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**FEATURES OF VITAMINS AND MICROELEMENTS AMONG CHILDREN WITH POST-COVID SYNDROME**

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✓ **Resume**

*The article is devoted to the study of the composition of vitamins (B6, C, D) and trace elements (calcium, phosphorus and iron) in children with post-Covid syndrome. The study is based on data from a prospective examination of 253 children with confirmed COVID-19 (by nasopharyngeal smear or IgM COVID-19 blood enzyme-linked immunosorbent assay (ELISA) PCR diagnosis) who complained of subsequent symptoms. Covid syndrome (PCS) 12 weeks after COVID-19. As a result, it has been proven that the development of post-Covid syndrome in children infected with COVID-19 is 65.6%. Typical variants of the post-Covid syndrome in children: asthenic (7.1%), respiratory (8.3%), cardiac (18.6%), recurrent diseases of the ENT organs (7.9%), functional gastrointestinal diseases (38.7%), mixed version (19.4%). Children with PCS have deficiencies in electrolytes such as phosphorus, calcium, and iron, as well as vitamins B6, C, and D, indicating a strained immune system.*

**Key words:** post-Covid syndrome, diagnosis, micronutrients, vitamin levels, children

**ОСОБЕННОСТИ СОДЕРЖАНИЯ ВИТАМИНОВ И МИКРОЭЛЕМЕНТОВ У ДЕТЕЙ С ПОСТКОВИДНЫМ СИНДРОМОМ**

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✓ **Резюме**

*Статья посвящена изучению содержания витаминов (B6, C, D) и микроэлементов (кальций фосфор и железо) у детей с постковидным синдромом. В основу исследования положены данные проспективного обследования 253 детей с подтвержденным COVID-19 (методом ПЦР-диагностики мазка из носоглотки или иммуноферментным анализом (ИФА) крови IgM COVID-19), обратившихся с жалобами на возникшие симптомы постковидного синдрома (ПКС) спустя 12 нед после COVID-19. В результате было доказано, что развитие постковидного синдрома у детей, перенесших COVID-19 составляет 65,6%. Характерными вариантами постковидного синдрома у детей являются: астенический (7,1%), респираторный (8,3%), кардиальный (18,6%), рецидивирующие заболевания ЛОР-органов (7,9%), функциональные гастроинтестинальные расстройства (38,7%), смешанный вариант (19,4%). У детей с ПКС отмечается дефицит таких электролитов как фосфор, кальций и железо, а также дефицит витаминов B6, C и D, что свидетельствует о напряженности иммунной системы.*

**Ключевые слова:** постковидный синдром, диагностика, микроэлементы, уровень витаминов, дети

## POST-COVID SINDROMLI BOLALARDA VITAMINLAR VA MIKROELEMENTLAR TARKIBINING XUSUSIYATLARI

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✓ **Rezyume**

*Maqola post-Covid sindromi bo'lgan bolalarda vitaminlar (B6, C, D) va mikroelementlar (kaltsiy fosfor va temir) tarkibini o'rganishga bag'ishlangan. Tadqiqot COVID-19 bilan tasdiqlangan (nazofarengial smear yoki IgM COVID-19 qon fermenti bilan bog'liq immunosorbent tahlilining (ELISA) PCR diagnostikasi bo'yicha) 253 bolani prospektiv tekshirish ma'lumotlariga asoslanadi, ular keyingi alomatlardan shikoyat qiladilar. Covid sindromi (PCS) COVID-19dan 12 hafta o'tgach. Natijada, COVID-19 bilan kasallangan bolalarda post-Covid sindromining rivojlanishi 65,6% ni tashkil etishi isbotlangan. Bolalarda post-Covid sindromining tipik variantlari: astenik (7,1%), nafas olish (8,3%), yurak (18,6%), LOR a'zolarining takroriy kasalliklari (7,9%), funktsional oshqozonichak kasalliklari (38,7%), aralash versiya (19,4%). PCS bilan og'rigan bolalarda fosfor, kaltsiy va temir kabi elektrolitlar, shuningdek, B6, C va D vitaminlari etishmovchiligi mavjud bo'lib, bu immunitet tizimining zo'riqishini ko'rsatadi.*

**Kalit so'zlar:** post-Covid sindromi, tashxis, mikroelementlar, vitaminlar darajasi, bolalar

### Relevance

The results of population studies indicate extremely insufficient consumption and an increasingly increasing deficiency of vitamins (A, group B, C, E), as well as microelements (iron, zinc, iodine) among a significant part of the population of the Russian Federation. Thus, deficiency of B vitamins is detected in 30–40%, b-carotene in more than 40%, and vitamin C in 70–90% of subjects [3]. In this case, the identified deficiency often has the character of a combined vitamin deficiency.

The intense level of metabolism among children, which not only supports vital functions, but also ensures the growth and development of the child's body, requires sufficient and regular intake of micronutrients. Therefore, the development of deficiency of vitamins and microelements among children may be accompanied by various health disorders [9]. Unbalanced and insufficient (both qualitatively and quantitatively) nutrition of Russian children has led to the fact that most of them have a deficiency of microelements and vitamins, 16–47% have anemia, and 24–63% have latent iron deficiency [3, 6]. In addition, as a result of nutritional deficiency of microelements such as iron and iodine, in recent years there has been a clear trend towards a deterioration in the mental health of children. It should be noted that the frequency of detection of iodine deficiency is increasing [5]. With iodine deficiency, irreversible changes occur in the brain of a growing child's body, mental retardation and cretinism develop. Iodine deficiency is the most common preventable cause of intellectual disability [12]. However, in Russia, the activity of measures to prevent iodine deficiency in the last decade has been significantly reduced. This could not but affect the somatic health of children.

It is believed that the main role in the regulation of immune function belongs to vitamins D and A [2, 11]. Even a slight deficiency of vitamins A and C leads to increased sensitivity of the body to infections. The intake of sufficient amounts of vitamin A into the child's body is a prerequisite for the differentiation of cells of the immune system and the barrier function of the mucous membranes. Using modern methods of data mining, it was found that a reduced supply of vitamins A, PP, B6, B12, E was statistically significantly associated with decreased immunity, increased body weight, reduced activity of the detoxification systems of the child's body, increased frequency of asthma attacks, headaches (vegetative -vascular dystonia) and myopia [1, 3]

It has been established that a deficiency of vitamins C, D, B6 and B12 is associated with a 1.4–6.9 times increase in the risk of elevated concentrations of organic substances of technogenic origin in the blood, and unfavorable environmental conditions contribute to the occurrence of vitamin deficiency [4, 6]. Among children with subclinical polyhypovitaminosis, under conditions of technogenic toxicant load, the intensity of erythropoiesis increases, the activity of proliferative processes of the



lymphomonocytic lineage, cellular factors of nonspecific resistance decreases, and the activity of the antioxidant defense system decreases [6, 8].

Research into the pathogenesis and clinical course of the new coronavirus disease (COVID-19) is being conducted around the world. At the same time, various dietary therapy options and alternative supportive treatments are being tested. All this work is aimed at reducing mortality, the severity of the disease and the severity of post-Covid syndrome [7, 10].

It should be taken into account that the use of antibiotics, which are prescribed, including for the treatment of COVID-19 in a hospital, aggravates the development of B vitamin deficiency [4, 6], and prescribed glucocorticosteroids deplete vitamin C reserves in the body. Conversely, simultaneous use of retinol and corticosteroids reduces the risk of side effects of the vitamin A drug. It has also been proven that the simultaneous use of ascorbic acid and indirect anticoagulants, heparin, leads to a decrease in the effectiveness of the latter. [4, 10, 12]

The results obtained confirm the advisability of including a complex of vitamins in combination with various drugs in pharmacological doses in multitherapeutic regimens for the treatment of SARS-CoV-2 and post-Covid syndrome [10, 12].

Vitamin-mineral complexes containing up to 100% of the daily requirement of vitamins, which the patient can take without a doctor's prescription, are known as biologically active food supplements [6, 8, 12]. However, the timing, dosage and interactions of these micronutrients must be carefully considered.

**Purpose of the study:** to study the content of vitamins (B6, C, D) and microelements (calcium phosphorus and iron) among children with post-Covid syndrome.

### Materials and methods

The study was conducted on the basis of a children's diagnostic center and family clinics in the city of Tashkent. We examined 253 children with confirmed COVID-19 (by PCR diagnosis of a nasopharyngeal smear or enzyme-linked immunosorbent assay (ELISA) of IgM COVID-19 blood), who complained of symptoms of post-Covid syndrome (PCS) 12 weeks after COVID-19. The age of patients is from 1 to 17 years.

This group of patients was examined by an allergist-immunologist, cardiologist, neurologist, gastroenterologist, and pediatrician.

As a result, 2 groups were formed: the main group - 166 children with PCL, the comparison group - 87 children who had a history of covid infection without PCL.

Laboratory studies consisted of studying the level of vitamin D (25-OH.) (enzyme immunoassay and chemiluminescence immunoassay), vitamin B6 and C (by high-performance liquid chromatography with tandem mass spectrometry).

Biochemical analysis of calcium, phosphorus and iron in peripheral blood was carried out according to generally accepted methods.

The analysis of the statistical type of the final data of the study was carried out on a personal computer using a specialized software package "Microsoft Excel". Correlation type analysis was carried out using Spearman's correlation indices. Discrepancies between statistical type values were significant at P values <0.05.

### Result and discussions

When distributed depending on age, we found that the largest percentage of children were under 10 years of age. Thus, 21.7% (55 children) of children suffered COVID-19 under the age of 3 years, 22.2% (56 children) aged 3-6 years and 23.3% (59 children) - in the age period from 7 to 10 years. At the age of 11-14 years, 22.1% of children (56 children) suffered from COVID-19, and at 15-17 years old - 10.7% (27 adolescents).

Among 253 children, 37 children (14.6%) had CVI asymptotically; a mild form was observed in 53.7% (136 out of 253 children), a moderate-severe course was noted in 17.4% (44 out of 253), a severe form was observed in 8.7% (22 out of 253), extremely severe - 5.5% (14 out of 253).

Among 253 children with confirmed COVID-19, 168 patients received outpatient treatment, which was 66.4%, and 85 children (33.3%) received inpatient treatment.

We found that children went to family clinics with complaints related to PCS on average  $4.8 \pm 0.3$  months after recovery from COVID-19.

Among the examined children, the following clinical variants of PCS were identified: asthenic, respiratory, cardiac, recurrent diseases of the ENT organs, functional gastrointestinal disorders, mixed variant.

The asthenic variant of PCS occurred in 7.1% of children (18 children), which was characterized by complaints of general weakness, increased fatigue, loss of appetite, decreased physical and cognitive activity, and deterioration of appetite. An objective examination revealed symptoms of autonomic dysfunction (bright red or white dermographism, increased sweating).

Respiratory syndrome occurred in 8.3% of the examined children (21 children), which was characterized by the presence of a clinical picture of recurrent bronchitis. Among children, general weakness, low-grade fever (85.7%), and diffuse dry wheezing were noted.

The cardiac variant of PCS was registered in 47 children (18.6%). The following complaints characteristic of this variant of PCS were identified: sensation of arrhythmic heart contractions (85.1%; 40 out of 47 children), stabbing pain in the pericardial region. Tachycardia was noted in 41 (87.2%) examined children. During electrocardiography, sinus rhythm was recorded in all, and supraventricular extrasystole was recorded in 29 (61.7%). Ventricular extrasystole was registered in 8 (17.0%) cases.

Recurrent lesions of the ENT organs were recorded in (7.9%; 20 children out of 253) of the examined children. From 3 to 5 relapses of inflammatory diseases after coronavirus infection were noted: laryngotracheitis, rhinosinusitis, nasopharyngitis, otitis media.

Functional gastrointestinal disorders were observed in 38.7% (98 of 253 children), which were characterized in 85.7% (84 of 98 patients) of cases by the presence of a clinical picture of functional dyspepsia in most cases of the type of epigastric pain, in 10.2% - functional constipation, in 5.1% - a clinical picture of functional diarrhea.

A mixed variant of PCS was registered in 49 children (19.4%): a combination of asthenic and cardiac complaints (69.8%), a combination of a respiratory variant of PCS and recurrent diseases of the ENT organs (19.8%), a combination of gastrointestinal and cardiac complaints - 12.8%

Characteristic differences in the clinical variants of PCS depending on age were established. Among children 1–3 years old, mixed and respiratory were more common (9.7 and 9.0%, respectively), and the gender difference was insignificant.

In the group of children 4–6 years old, the leading role is played by recurrent lesions of the ENT organs (10.2%) and, to a lesser extent, the respiratory variant (9.0%), the gender difference is also insignificant.

At 7–9 years old, the leading variants of PCS were recurrent lesions of the ENT organs (10.9%) and respiratory (9.2%), boys and girls suffered equally.

Among children 10–12 years old, functional gastrointestinal disorders (10.2%) and the respiratory variant of PCS (9.0%) are more common; in this age group, no gender difference is observed within these variants.

At 13–15 years of age, the dominant variant of PCS in both boys and girls is functional gastrointestinal disorders, which account for 13.4%. Boys and girls aged 16–17 years most often experience functional gastrointestinal disorders (13.5%), without gender difference, while the cardiac variant in this age group is more common in girls - almost 10.3% versus 8.1%.

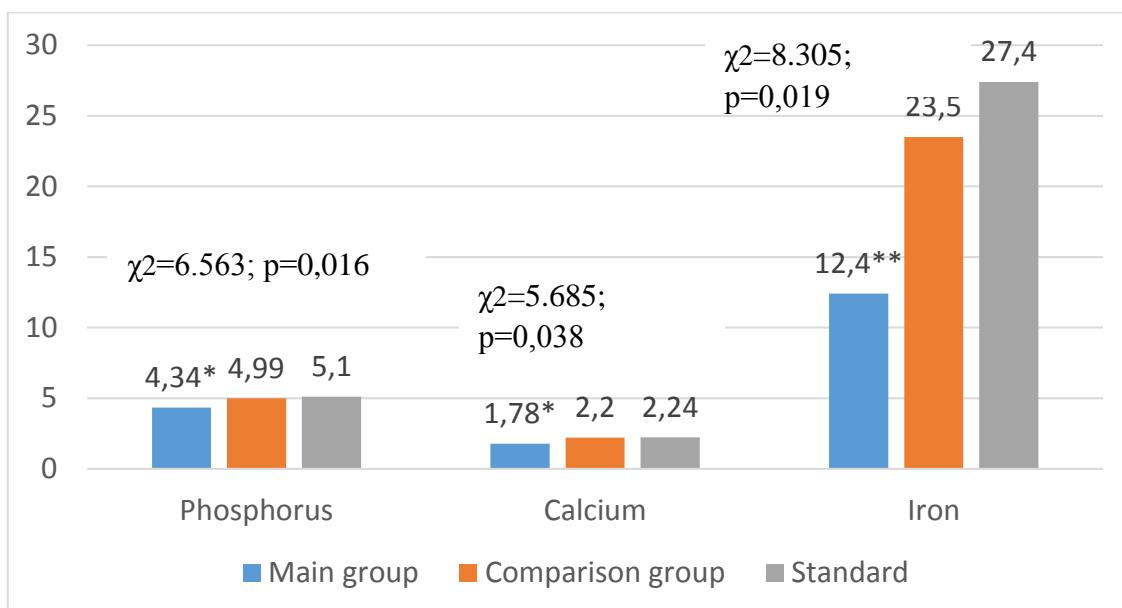
When assessing clinical variants of PCS in terms of age, an increase in the asthenic variant is determined at 1–3 years and 10–15 years, then its frequency decreases to minimum values by 16–17 years. The respiratory variant occurs approximately equally in all age periods. The frequency of the cardiac variant is the same up to 12 years of age, and starting from 13 years of age, its frequency increases, especially in girls. The frequency of recurrent lesions of the ENT organs increases to a maximum by the age of 9 years, then gradually decreases by more than 2 times by the age of 17 years. The frequency of functional gastrointestinal disorders decreases slightly from 1 year to 9 years, and in subsequent age periods increases up to 2 times. The mixed version of PCS has a maximum frequency of 1–3 years, then gradually decreases to 17.

As is known, the phosphorus content in the body is responsible for many functions, in particular it serves to normalize the functioning of the heart muscle (Fig. 1). In our studies, this electrolyte was significantly reduced among children with PCS in relation to normative values and the indicators of the comparison group of children without PCS ( $4.3 \pm 0.02$  mmol/l versus  $4.9 \pm 0.03$  mmol/l ( $P < 0.05$ ) and  $5.1 \pm 0.04$  mmol/l ( $P < 0.05$ ), respectively). Inorganic phosphorus deficiency leads to hypophosphatemia, which develops as a result of insufficient dietary intake, high calcium content, poor intestinal absorption,

or excess urinary excretion. The pathology is manifested by impaired consciousness and weakness of skeletal muscles.

Calcium is one of the key macronutrients, it is necessary for the construction of bones and teeth. Participates in the functioning of the muscular and cardiovascular systems and is necessary for the normal functioning of many enzymes. The calcium content among children in the main group decreased in relation to standard values ( $1.78 \pm 0.1$  mmol/l versus  $2.24 \pm 0.06$  mmol/l;  $P < 0.05$ ), and there was also a tendency for this element to decrease and in the comparison group (Fig. 1).

**Fig. 1. Features of the content of microelements in the blood of children with and without post-Covid syndrome in a comparative aspect**



Note: \* - reliability of data to the indicators of the control group (\* -  $P < 0.05$ ; \*\* -  $P < 0.01$ )

Iron is a trace element that is absorbed from food and then transported throughout the body by transferrin, a special protein produced in the liver. Iron is necessary for the formation of red blood cells. It is an essential component of hemoglobin, a protein that fills red blood cells, which allows them to carry oxygen from the lungs to organs and tissues. Iron is also a component of the muscle protein myoglobin and some enzymes. Among children with PCS, the level of iron in the peripheral blood is significantly reduced by 2.2 times ( $12.4 \pm 0.3$  mmol/l versus  $27.4 \pm 0.04$  mmol/l;  $P < 0.05$ ). In the group of children with a history of covid infection without PCS, there was a tendency for iron levels to decrease by 1.2 times ( $23.5 \pm 0.5$  mmol/l versus  $27.4 \pm 0.2$  mmol/l).

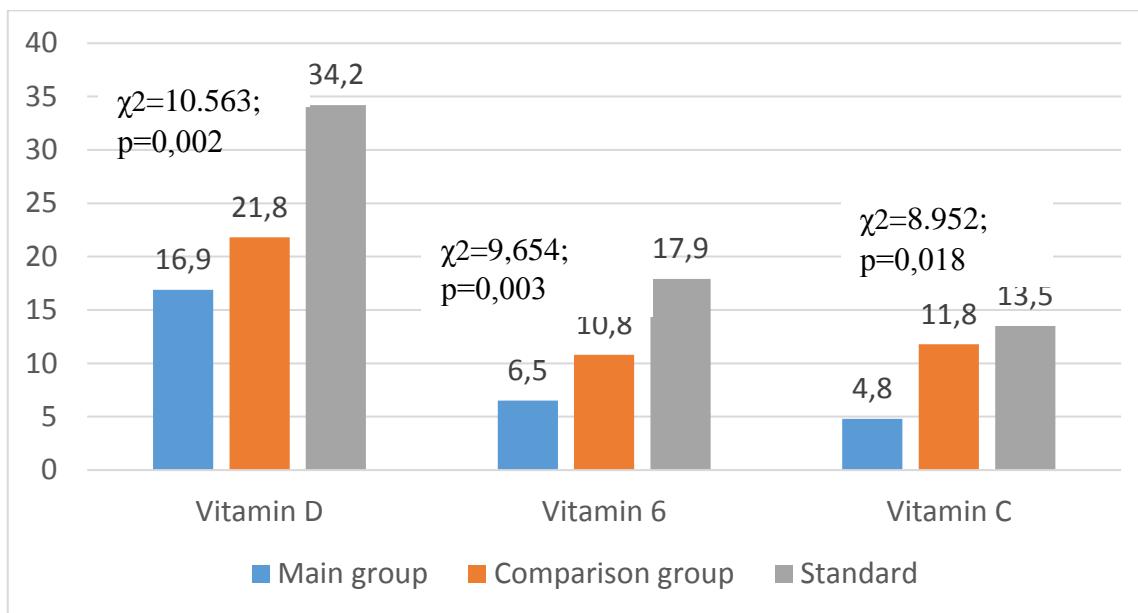
Insufficient provision of children's bodies with vitamins D, C and B6 leads to a weakened immune response, which may increase the likelihood of developing complications after suffering from COVID-19.

Our study established a significant decrease in the levels of vitamin B6, vitamin C and D among children with PCS and the comparison group in relation to the norm (Fig. 2).

The vitamin D content in the main group was reduced by 2 times compared to the norm, its average values were  $16.9 \pm 0.6$  ng/ml ( $P < 0.001$ ), which indicates a deficiency of this vitamin among children with PCS. In the comparison group among children who had COVID-19, the average values corresponded to vitamin D deficiency ( $21.8 \pm 0.7$  ng/ml) and were significantly reduced compared to the norm ( $P < 0.01$ ).

A similar picture is observed when analyzing the average levels of vitamin B6 among children in the main group, where the level was 2.7 times lower in relation to the norm ( $P < 0.01$ ) and 1.7 times lower in relation to the comparison group ( $P < 0.05$ ).

**Fig. 2. Features of the content of vitamins D, B6 and C in the blood of children with and without post-Covid syndrome in a comparative aspect**



The level of vitamin C among children of the main group decreased by 2.8 times in relation to the norm ( $P<0.001$ ) and by 2.5 times in relation to the comparison group ( $P<0.001$ ). Among children who had COVID-19, the average vitamin C levels were 1.1 times lower than normal ( $P<0.05$ ).

Thus, children with PCS have an imbalance of both electrolytes and vitamins B6, C and D, which may indicate a strained immune system. In the comparison group, children who have had COVID-19 also show an imbalance in the studied indicators, which indicates that these children are classified as a high-risk group for the development of PCS.

### Conclusions

1. The development of post-Covid syndrome among children who have had COVID-19 is 65.6%. Typical variants of post-Covid syndrome among children are: asthenic (7.1%), respiratory (8.3%), cardiac (18.6%), recurrent diseases of the ENT organs (7.9%), functional gastrointestinal disorders (38.7%), mixed version (19.4%).

2. When assessing the clinical variants of PCS in the age aspect, an increase in the asthenic variant is determined at 1–3 years and 10–15 years, then its frequency decreases to minimum values by 16–17 years. The frequency of the cardiac variant is the same up to 12 years of age, and starting from 13 years of age, its frequency increases. The frequency of recurrent lesions of the ENT organs increases to a maximum by the age of 9 years, then gradually decreases by more than 2 times by the age of 17 years. The frequency of functional gastrointestinal disorders among children after 9 years of age increases up to 2 times. The mixed version of PCS gradually decreases with age.

3. Children with PCS have a deficiency of electrolytes such as phosphorus, calcium and iron, as well as a deficiency of vitamins B6, C and D, which indicates a strained immune system.

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