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VITAMIN D LEVELS IN NEWBORNS CHILDREN OF STAVROPOL REGION

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ОБЕСПЕЧЕННОСТЬ ВИТАМИНОМ D НОВОРОЖДЁННЫХ ДЕТЕЙ СТАВРОПОЛЬСКОГО КРАЯ

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Vitamin D has a wide range of biological effects. There is evidence suggesting an important role of vitamin D in women's reproductive health, yet there has been no research focusing on newborns in South Russia. The purpose of this current study was to analyze the levels of vitamin D in newborns in the Stavropol Region. The clinical, anamnestic, and laboratory examination involved 60 newborns. The levels of vitamin D were assessed based on serum content of calcidiol, while the mothers' pregnancy courses were also taken into account. The mean content of serum 25(OH)D₃ was 9.9±0.7 ng/ml. The study showed that the vast majority of the patients (98.3%) lacked vitamin D while in over a half of them (56.7%) the deficiency was severe. It was shown that complicated somatic, obstetric and gynecological history is an important factor for antenatal hypovitaminosis D in newborns (p<0.05). In case of mothers' taking multivitamin preparations through pregnancies, severe vitamin D deficiency in newborns had an occurrence twice below that in infants whose mothers failed to take additional vitamin supply (p<0.001). There is confirmation to the need for targeted antenatal prevention of hypovitaminosis D in order to reach proper levels of calciferol in the early neonatal period.

Key words: vitamin D, newborn, hypovitaminosis d, pregnancy failure, antenatal prophylaxis

Витамин D оказывает широкий спектр биологических эффектов. Имеются данные, указывающие на значимую роль витамина D в репродуктивном здоровье женщин, но до настоящего времени показатели у новорожденных юга России не изучались. Целью исследования был анализ обеспеченности витамином D новорождённых детей Ставропольского края. Проведено клинико-анамнестическое и лабораторное обследование 60 новорождённых. Обеспеченность витамином D оценивалась по содержанию кальцидиола в сыворотке крови, из анамнестических данных подробно анализировалось течение беременности у матери. Среднее содержание 25(OH)D₃ сыворотки составляло 9,9±0,7 нг/мл. Установлено, что у подавляющего большинства пациентов (98,3%) имеет место недостаточное содержание витамина D, более половины (56,7%) страдают тяжёлым дефицитом. Показано, что осложнённый соматический и акушерско-гинекологический анамнез являет-

ся значимым антенатальным фактором формирования тяжёлого гиповитаминоза D у новорождённых ($p < 0,05$). На фоне приёма матерью поливитаминных препаратов тяжёлый дефицит витамина D у новорождённых встречается в 2 раза реже, чем у младенцев, рождённых от матерей без дополнительной дотации ($p < 0,001$). Подтверждена необходимость целенаправленной антенатальной профилактики гиповитаминоза D для достижения нормального уровня обеспеченности кальциферолом в раннем неонатальном периоде.

Ключевые слова: витамин D, новорождённые, гиповитаминоз D, патология беременности, антенатальная профилактика

Despite the fact that vitamin D and its role in the regulation of calcium-phosphorus metabolism were discovered over eight decades ago, the interest in the effects of cholecalciferol and its active metabolites are growing steadily nowadays [1, 4, 12]. Lack of vitamin D is not only a triggering factor in the development of musculoskeletal disorders (rickets, osteoporosis, myofascial dysfunction) yet it is also closely associated with an increased risk of autoimmune (multiple sclerosis, Crohn's disease, celiac disease, type I diabetes mellitus, autoimmune thyroiditis), cardiovascular (acute myocardial infarction, hypertension) and oncology diseases [6, 9, 13, 14, 17].

Vitamin D deficiency is a widespread condition in the postnatal period [2, 13]. In particular, 70% of American children have their level of 25(OH)D below 30 ng/ml, while 9% of them have the content of calcidiol under 15 ng/ml [16].

Newborns and young children are at special risk in terms of vitamin D deficiency due to relatively higher need for it, which is accounted for by a high growth rate and skeletal mineralization [2, 3]. Polluted air, including South Russia, is one of the adverse factors hindering the synthesis of cholecalciferol in the skin [5, 15].

Of special interest here are the studies focusing on the impact that vitamin D has on pregnancy. Active metabolite $1.25(\text{OH})_2\text{D}_3$ has been shown to regulate the secretion of human chorionic gonadotropin and it increases the production of reproductive hormones in placenta [7]. Calcitriol promotes placental calcium transport, stimulates the secretion of placental lactogen, and increases the sensitivity of the endometrium to implantation [4]. Vitamin D deficiency has been proven to have a role in occurrence of pregnancy complications: hypertension, nephropathy [19], increased frequency of spontaneous preterm birth and cesarean section [8], vaginosis in early pregnancy [11], increased risk of gestational diabetes [4], etc.

Newborns have vitamin D acquired prenatally, which is maintained at a certain level for the first months of life [18]. There has been no research until now focusing on vitamin D and the occurrence of its deficiency among newborns in South Russia.

The purpose of this study was to investigate the levels of vitamin D in newborns in the Stavropol Region.

Material and Methods. This clinical, anamnestic, laboratory and instrumental examination of 60

newborns was held on the premises of the Department for Newborns at the Stavropol Regional Clinical Perinatal Center.

A detailed analysis was performed into the comorbidities in the mothers and the course of pregnancy. Taking blood samples of 25(OH)D was done in the first three days of the newborns' life.

The levels of vitamin D were assessed based on the total content of the intermediate metabolite calcidiol ($25(\text{OH})\text{D}_3$) in the blood serum, which was determined using immunofluorescence analyzer Liason DiaSorin Pleutschland GmbH (Germany).

The assessment of the results was carried out in accordance with the recommendations of the International Society of Endocrinology (2011): vitamin D deficiency – $25(\text{OH})\text{D}_3$ below 20 ng/ml; lack of vitamin D – 21–29 ng/ml; proper level of vitamin D – 30–100 ng/ml. Concentrations below 10 ng/ml are interpreted as severe vitamin D deficiency while level above 100 ng/ml is seen as excessive [1, 12].

The mathematical processing of the research data was carried out using the software package STATISTICA ver.10.0 and AtteStat employing parametric and nonparametric methods. To determine the type of data distribution the Shapiro-Wilk test was used. For parametric quantitative data arithmetic mean (M) and error of the arithmetic mean (m) were calculated. For the non-parametric quantitative data the median and the 25th and 75th quartiles were determined.

To assess the intergroup differences Student's t-test was employed in the analysis of quantitative parametric data, in the groups with non-parametric quantitative data – U-Wilcoxon, Mann-Whitney test with amendments for small samples: in case a value was below 4 then Yates' correction was introduced; however, if a value was below 4 with a total number of values under 30, the Fisher's test was used. To identify the links between the quantitative data Pearson's chi-square test was used. The differences were considered statistically significant at $p \leq 0.05$.

Results and Discussion. A detailed study of maternal history in the children enrolled in our study showed that 45 (75.0%) of them suffered from chronic extragenital diseases, while 38 (63.3%) of the women had a gynecological pathology.

The current pregnancy in most cases was pathological: in the 1st trimester – in 52 (86.7%) women; in the 2nd – in 54 (90.0%), and in the 3rd trimester – in 54 (90.0%) of them. Up to 12 weeks of gestation the most frequent were severe toxicosis, danger of spontaneous abortion, anemia and

various somatic diseases. In the second and third trimesters the threatened miscarriage, anemia, isolated increased blood pressure and preeclampsia, alongside with extragenital diseases and fetoplacental insufficiency were observed (Table).

Table

Pathology of pregnancy in mothers of newborns

Index	1 st tri- mester of gestation		2 nd tri- mester of gestation		3 rd tri- mester of gestation	
	Abs.	%	Abs.	%	Abs.	%
Severe toxico- sis in the first half of pregnancy	13	25.0	-	-	-	-
Threatened miscarriage	22	42.3	19	35.2	10	18.5
Anemia	7	13.5	5	9.3	12	22.2
Increased blood pressure	2	3.8	8	14.8	9	16.6
Pre-eclampsia	-	-	9	16.6	11	20.4
Fetoplacental insufficiency	-	-	3	5.6	5	9.3
Extragenital pathology	8	15.4	10	18.5	7	13.0
TOTAL	52	100	54	100	54	100

The levels of vitamin D in the newborns of the Stavropol Region is extremely low, the average serum levels of 25(OH)D₃ being 9.9±0.7 ng/ml. Severe deficiency (below 10 ng/ml) was identified in 34 (56.7%) babies; 23 (38.3%) new borns had the vitamin D level at 10–20 ng/ml; lack of vitamin D (20–30 ng/ml) was found in 2 (3.3%) babies and only 1 (1.7%) of the newborn had an optimal level of vitamin D (over 30 ng/ml).

The outcomes are comparable with those of our Asian colleagues. A similar study involving newborns, which was held in China (Beijing – 39.60 N) showed severe deficiency in 46.6% of the cases while no baby was detected with a proper level of vitamin D [20].

A comparison of our data with those of North American colleagues revealed significant differences. A study held in Omaha (41 N; Nebraska, USA) in particular manifested that the average level of serum calcidiol in newborns was 17.8±4.7 ng/ml (p=0.007) [10].

Since vitamin D is not synthesized through the intrauterine development and its only source is the mother's body, the blood calcidiol levels in the newborns serve an indirect indication of vitamin D in the mother. As stated earlier, hypovitaminosis D can be a predictor of pregnancy pathology and the results yielded through this present study support the view of the high frequency of abnormal pregnancy when combined with severe hypovitaminosis D. On the other hand, a pathological pregnancy will inevitably entail certain disturbances in the utero-placental blood flow and reduce the availability of nutrients to the fetus, which can naturally lead to vitamin D deficiency.

Figure 1 shows that in pathological pregnancies newborns had significantly lower levels of vitamin D. Significantly lower values were obtained in infants marked with the burdened obstetric and gynecological history in the 1st and 2nd trimesters of pregnancy.

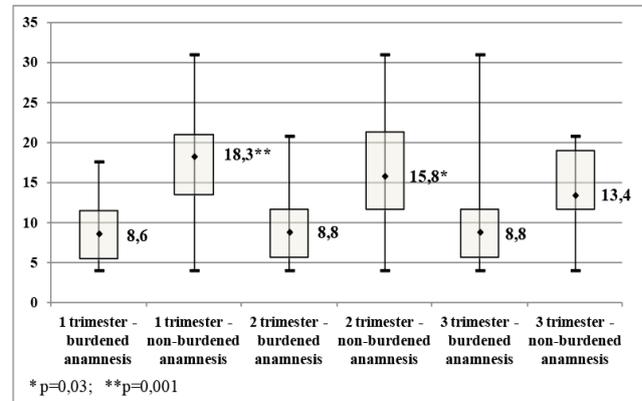


Fig 1. Comparative analysis of vitamin D levels in newborns depending on complications through pregnancy

31 (51.7%) babies of the general group involved into this study were born at a gestational age of 37 to 42 weeks; 29 (48.3%) of the patients were born premature. Among the full-term newborns the average level of 25(OH)D₃ was 9.2±0.8 ng/ml; in those born prematurely the average concentration of calcidiol was 10.7±1.1 ng/ml. There were no significant differences between the groups of patients with various gestational ages (p>0.05). Vitamin D deficiency was identified in 30 (96.8%) full-term babies and in 20 (64.5%) premature newborns; severe hypovitaminosis D was found in 22 (64.5%) and in 14 (48.3%) infants, respectively (p>0.05) (Fig. 2).

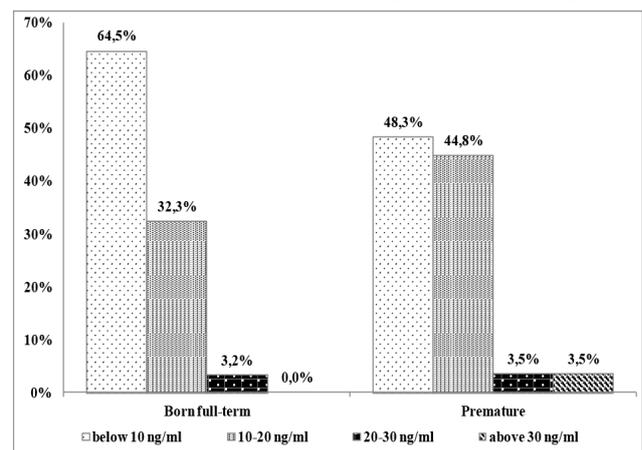


Fig. 2. Comparative description of vitamin D levels depending on gestation age

Despite all the recommendation regarding maximum intake of vitamin and mineral supplements through pregnancies, only 22 (36.7%) of the women took those while another 38 (63.3%) women never took them. Naturally, vitamin D levels in infants whose mothers took multivitamins were significantly higher if compared to the infants whose mothers failed to take vitamin and mineral supplements – 12.8±1.4 ng/ml vs 8.3±0.6 ng/ml, respectively (p<0.01).

The data in the Figure 3 shows that intake of the medications, containing calciferol during pregnancy will reduce significantly the proportion of babies with severe hypovitaminosis D ($p < 0.001$). The level of 25(OH)D₃ above 20 ng/ml was observed only in those infants whose mothers took multivitamins during pregnancy.

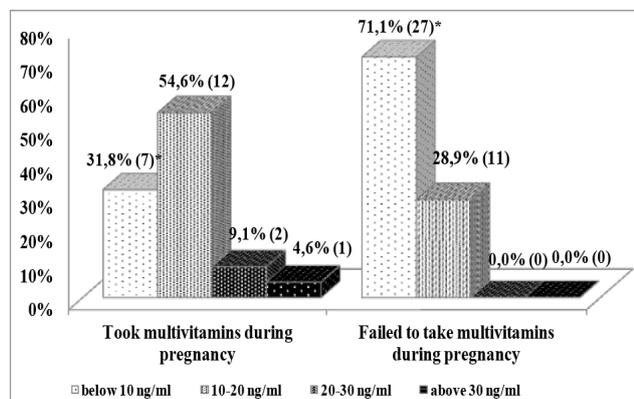


Fig. 3. Vitamin D in newborns depending on multivitamins intake by mothers during pregnancy

Of the cohort of the patients examined, 23 children were born to primiparas, while 26 patients were second born, and 11 – third born. The mean age of the mothers giving birth to the second and third children was basically the same – 31.2 ± 1.5 ; the mean age of primiparas was 26.5 ± 1.5 .

The levels of vitamin D in the first born infants was found to be lower than in case of the second and third labours (9.7 ± 1.3 and 11.0 ± 1.2 ng/ml, respectively) yet in the subsequent delivery its content decreases significantly, becoming lower than that of primiparas (7.2 ± 0.6 ng/ml).

The distribution of patients based on the level of the deficiency produced a similar picture.

Among those born to primiparas, severe deficiency was observed in 15 (65.3%) patients; among the second born – in 11 (42.3%), and among the third born – in 11 (100%) infants. Hypovitaminosis D at 10–20 ng/ml was registered in 6 (26.2%) first born infants and in 15 (57.7%) second born. Only 2 (8.6%) cases born to primiparas had 25(OH)D above 20 ng/ml.

Conclusions. The vast majority of the newborns in the Stavropol Region were found to suffer from vitamin D deficiency, and in more than half of the cases the deficiency was severe.

Chronic somatic pathologies complicated by burdened obstetric and gynecological history alongside with pathology of pregnancy are significant factors in antenatal development of severe hypovitaminosis D in newborns. In our region, pregnancy through spring and summer time where exposure to sunlight is high, with no targeted antenatal prophylaxis of hypovitaminosis D, will not allow reaching proper levels of vitamin D supply in the early neonatal period.

Taking vitamin and mineral supplements for pregnant women, which contain minimal dose of vitamin D (200–500 IU) reduces significantly the risk of developing severe hypovitaminosis D in newborns. A promising area here is an investigation into the link between vitamin D levels in pregnant women and the risk of obstetrical pathology.

The results obtained through our study show that only well-coordinated work by obstetric, gynecological, and pediatric services aiming at antenatal prophylaxis of hypovitaminosis D may not just reduce the frequency of abnormal pregnancies yet also dramatically increase the availability of cholecalciferol in child population, starting from their neonatal period.

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DEVELOPMENT OF A PHARMACETICAL ANTICANCER GEL BASED ON DOXORUBICIN AND SILICONE NANOTECHNOLOGY

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РАЗРАБОТКА ФАРМАЦЕВТИЧЕСКОГО ПРОТИВООПУХОЛЕВОГО ГЕЛЯ С НИОСОМАЛЬНЫМ ДОКСОРУБИЦИНОМ

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Developed a gel based on pharmacological niosomes silicone nature incorporated with the anticancer drug – doxorubicin at 5 mg/ml to enhance the efficacy of cancer treatment. Using prototype gel doxorubicin niosomes composition provides greater bioavailability of the antibiotic and significantly prolongs its retention time in blood concentrations. Even 48 hours after gel application prototype drug concentration in the blood exceeds control values three times. The transdermal route of administration of doxorubicin can reduce the cardiotoxic effect of the drug, dyspeptic reactions, reduce the likelihood of necrosis at the injection site, which significantly extends the use of the drug among patients with heart failure, diseases of the gastrointestinal tract.

Key words: doxorubicin, niosomes, niosomal gel, skin cancer