alleles of the gene associated with the development of osteoporosis is 10–15 times higher than the average in the population, allows timely initiation of therapeutic measures to prevent these diseases.

Summing up, we can say that vitamin D takes an active part in the physiological regulation of bone metabolism, including bone growth and the process of bone remodeling in the future, which indicates the need for further study.

## CONCLUSION

In accordance with the purpose and objectives of the study, for the reporting period, a comprehensive examination of children under one year old of the Kazakh population was carried out. The results obtained were evaluated by the totality of the surveyed and by the method of comparison of research data. Based on the results obtained, the following results and conclusions were made.

Conclusions:

1) According to the results of the study, 80.2% of the mothers of the surveyed group had deviations in their health status. It has been proven that the presence of infectious and inflammatory diseases in mothers before and during pregnancy, as well as the absence of D-vitamin prophylaxis, increases the risk of vitamin D deficiency and D deficiency in their children, respectively, by 2.5 (OR = 2.4 CI95% [ 1.1 ÷ 4.8]); 4 (OR = 4.2 CI95% [1.9 ÷ 9.1]) times;

2) It was revealed that children of mothers who did not receive calcium and vitamin D3 preparations or received them from the 2nd trimester and later, significantly more often had a decrease in bone strength ($p < 0.05$), impaired mineral metabolism ($p < 0.05$) and bone metabolism ($p < 0.05$);

3) In children under one year old, osteopenia is caused by unfavorable factors of the antenatal and postnatal periods: complicated course of the present pregnancy (AR = 34.9%; p = 0.01); early irrational artificial feeding (AR = 42.3%; p = 0.03); rickets transferred in the first year of life (AR = 38.1%; p = 0.02);

4)Prenatal use of VMC (vitamin-mineral complex) in 24 women (18.5%) was completely absent during pregnancy; the rest (n = 57; 81.5%) of them: in 20.2% (n = 14) women received only calcium supplements; in 35.7% (n = 25) - a combination of VMC with calcium preparations; in 25.6% (n = 32) - only VMC;

5) The mean time to discontinue vitamin D prophylaxis was 12.4 ± 1.7 months. In 86.2% of cases, the prophylactic dose of vitamin D was 500 IU, in 13.8% of children - 1000 IU);

6) The average level of vitamin D supply in children corresponded to vitamin D deficiency and averaged 20.16 ± 1.7 ng / ml. The best indicators of vitamin D supply were observed in children 7-12 months old (43.54 ± 1.7 ng / ml); the lowest rates are in children from 2 to 6 months (12.3 ± 2.7 ng / ml);

7) The introduction of complementary foods increased the chances of normalizing vitamin D levels by 5 times. With BF + BC (OR = 5.6; CI 95% [2.46 ÷ 12.8]) and with AF + AC- 4 times (OR = 4.0; CI 95% [0.87 ÷ 18, 25]);

8) It was determined that in 54% of children homozygous CC type is determined according to RANKLrs9594759 and TT-17%, respectively, heterozygous CT-33%. According to RANKL rs9594738, homozygous CC in 59% and TT in 28%, heterozygous CT in 15%. According to VDR rs2228570, homozygous CC type in 52% and TT-17%, heterozygous CT-31%. VDR for rs 2228570 homozygous type GG is observed in 76%, AA-4% and heterozygous GA-20%;

9) It was found that RANKLrs 9594738 has an average relationship between the CC-CT genotypes and vitamin D ($p = 0.043$) and a relatively strong relationship between the CT-TT genotypes and vitamin D ($p = 0.008$)

According to RANKL rs9594759, the average relationship between the CC-CT genotypes and vitamin D ($p = 0.033$) and a relatively strong relationship between the CT-TT genotypes and vitamin D ($p = 0.026$).

According to VDR rs2228570, the average relationship between CC-CT genotypes and vitamin D ($p = 0.047$);

10) It was revealed that the nature of the relationship between the T / T and T / C genotypes of the VDR gene and changes in the concentration of vitamin D below the normal value is relatively strong, which proves the presence of a direct relationship between the level of vitamin D and the risk of developing pathology of the skeletal system in children (F> 0, 05 units));

Practical significance

1) It has been proven that the mother's intake of calcium and vitamin D preparations from the first trimester of pregnancy has a positive effect on the bone strength of the child's skeleton, reduces the severity of rickets symptoms and the risk of mineral metabolism disorders in infants;

2) Taking calcium supplements (1000 mg) and vitamin D (400 IU), starting from the first trimester, has a positive effect on the bone quality of the mother and child;

3) It has been proven that there is a direct relationship between the level of vitamin D and the risk of developing pathology of the skeletal system in children (F> 0.05 units);

Practical advice

1) It is advisable for children with antenatal calcium deficiency during the neonatal period to study mineral metabolism and markers of bone remodeling in the first year of life - bone strength;

2) For children of mothers at risk of calcium deficiency, prevention of mineral metabolism disorders, linear growth, bone strength, skeletal deformities and the development of rickets should be carried out with vitamin D in conjunction with calcium supplements;

3) Recommend to revise the prophylactic and therapeutic dose of vitamin D in children under one year old of the Kazakh population;

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**ANNEX A**

**Application form**

| | | |
|---|---|---|
| 1 | PatientCode | |
| 2 | Date | |
| 3 | FCs | |
| 4 | IIN | |
| 5 | Placeofresidence | |
| 6 | Birthday (date, month, year) | |
| 7 | Nationality | |
| 8 | Genus (tribe) | |

| | **Mother** | **Father** |
|---|---|---|
| **Nationality** | | |
| **Genus (tribe)** | | |
| **Placeofbirth** | | |
| | **Grandma (my mom's mom)** | **Grandma (my father's mom)** |
| **Nationality** | | |
| **Genus (tribe)** | | |
| **Placeofbirth** | | |
| | **Grandfather (mymother'sfather)** | **Grandfather (myfather'sfather)** |
| **Nationality** | | |
| **Genus (tribe)** | | |
| **Placeofbirth** | | |
| | **Great-grandmother (my grandmother's mother)** | **Great-grandmother (my grandfather's mother)** |
| **Nationality** | | |
| **Genus (tribe)** | | |
| **Placeofbirth** | | |
| | **Great-grandfather (my grandmother's father)** | **Great-grandfather (my grandfather's father)** |
| **Nationality** | | |
| **Genus (tribe)** | | |
| **Placeofbirth** | | |

**Participant'sfullname**_____

_____

**Participant'ssignature**_____

**Date**_____

**Full name of the researcher**_____

**Signature of the researcher** _____

**Date**_____

**ANNEXES B**

**Individual patient registration card no.____**

Full name of the child
Date of birth_____Age _____
Mother's full name
Contactphonenumber
Mother'sage
Address

| | YES/NO |
|---|---|
| Toxicosis | |
| Threatofinterruption | |
| Nephropathy (proteininurine) | |
| Bloodpressure | |
| Anemia (hemoglobinfigure ) | |
| Examinationforinfections | |
| Diseases of the mother (kidney, heart, etc.) | |
| Risk factors for osteoporosis/osteopenia hereditary predisposition, frequent previous fractures | |
| Takingmedications (anticonvulsants, glucocorticosteroids) | |
| Badhabits (smoking / alcohol) | |
| Intake of calcium, vitamin D | |

What is the pregnancy count _____
Childbirth _____
Information about the child:
Birth weight _____ Height at birth _____Apgar _____
Shouted / not immediately
Attached to the chest
Feeding
The presence of allergic reactions in the child:
Weight _____ (at the moment )Growth____ (at the moment )
Prevention of rickets (taking vitamin D): YES / NO
Initial signs of rickets (restlessness, timidity, sleep disturbance, sweating, baldness of the back of the head)
Number of teeth at the moment

**ANNEXES C**
**Calendar plan**

1. NON-PROFIT JOINT STOCK COMPANY "WEST KAZAKHSTAN MEDICAL UNIVERSITY NAMED AFTER MARAT OSPANOVA"

1.1 By priority: The science of Life and Health.

1.2 By priority: Biotechnologies in medicine

1.3 On the topic of the project: IRN AP09563003 "Clinical and genetic markers of vitamin status in children under one year of the Kazakh population"

1.4 The total amount of the project for 2021 is 7967,867 (seven million nine hundred sixty-seven thousand eight hundred sixty-seven) tenge for the performance of works according to paragraph 3.

2. Characteristics of scientific and technical products by qualification criteria economic indicators

2.1 Direction of work: Applied scientific research in the field of medical sciences.

2.2 Scope of application: Neonatology, medical genetics, laboratory diagnostics, pediatrics

2.3 Final result for 2021: 1 article will be published, accepted for publication or submitted to a peer-reviewed scientific publication indexed in the Web of Science database and (or) having a CiteScore percentile in the Scopus database of at least 35 percentile.

2.4 Patentability: 1 certificate of state registration of rights to the copyright object will be received.

2.5 Scientific and technical level (novelty): Determination of the role of gene polymorphism in the diagnosis of bone health in children under one year of the Kazakh population.

2.6 The use of scientific and technical products is carried out by: The Customer and The performer.

2.7 Type of use of the result of scientific and (or) scientific and technical activities:

Protocols for the diagnosis and treatment of bone metabolism.

3. Name of works, terms of their implementation and results

| Code | The names of the works under the Contract and the main stages of its implementation | Deadlines for implementation | | Expected result |
|---|---|---|---|---|
| | | beginning | ending | |
| 1. | Determine the content of the questionnaire and conduct a questionnaire procedure to assess the initial status of children 2. Make a plan for the implementation of the NTP by year, by quarter To determine the methods and materials of the study 3. Assessment of the initial condition of children of the Kazakh population based on the results of examination and analysis of primary medical documentation - filling out questionnaires - transferring data to electronic media for subsequent processing. Study D vitaminstatus | May 2021 | August 2021 | B the result of the execution The STP will present an in-depth analysis of the assessment of children of the Kazakh population (anamnesis, examination), which will allow assessing the health status of children in the Kazakh population. Risk groups forvitamin D deficiency will be identified |
| 2. | To determine the frequency of allelic variants of the VDR (rs1544410, rs2228570), RANKL (rs9594738, rs9594759) genes in children under one year of the Kazakh population | September 2021 | November 1, 2021 | For the first time, the frequency of different allelic variants of genes will be determined VDR (rs1544410, rs2228570), RANKL(rs9594738, rs9594759) in children of the Kazakh population |
| 3. | To study the relationship between the allelic polymorphism of the VDR genes (rs1544410, rs2228570), RANKL (rs 9594738, rs9594759) and the degree of vitamin D deficiency and deficiency in children under one year of the Kazakh population | September 2021 | November 1, 2021 | For the first time, the link between the presence of genes will be revealed VDR (rs1544410, rs2228570),RANKL (rs9594738,rs9594759) and severity To vitamin status in children under one year of Kazakh populations |
| 4. | To make the role of determining the polymorphism of genes VDR (rs1544410, rs2228570), RANKL (rs 9594738, | September 2021 | November 1, 2021 | The role of polymorphism of VDR genes (rs1544410, rs2228570) will be proved for the first time, RANKL (rs9594738, rs9594759) as |

| | | | | |
|---|---|---|---|---|
| | rs9594759,) in the diagnosis of bone health in children under one year old Kazakh population 2. Publish 1 article in journals with a CiteScore rating of at least 35 (thirty-five) percentile in the database Scopus data. | | | a risk factor for low vitamin D status in children under one year of the Kazakh population. There will be 1 article published, accepted for publication or submitted to a peer-reviewed scientific publication indexed in the Web of Science database and (or) having a CiteScore percentile in the Scopus database of at least 35 percentile |

by customer:
chairman
GU "Science Committee of the Ministry education and science of the RK "
_____ Kurmangaliyeva Zh.D.

from the performer:
Chairman of the Board-Rector
JS West Kazakhstan Medical University named after Marat Ospanov
_____ Teleuov M.K.

familiarized with:
Scientific supervisor of the project
_____ Zhumalina A.K.

**ANNEXES D**
**List of scientific products**

SCIENTIFIC PUBLICATIONS
publ.science

**Certificate**

This is to certify that the article entitled «Особенности D-витаминного статуса у детей раннего возраста в казахской популяции» and authored by Zhumalina Akmaral, Kim Irina, Tusupkaliev Balash, Zharlikasinova Mairamkul, Zhekeyeva Botagoz is being prepared for publication in the journal, which is currently indexed by the Scopus database.

Date: 07.10.2021 Head of Scientific Projects Implementation Department,
Viacheslav Kerner

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ҚАЗАҚСТАН РЕСПУБЛИКАСЫ

РЕСПУБЛИКА КАЗАХСТАН

**АВТОРЛЫҚ ҚҰҚЫҚПЕН ҚОРҒАЛАТЫН ОБЪЕКТІЛЕРГЕ ҚҰҚЫҚТАРДЫҢ МЕМЛЕКЕТТІК ТІЗІЛІМГЕ МӘЛІМЕТТЕРДІ ЕНГІЗУ ТУРАЛЫ**

# КУӘЛІК

**2021 жылғы «22» қыркүйек № 20379**

**Автордың (лардың) жеке, аты, әкесінің аты (егер ол жеке басын куәландыратын құжатта көрсетілсе):**
**ЖУМАЛИНА АКМАРАЛ КАНАШЕВНА, Тусупкалиев Балаш, Ким Ирина Сергеевна, Жарлыкасинова Майрамкуль Буркутбаевна**

**Авторлық құқық объектісі: қылыми туынды**

**Объектінің атауы: Vitamin D receptor gene polymorphism among children (literature review)**

**Объектіні жасаған күні: 11.11.2020**

ЭЦҚ қол қойылды

Оспанов Е.К.

ЗАПАДНО - КАЗАХСТАНСКИЙ
МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
имени Марата Оспанова

# Программа

Международной научно - практической конференции «СОВРЕМЕННАЯ МЕДИЦИНА: НОВЫЙ ПОДХОД И АКТУАЛЬНЫЕ ИССЛЕДОВАНИЯ» среди медицинских организаций образования Казахстана, ближнего и дальнего зарубежья, приуроченной ко дню Всемирного дня борьбы с остеопорозом.

20 октября 2021 года г. Актобе

## Секция 1: «Проблемные аспекты в медицине, связанные с дефицитом витамина D»

**https://wkmu.webex.com/meet/webex2**

**Модераторы:**

**Сапарбаев Самат Сагатович** – Проректор по стратегическому развитию, науке и международному сотрудничеству, член Правления, кандидат медицинских наук, ассоциированный профессор

**Климов Леонид Яковлевич** – заведующий кафедрой факультетской педиатрии, декан педиатрического факультета Ставропольского государственного медицинского университета, доктор медицинских наук, доцент.

**Время Актобе**

**11.50–12.05**

**Верисокина Наталья Евгеньевна,** ГБОУ ВО «Ставропольский государственный медицинский университет» МЗ РФ - "Обеспеченность витамином D и гипокальциемия у новорожденных и недоношенных детей".

**12.05-12.20**

**Бейшебай кызы Гулнур,** Кыргызская государственная медицинская академия им. И.К. Ахунбаева, г. Бишкек, Кыргызстан – "Морфологические особенности тимуса у новорожденных крыс в условиях горной гипоксии Кыргызстана".

**12.20-12.35**

**Дёмин Евгений Павлович,** ТОО «МЦ Тау Сункар», г.Алматы, Республика Казахстан - "Перспективы применения ТриДаль® спрей у пациентов с остеопорозом и саркопенией".

**15.30-15.45**

**Ким Ирина Сергеевна,** НАО «Западно-Казахстанский медицинский университет имени Марата Оспанова», г. Актобе, РК. - "Полиморфизм генов ассоциированный с риском развития гиповитаминоза D у детей раннего возраста казахской популяции".

**15.45-16.00**

**Донаева Айнур Ергалиевна,** НАО «Западно-Казахстанский медицинский университет имени Марата Оспанова», г. Актобе, РК. - "Полиморфизм гена рецептора витамина D VDR и минеральной плотности костной ткани у азиатских девочек-подростков с первичной дисменореей".

**16.00-16.15**

**Кульжанова Динара Сандибаевна,** НАО «Западно-Казахстанский медицинский университет имени Марата Оспанова», г. Актобе, РК. - "Статус витамина D у девочек-подростков с первичной дисменореей".

Приложение к приказу СГМУ
№ _____ _____

**Программа**
**IV Межрегиональной научно-практической конференции**
**с международным участием**
**«Актуальные проблемы современной педиатрии»**
**в рамках информационного проекта Министерства здравоохранения Саратовской области и ФГБОУ ВО «Саратовский ГМУ им. В. И. Разумовского» Минздрава России**
**«Мастер-классы и конференции для сельского доктора»**
**Ссылка для регистрации и подключения:**
**https://events.webinar.ru/29333781/8851265**
**23 октября 2021 года**

10:00-10:05 **Приветственное слово.**
10:05-10:35 **Лекция: «Острые респираторные вирусные инфекции: сложности дифференциальной диагностики в эпоху пандемии».**
**Михайлова Е.В.** - д.м.н., профессор, заведующая кафедрой детских инфекционных болезней и поликлинической педиатрии им. Н.Р. Иванова ФГБОУ ВО «Саратовский ГМУ им. В. И. Разумовского» Минздрава России, главный внештатный специалист по детским инфекционным заболеваниям Министерства здравоохранения Саратовской области;
**Малюгина Т.Н.** - д.м.н., профессор кафедры детских инфекционных болезней и поликлинической педиатрии им. Н.Р.Иванова ФГБОУ ВО «Саратовский ГМУ им. В. И. Разумовского» Минздрава России
10:35 -10:40 **Дискуссия. Ответы на вопросы.**

10:40-11:10 **Лекция: «Ожирение -современная проблема педиатрии».**
**Болотова Н.В.** — д.м.н., профессор, профессор кафедры пропедевтики детских болезней, детской эндокринологии и диабетологии ФГБОУ ВО «Саратовский ГМУ им. В. И. Разумовского» Минздрава России.
11:10-11:15 **Дискуссия. Ответы на вопросы.**

11:15 -11:45 **Лекция: «Ювенильные гемангиомы: на пути от хирургии к соматической педиатрии. Что должен знать педиатр о консервативном лечении гемангиом».**
**Спиваковский Ю.М.** - к.м.н., доцент, заведующий кафедрой факультетской педиатрии ФГБОУ ВО «Саратовский ГМУ им. В. И. Разумовского» Минздрава России, главный внештатный специалист по детской ревматологии министерства здравоохранения Саратовской области.
11: 40-11:45 **Дискуссия. Ответы на вопросы.**

11:45-12:10 **Лекция: «Дефицит витамина Д: актуальные вопросы профилактики и лечения».**
**Филина Н.Ю.** — д.м.н., доцент, заведующая кафедрой пропедевтики детских болезней, детской эндокринологии и диабетологии ФГБОУ ВО «Саратовский ГМУ им. В. И. Разумовского» Минздрава России.
12:10-12:15 **Дискуссия. Ответы на вопросы.**

12:15-12:40 **Лекция: «Генетический полиморфизм недостаточности витамина Д у детей казахской популяции».**
**Жумалина А. К.**- доктор медицинских наук, профессор, руководитель кафедры детских болезней № 1 с неонатологией Западно-Казахстанского государственного медицинского университета имени Марата Оспанова (Актобе, Казахстан);
**Ким И.С.**- ассистент кафедры детских болезней №1 с неонатологией Западно-Казахстанского государственного медицинского университета им. Марата Оспанова (Актобе, Казахстан)
**Тусупкалиев Б.Т.**- доктор медицинских наук, профессор, Академик РАЕ, профессор кафедры детских болезней №1 с неонатологией Западно-Казахстанского государственного медицинского университета им. Марата Оспанова (Актобе, Казахстан);
**Саханова С. К.**- д.м.н., доцент, руководитель Научно-практического центра Западно-Казахстанского медицинского университета имени М.Оспанова (Актобе, Казахстан);
12:40-12:45 **Дискуссия. Ответы на вопросы.**

12:45-13:05 **Лекция: «Остеопороз и остеопения у пациентов с ювенильными артритами: роль витамина Д».**
**Спиваковская А.Ю.** - к.м.н., доцент кафедры госпитальной педиатрии и неонатологии ФГБОУ ВО «Саратовский ГМУ им. В. И. Разумовского» Минздрава России, руководитель курса по детской ревматологии.
**13:05 -13:10 Дискуссия. Ответы на вопросы.**

**13:10-13:40 Лекция: «Пищевая аллергия: что мы должны знать и что мы должны делать».**
**Гузеева Г.В.** — к.м.н., врач-педиатр консультативной поликлиники СОДКБ, главный специалист по детской гастроэнтерологии и эндоскопии Министерства здравоохранения Саратовской области.
13:40-13:45 **Дискуссия. Ответы на вопросы.**

13:45-14:15 **Лекция: «Вакцинопрофилактика: законы и правила. Вакцинопрофилактика иммунокомпрометированных детей».**
**Алешина Л.В.** – к.м.н., асситстент кафедры клинической иммунологии и аллергологии ФГБОУ ВО «Саратовский ГМУ им. В. И. Разумовского» Минздрава России, внештатный специалист по иммунологии МЗ Саратовской области.
**14:15-14:20 Дискуссия. Ответы на вопросы.**

СОГЛАСОВАНО
Проректор по стратегическому развитию,
науке и международному сотрудничеству,
член Правления ЗКМУ имени Марат Оспанова
_____ С.С.Сапарбаев
«25» 10 2021г.

АКТ №178
От «25» 10 2021 г
внедрение научно-исследовательской работы
Западно-Казахстанский медицинский университет имени Марата Оспанова
Кафедра детских болезней №1 с неонатологией
( наименование учреждения, где внедряется работа)

**Наименование предложения**: «Использование показателя витамина Д сыворотки крови в оценке уровня нарушения метаболизма у новорожденных».
**Работа включена:** для улучшения плана работы кафедры детских болезней №1 с неонатологией на 2021-2022 учебный год. Внедрена в инициативном порядке.
**Форма внедрения:** В вопросах практических занятии на 4 курсе по следующим темам: Организация педиатрической помощи. Новорожденный. Доношенный ребенок. Недоношенный ребенок. Первичный патронаж новорожденного. На 4 курсе будут дополнительно рассматриваться особенности определения витамина Д в крови и использование их показателей в оценке уровня нарушения метаболизма у новорожденных.
**Ответственный за внедрение и исполнитель:** рук. каф. Жумалина А.К., проф. Тусупкалиев Б.Т., доц. Волошина Л.В., Ким И.С., Егшатян Н.В., Замэ Ю.А.
**Эффективность внедрения:** диагностическая.
**Предложения, замечания учреждения, осуществляющего внедрение:**
Повышение знаний студентов по вопросам современной диагностики дефицита витамина Д и оценке уровня нарушения метаболизма в крови у новорожденных при проведении практического занятия на 4 курсе будет способствовать улучшению знании по следующим темам: Организация педиатрической помощи. Новорожденный. Доношенный ребенок. Недоношенный ребенок. Первичный патронаж новорожденного.
**Срок внедрения:** сентябрь 2021 года- сентябрь 2022 года

**Председатель комиссии** Жумалина А.К.

**Члены (ответственные за внедрение):** Жумалина А.К.
Тусупкалиев Б.Т.
Волошина Л.В.
Ким И.С.
Егшатян Н.В.
Замэ Ю.А.

**Исполнитель:** Жекеева Б.А.

СОГЛАСОВАНО
Проректор по стратегическому развитию,
науке и международному сотрудничеству,
член Правления ЗКМУ имени Марат Оспанова
_____ С.С.Сапарбаев
«25» 10 2021г.

АКТ № 176
От «25» 10 2021г.
внедрение научно-исследовательской работы
Западно-Казахстанский медицинский университет имени Марата Оспанова
Кафедра детских болезней №1 с неонатологией
( наименование учреждения, где внедряется работа)

**Наименование предложения**: «Использование показателя витамина Д сыворотки крови в оценке уровня нарушения метаболизма у новорожденных».
**Работа включена:** для улучшения плана работы кафедры детских болезней №1 с неонатологией на 2021-2022 учебный год. Внедрена в инициативном порядке.
**Форма внедрения:** В резидентуру по специальности 7R031 – Неонатология. В вопросах по следующим темам: Организация неонатальной помощи. Неонатальный скрининг. Уход и лечение новорожденных после перенесенной асфиксии. Устранение гипоксемии и нормализации кровообращения. Лечение мекониальной аспирации. Онтогенетические особенности иммунной системы у новорожденных. Резидентами неонатологами дополнительно будут рассматриваться особенности определения витамина Д в крови и использование их показателей в оценке уровня нарушения метаболизма у новорожденных.
**Ответственный за внедрение и исполнитель:** рук. каф. Жумалина А.К., проф. Тусупкалиев Б.Т., доц. Жарлыкасинова М.Б., и.о. доц. Жекеева Б.А., Зав.ОРИТН ОПЦ Асанова С.С., Зав ОПН АМЦ родильного отделения Ергалиева Г.Ж.
**Эффективность внедрения:** диагностическая.
**Предложения, замечания учреждения, осуществляющего внедрение** Повышение знаний резидентов-неонатологов по вопросам современной диагностики дефицита витамина Д и оценке уровня нарушения метаболизма в крови у новорожденных при проведении практических занятии резидентам неонатологам 1 и 2 года обучения будут способствовать улучшению знаний по следующим темам: Организация неонатальной помощи. Новорожденные. Доношенный ребенок. Недоношенный ребенок. Неонатальный скрининг. Уход и лечение новорожденных после перенесенной асфиксии. Устранение гипоксемии и нормализации кровообращения. Лечение мекониальной аспирации. Онтогенетические особенности иммунной системы у новорожденных.
**Срок внедрения:** сентябрь 2021 года- сентябрь 2022 года

**Председатель комиссии** Жумалина А.К.

**Члены (ответственные за внедрение):** Жумалина А.К.
Тусупкалиев Б.Т.
Жарлыкасинова М.Б.,
Жекеева Б.А.
Асанова С.С.
Ергалиева Г.Ж.

**Исполнитель:** Жекеева Б.А.

ПРО БҚМУ 605-03-2020. Ғылыми-зерттеу жұмысын енгізу акті. Алтыншы басылым.
Ф ПРО ЗКМУ 605-03-2020. Акт внедрения научно-исследовательской работы. Издание шестое.