MINISTRY OF HEALTH OF THE REPUBLIC OF UZBEKISTAN

SAMARKAND STATE MEDICAL UNIVERSITY

MAKSUDA ZHAMSHEDOVNA ASHUROVA

"PECULIARITIES OF FORMATION OF METABOLIC AND OSTEOPENIC DISORDERS CAUSED BY VITAMIN D DEFICIENCY RELATED TO CHILDHOOD OBESITY"

(Monograph)

Samarkand 2025

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The monograph presents the substantiation and a new method of solving the recent problem of modern pediatrics, which consists in studying the features of carbohydrate and lipid metabolism in interrelation with phosphorus-calcium metabolism, related to deficit of vitamin D in children with obesity. The monograph represents an interest for pediatricians and general practice doctors, as well as master's and clinical residents. Monograph may be used in the structure of work of medical-polyclinic health care institutions

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INTRODUCTION

At the present, the problem of obesity in children and adolescents has acquired the character of one of the significant problems of medicine. According to the World Health Organization (WHO) "...overweight and obesity affect almost 60% of the adult population, with 7.9% of children under 5 years of age suffering from this pathology...every third school-age child, and every fourth child from 10 to 19 years of age is overweight or obese...". Along with the problem of childhood obesity, there is a great interest in insufficient vitamin D supply, this dual problem determines the study of early diagnosis of occurrence, development risk factors, features of clinical, laboratory and instrumental implications, as well as the search for important pathogenetically substantiated methods of treatment for the prevention of complications, reducing the number of recurrences of diseases, which is considered one of the problems that need to be solved in medicine

All over the world, a number of scientific studies are being conducted to find the mechanisms of metabolic disorders, especially vitamin D deficiency in obese children and adolescents, to improve early diagnosis, treatment and prophylaxis. Therefore, it is important to conduct scientific research of childhood obesity and other comorbid diseases with vitamin D deficiency to improve regional methods of treatment, taking into account the degree of metabolic disorders, as well as osteopenic conditions developed related to vitamin D deficit, which affect the children's life quality at the present stage and further in adult life, as well as focused on the development of optimal recommendations for the prevention of vitamin D deficiency. Therefore, the study of the degree of pathology of metabolic disorders, including the development of osteopenic conditions, related to vitamin D deficit, which can affect the quality of life of children at the present stage and in adulthood, represent a high relevance and formed the basis of scientific research.

For the development of the medical industry in our country, large-scale activities are carried out to detect and prevent non-infectious pathology in adults and children, which includes obesity. Therefore, the following tasks are indicated

“...strategic priorities of the Concept: is the control of such risk factors of non-infectious diseases as: overweight, obesity, high blood pressure...”.

The solution of these problems was the identification of significant deficiency and insufficiency of vitamin D in school-age children with different body weight in the Samarkand region, significant violations of lipid and carbohydrate metabolism related to the vitamin D deficiency within the group of children with severe obesity were evaluated, the level of phosphorus-calcium metabolism and activity of parathyroid hormone was determined, which allows to reduce disability and mortality in the subsequent period of life.

WHO data shows that obesity and overweight affects 41 million children under the age of 5 and 340 million children and adolescents aged 5-19 worldwide. At the present, the pandemic of obesity, and similarly, the pandemic of vitamin D deficiency in the child population is actively discussed in the domestic and foreign literature. According to various authors, there is a wide prevalence of decreased vitamin D supply due to various factors up to 90% of the population (Dedov I.I. et al. 2020; Todieva A.M., 2018; Karonova T.L. 2016; Gromova O.A. 2015). Moreover, vitamin D deficiency is as widespread in the child population as in adults (Zakharova I.N. et al. 2017; Baranov A.A. et al. 2018, Maltsev S.V. 2020; Holick M.F.et al., 2021).

Studies conducted in Uzbekistan to determine vitamin D deficiency and insufficiency showed that the examinations were mainly conducted in young children and frequently ill school-aged children (Rasulova N.A. 2021, Shomansurova E.A. 2018). It has been determined that the population in Uzbekistan does not sufficiently consume foods containing vitamin D (UNICEF Report 2017).

Chapter I. LITERATURE REVIEW

Obesity in children and adolescents: an recent problem of modern pediatrics

In modern public healthcare, the problem of obesity is one of the most relevant, a trend towards an increase in its prevalence has been identified, acquiring in most countries the character of a non-infectious pandemic [45: p.214-215; 106: p.377. 557-567]. Overweight is a condition in which there is excessive accumulation of adipose tissue in the body, and the body weight exceeds the typical weight for that age and sex. Obesity is a complex of heterogeneous hereditary and acquired diseases associated with excessive accumulation of adipose tissue in the body [51: p.125-132]. According to various authors, overweight, obesity and related complications have led to the death of 4 million people in the world, 5-6% of the population annually have a reduced quality of life, 4% become disabled [45: p. 214-217; 125: p.2224-2260].

It is well known that the skills of proper nutrition are laid in childhood, in the conditions of excess or deficiency of certain nutrients may develop in the future chronic forms of nutrient-dependent pathology. Studies have shown that the number of obese children worldwide is increasing exponentially, doubling every three decades [65: p.28-31]. A number of authors attribute the relevance of studying the problem of obesity in children and adolescents not only to the increasing prevalence of the disease, but also to the high probability of its transition in subsequent periods of life [5: c186-193]. This is the notion of "transference", "tracking'" of obesity and comorbid problems into adulthood, in which a worsening of the condition may occur [63: p.8-9]. In other words, it is an assessment of the "evolution" of the disease during the life course or the "predictability" of risk factor values in the future based on previous changes [32: p.128-135]. Long-term randomized studies have established that 80% of obese children are not deprived of this problem and in adulthood, have a severe course of the disease, a high degree of overweight, comorbid pathology. "Companion diseases" (cardiovascular and hepatobiliary pathology, arthragra, diabetes, etc.) serve as a cause of death, reducing the average

life expectancy of obese people by 7-10 years [27: p.279, 148: p.1255-1260, 160: p.132-134]. Bhargava S. et al. calculated the tracking of adolescent and childhood obesity into adulthood: 20% - obesity formed in children under 4 years of age and up to 80% in adolescents [63:p.15-20; 150: p.865-875].

According to a 2016 WHO report, there are more than 1.9 billion overweight people on the globe, 650 million of them are obese [48:]. Between 1975 and 2016, the number of obese individuals has increased more than threefold [32: p.8-12; 48:, 110:p.766-781].

Statistics from the previous decade indicated that the problem of overweight was mainly confined to the economically developed countries of the world: the number of obese people with varying degrees of obesity ranged from 20-30 to 40-60% of the population [155: p.408]. The leading position was held by the USA, where 64-65% of the adult population was overweight, one third of whom were obese (BMI >30 kg/m²) [32: p.15-18; 63: p.15-21; 143: p.806-814]. This indicator is slightly lower in the countries of Western Europe [32: p.20-23]. In Italy, France and Germany, overweight has been reported in 25% of the population [110: p766-781]. In the UK, obesity affects about 17-20% of the adult population [155: p.408]. In Asian countries (Japan), up to 16% of the population was overweight, 3.7% of whom were obese [124: p.581-592].

Presently, it can be noted that the problem of obesity has also become an issue in developing countries. The number of overweight and obese people in such countries was 30% higher than in the USA and Europe [27: c.279; 48:]. In 2016, Pacific Islands countries as well as Middle Eastern countries (35-60% of the population) have the highest prevalence of overweight and obesity in the population [110: p.766-781]. The main cause of this situation is unbalanced nutrition since the birth of the child, as well as sedentary lifestyle [84:p. 226-243, 97:p.1183-1190, 98:p.90-99]. The so-called "double burden of disease" is not uncommon: while the problems of infectious diseases and malnutrition continue to exist, the problem of non-infectious diseases and obesity is emerging and growing [32: p.22-25; 48].

WHO reports show a growing problem of overweight or obesity in childhood: in 2016, 41 million children under 5 years and 340 million children and adolescents 5-19 years had this pathology. Meanwhile, the age group above 5 years recorded a dramatic spike in rates from 4% in 1975 to 18% in 2016 [48]. WHO predicts that by 2022, more children in the world will be overweight than underweight. In recent years, the problem of childhood obesity [32: p.20-24] has been reported more frequently in countries on the Asian continent, while rates have stabilized in the United States and Europe [84:p. 226-243, 88:p.2430-2440]. In a 2015 epidemiologic study conducted in Shanghai, the prevalence of overweight and obesity was 18.1% and 8.6%, correspondingly [32: p.17-18; 145: p.642-643]. In the United States, obesity rates among children and adolescents were about 18.0%, nearly three times the national rate in 1980 [144: p.483-490]. Research data from European countries (UK, Sweden, Greece, Norway) show that the prevalence of obesity in the children population remains relatively stable at about 16.8% [146: p.244-258]. In Russia, a multicenter study found that the prevalence of overweight in children was 19.9%, obesity - 5.6% [65: p.28-31].

However, epidemiologic studies show that the actual incidence of obesity is significantly higher than official statistics [32: p.11-15; 143: p.806-814, 145: p.642-643, 146: p.244-258].

The question about the frequency of the pathology we studied in terms of whether the respondents of the study live in urban or rural areas remains controversial. The prevalence of obesity in urban child population has also been noted in China and Greece [32: p.22; 141: p.710-714; 145: p.642-643; 146: p.244-258]. The data for the Russian Federation are similar: obesity was found in 8.5% of children living in urban areas and 5.5% of children living in rural areas [52: p.17-23]. The predominance of the incidence of obesity in children and adolescents in rural areas in African and American countries is explained by the worse socioeconomic situation of the rural population, which leads to the choice of cheaper food products with high caloric content and lower biological value [77: p.47-54; 142: p.370-375; 143: p.483-490; 13: p.108-111; 29: p.93-97; 38: p.52-55; 50: p.143-

145]. Rural adolescents are more prone to emotional chronic stress and show greater adherence to fast and street foods [29: p.93-97; 104: p.341-402]. However, it should be noted that in some countries no differences in the incidence of obesity have been found between urban and rural children [99: p.282-287].

To date, the gender specificity of childhood obesity has been controversial. In studies conducted in Russia, Brazil and Spain, the incidence of obesity was found to be approximately the same in both boys (1.7-9.1%) and girls (2.0-6.5%) [77: p.47-54; 4: p.146; 12: p.311; 49: p.5-13; 129:p. 3341-3352; 70: p.37-40; 94: p.1-8; 98: p.90-99]. In 2016, the highest prevalence of childhood obesity was observed in several island nations and was 25.4% in girls and 22.4% in boys [32: p.14; 48]. Studies in China have proven an unequivocally higher prevalence of obesity in boys: the increase in obesity rates in boys and girls increased from 0.5% and 0.2% correspondingly in 1985 to 18.2% and 6.6% correspondingly in 2014 [98: p.90-99; 141: p.710-714; 145: p.642-643]. In contrast, in some regions of the Middle East, Eastern Europe, and Turkey, there is a predominance of girls in the children obese population [32: p.32] (14.4-19.2% in boys and 11.8-17.6% in girls) [137: p. 2062-2069; 99:p.282-287; 104:p.341-402]. According to some authors, an increased prevalence of overweight and obesity in adolescent girls is a poor prognostic sign because maternal obesity has a significant impact on the formation of obesity of the future child [27:c. 279; 12:c.311; 134:p.372-381].

The mutual influences of obesity, reduced vitamin D supply and bone metabolism

For the past decades, vitamin D levels have been considered a predictor of metabolic diseases and have been widely discussed in the academic medical communities. A number of authors consider the problem of hypovitaminosis of vitamin D to be global for many countries [60: p.195-200].

1	Absolutely toxic level	>200ng/mL;
2	Level with possible toxicity:	>100ng/mL;

3	Norm	30-100ng/mL;
4	Inefficiency	21-29ng/mL;
5	Deficiency	Less than 20ng/mL

Fig. 1. Normative values of vitamin D in children's blood

(National Program "Vitamin D Insufficiency in Children and Adolescents of the Russian Federation: Modern Approaches to Correction", 2021)

There are a number of diseases (inflamatory diseases, myocardial infarction, malignancies, diabetes, arterial hypertension, and decreased immunity) that have an association with vitamin D deficiency in the body [43:c. 96; 44:c.58-67; 119: p.1160; 159: p.1-6]. Thus the effect of vitamin D on glucose and insulin metabolism has been proven to lead to the formation of obesity [26: p.25-31; 40: p.213-219; 77:p. 447-452].

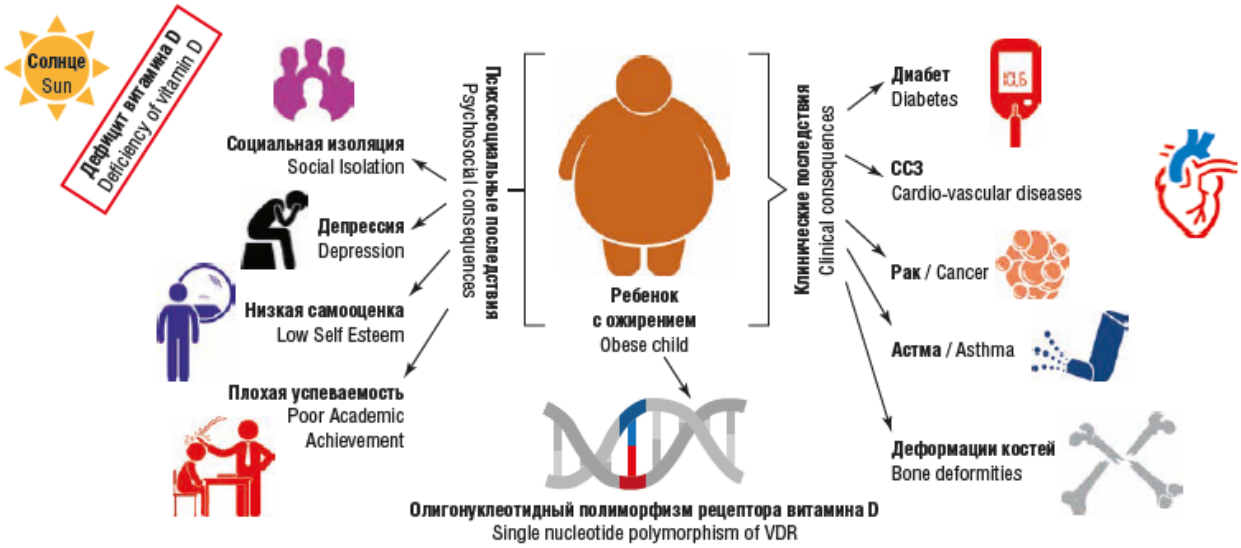


Fig. 2. Interconnection of childhood obesity with non-infectious diseases and psycho-emotional problems.

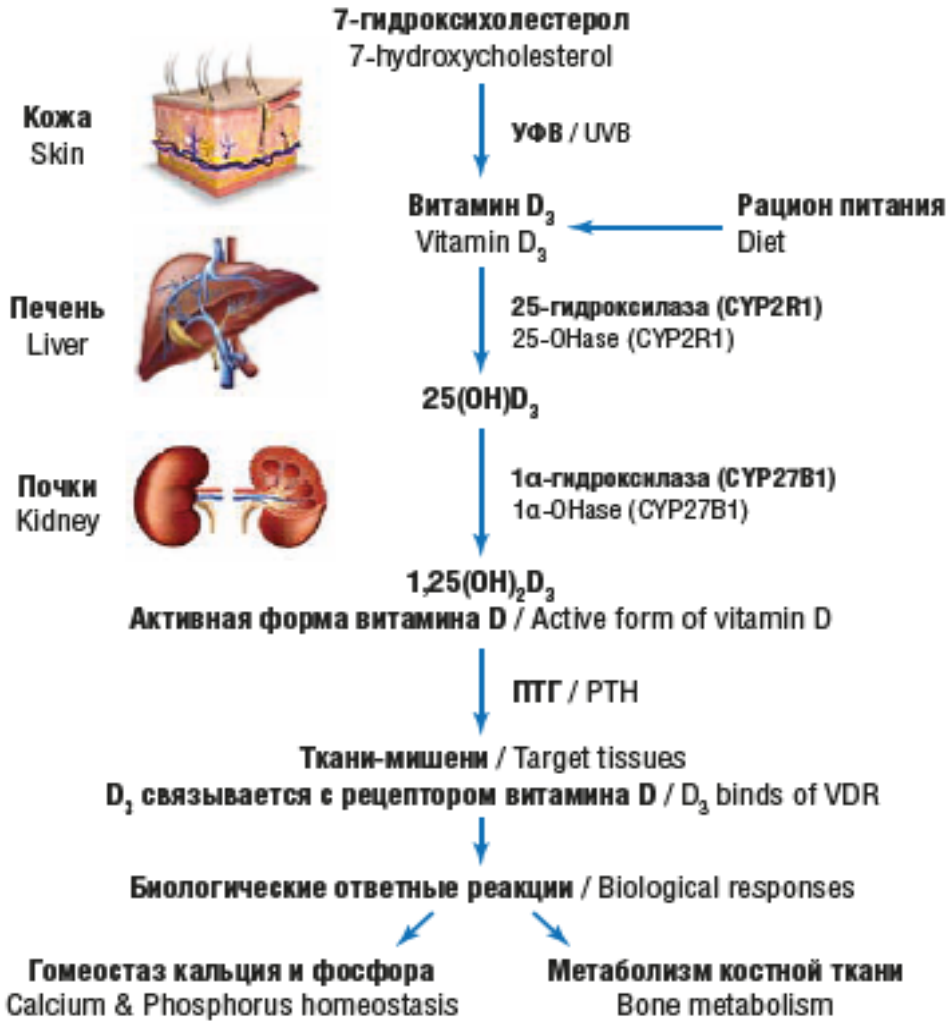


Fig. 3. Mechanism of vitamin D metabolism in the human body

Hypovitaminosis of vitamin D has been reported of the population of many countries [9: p.57-61; 22: p.22-28; 85: p.15-22; 109: p.1807-1820]. Some authors indicate that vitamin D insufficiency ranges from 60-80% of the adult population [43: p.95]. Vitamin D deficiency is registered in 66.0% of preschool children and 94.8-90.0% of elementary school children and adolescents [22: p.22-28; 46: p.30-34; 47: p.528-531].

The presence of a mutual influence of vitamin D deficiency and obesity has been established through numerous studies, for example, in a meta-analysis conducted in 2015 it was proved that there is a direct correlation between low vitamin D sufficiency and the risk of obesity [66: p.19-23; 87: p.157-161; 131: p.341-349]. Hypovitaminosis D has been reported 35% more frequently in obese

individuals than in normal weight individuals [26:c. 25-31;]. According to another meta-analysis, it was found that age, locality of residence, and standard of living do not affect vitamin D deficiency in obesity [133: p.260-264].

Vitamin D deficiency primarily affects disorders of calcium-phosphorus and bone metabolism. Because vitamin D normally increases calcium absorption in the intestine, its deficiency leads to increased PTH levels, secondary to hyperparathyroidism, which maintains normal calcium levels by mobilizing it from the skeleton. PTH increases osteoclast activity and thus leads to decreased MIC, osteopenia and osteoporosis [17: p.48;117: p.1911-30 93: p.1129-33; 118: p.3215-24; 163: p.51-108]. Vitamin D deficiency leads to myopathy, which can present with muscle weakness, especially in proximal muscle groups, difficulty walking, maintaining balance, and a tendency to fall, which accordingly increases the risk of fractures [154: p.470-7; 86: p.3692].

The issue of hypovitaminosis D in children and adolescents who are overweight or obese is being actively investigated. The results of an examination of more than 2,000 children showed that hypovitaminosis D was more common in obese children than in their healthy peers [131: p.341-349; 115: p.229-235]. In a study conducted in Denmark, vitamin D insufficiency was reported in 1/6 obese children and adolescents [132: p.53-61]. In addition to the effects of vitamin D on bone metabolism, its new effects on various tissues and systems have been investigated in recent years [14: p.463; 21: p.20-25].

To date, there are several mechanisms by which excess adipose tissue has a negative impact on vitamin D levels:

In a study by Worthman J. et al. in 2000, research methods included the assessment of vitamin D2 and D3 precursors in obese patients and people without excess body weight when exposed to direct sunlight and taking vitamin D2 preparations After a period of time equal to a day, the level of vitamin D precursors in the analyses of obese people was about 60% lower than in people with normal body weight [102: p.690-693; 121: p.183-191]. Decreased concentrations of vitamin

D2 in serum stimulate production of parathyroid hormone, which activates lipoprotein lipase and adipocyte growth [26:c.25-31; 79:p.2158-2164; 126:].

Chinese researches led by G. Chung published in 2016 the results of a cohort study of 6000 individuals, proving that a decrease of vitamin D2 formation is associated with a decrease in the rate of 25(OH)D synthesis in hepatocytes [158: p.146-151; 83: p.517-524; 107:p.513-520].

In vitro proved that vitamin D affects the processes of adipocyte differentiation [161: p.1915-1923].

Thus, studies concerning the mutual influence of obesity and hypovitaminosis D continue, the data obtained are contradictory, which necessitates further study of this problem especially in children and adolescents.

Childhood is characterized by a high prevalence of osteopenic syndrome rather than osteoporosis. This is the crux of the problem and the great advantage of pediatrics - the diagnosis of mineral metabolism disorders at the preclinical stage. The latter offers a unique opportunity to prevent progression and eliminate shifts in the rate of bone mass accumulation during childhood. This is the approach that will reduce the proportion of adult osteoporosis and ensure harmony in their lives.

Osteoporosis is the most common skeletal disease characterized by a progressive decrease in bone mass per unit of bone volume relative to normal in individuals of the respective sex, age. Osteoporosis belongs to the group of metabolic diseases. The severity of osteoporosis correlates with the degree of decrease in bone mineral density (BMD). The determination of BMD (or bone mineral density) is the accepted standard for diagnosing osteoporosis.

It important to emphasize that bone mass increases mainly due to endosteal deposits in long tubular bones and thickening of trabecular bones during pubertal and postpubertal periods. Bone formation during this period predominates over bone resorption. Maximum (peak) bone mass is regulated by genetic and external factors. Healthy individuals have no change in bone mass after reaching their "peak" (between the ages of 25 and 35). During this period, the rates of bone formation and

bone resorption are balanced. Subsequently, a natural age-dependent decline in bone mass begins at a rate of 0.3 to 0.5% per year [18].

Osteopenia (osteoporosis, bone thinning), a multifactorial pathology of bone metabolism, is nowadays widely spread worldwide and has unfavorable consequences. It is characterized by decreased bone mass, disruption of bone microstructure and bone fractures even with minimal trauma [30] Various somatic diseases can have a negative impact on metabolic processes in bone tissue starting in childhood and adolescence [3: p.76-83; 19: p.81-85; 42:p. 46-50].

Bone metabolism occurs throughout the human life and is called remodeling (includes several phases: activation, resorption, reversion, osteogenesis). Low or high level of bone metabolism with relative predominance of bone resorption or decreased bone formation, imbalance of bone remodeling phases leads to the formation of osteoporosis [32: p.12; 1; 19:p.81-85; 134:p.372-381].

Contemporary authors consider obesity as a precursor or companion to the development of osteopenia. A research conducted by Shapses S.A. et al. in 2017 showed that increased fat mass is associated with low bone mineral density [152: p.1-13; 103: p.526-546]. It has been shown that high obesity is strongly correlated with an increased risk of bone fractures [81: p.24-32; 135: p.947-956]. The negative effect of obesity on bone metabolism has been experimentally proven [91: p.1-7], while clinical studies either further convince or deny it [78: p.39-46; 80: p.98-100; 103: p.526-546; 123: p.514-527; 156: p.293-302].

V.Y. Schwartz et al. hypothesized in their studies that adipose tissue is regarded as an active endocrine organ that secretes proinflammatory (tumor-α necrosis factor, interleukin-6, leptin) and anti-inflammatory cytokines (adiponectin) into the blood [34: p.69-72; 61: p.44-60; 72: p.63-69]. Chronic elevation of pro-inflammatory cytokines in obesity promotes osteoclast activity and bone resorption, leading to an imbalance of the RANK / RANKL / ORG system, which is an important link in the balance between bone resorption and bone formation processes [32: p.15 ; 1; 19:p.81-85; 61:p.44-60; 91:p.1-7; 95:p.474-485; 101: p.273-280; 105:p.461-470; 134:p.372-381].

The effect of obesity on bone metabolism through cellular mechanisms has been proven [91:p.1-7]. The precursor of fat cells and osteoblasts is the common bone marrow stem cell growth factor; increased lipogenesis from the common mesenchymal growth factor leads to a deficiency of osteoblasts, and consequently causes the osteopenic process [112:p.273-286; 152:p.1-13]. Experimental studies support this, as agents that inhibit adipogenesis have been shown to stimulate osteoblastogenesis, and conversely, those that inhibit osteoblastogenesis have been shown to enhance adipogenesis [32: p.34; 91:p.1-7].

The role of insulin elevated in obesity has also been discussed in the literature [101:p.273-280; 157:p.237-245]. Obese individuals have excessive synthesis of adipose tissue production of sex hormones, which in turn reduce osteoclastogenesis and stimulate osteoblastogenesis [130:p.60-81].

All of the above studies have focused on bone metabolic status in obese adults. For obese children and adolescents, the problem remains understudied and highly debated. Some researchers prove the association of high body mass index in children and high risk of pathologic bone fractures [19: p.81-85; 103: p.526-546; 123: p.514-527]. Silva M. et al. studied bone fractures in obese children and adolescents according to gender [153:p.308-316].

The results of bone metabolism markers in obese children are highly inconsistent. Some studies have reported higher osteocalcin levels in obese children and adolescents [32: 46; 82:p.25-34; 90:p.275-284]. Other authors note a decrease in osteocalcin as a stimulator of osteoblastogenesis, in parallel noting an increase in markers of osteoclastogenesis, which leads to bone destruction [32: p.67; 25:p.45-50; 101:p.273-280].

The research results analyzing the relationship between obesity, hypovitaminosis D and bone metabolism are few, the issue is poorly studied in the pediatric population. This necessitates the need for further research in this domain.

Peculiarities of instrumental diagnostics of bone tissue condition

It is well known that the diagnosis of osteopenic condition can be made taking into account the data of objective examination, data of instrumental examination,

laboratory parameters [31:c.3]. Laboratory diagnosis of this condition is necessary, first of all, to exclude somatic pathology that runs with osteopenia; to clarify the etiology of osteoporosis, as well as to clarify metabolic changes in bone composition. Such methods of diagnostics of osteopenia as determination of mineral content in blood serum and urine, as well as methods of biochemical analysis of bone substance formation and resorption are known to science and have found wide application in practical activity [74:p.110-117].

The study of the mineral composition of blood and urine is advisable to begin with the analysis of calcium and phosphorus levels [10:p. 2-6]. In fasting state, the excretion of total or ionized calcium and phosphorus in the urine and their ratio to the creatinine level in the same portion are examined. A diet containing less than 10 mg/kg calcium and less than 1.5 g/kg body weight phosphorus is prescribed beforehand [3:p. 76-83]. Some authors also recommend examining the levels of magnesium, sodium, potassium salts, acid-base composition of blood, indirectly reflecting the level [69:p. 47-50]. There are publications in the literature concerning the investigation of parathyroid hormone (parathormone) and calcitonin levels in serum; calcitriol levels - 1,25(OH)2D - (active metabolite of vitamin D) and enzyme immunoassay (chromatography) of blood samples. These analyses are used to laboratory confirm or reject the diagnosis of osteopenia and osteoporosis [90:p.275-284; 92:p.245-50]. Moiseeva T.Y. in her study indicates the need to determine the level of 25-hydroxyvitamin D - 25(OH)D, which is the main metabolite of vitamin D, acts as a marker of the severity of the osteopenic process in the body [42:p. 46-50]. To date, automated systems such as "LIASON" analyzing the levels of all metabolites of vitamin D in human blood have been created and are actively used in practice.

Chapter II. CLINICAL MATERIAL AND RESEARCH METHODS

General characteristics of the examined patients

Clinical observation was conducted on the basis of Children's City Hospital No. 1, Samarkand, Samarkand branch of the Republican Scientific and Practical Specialized Center of Endocrinology, City Family Polyclinic No. 2, Samarkand. Samarkand in the period of 2020-2022.

The study included 106 children overweight and suffering from primary exogenous constitutional obesity (main group) living in Samarkand region at the age of 7 to 17 children (11,20± 0,25 years), where boys were 59 children (55,6%) and girls 47 children (44,4%).

The diagnosis of obesity was established according to WHO recommendations, and the standard deviation - SD (standart deviation) of BMI, taking into account the sex and age of children, was calculated with the programs WNO Antho, 2009. BMI values within ±1.0 SD were interpreted as normal body weight, BMI values between +1.0 and +2.0 SD were interpreted as overweight, and BMI equal to or greater than +2.0 SD was diagnosed as obesity [48]. The staging of the degree of obesity in children was performed according to the classification proposed by V.A. Peterkova et al., 2014. [52]:

SD BMI 2.0 - 2.5 - Grade I;

SD BMI 2.6 - 3.0 - Grade II;

SD BMI 3.1 - 3.9 - Grade III;

SD BMI 4.0 and more - Grade IV.

Inclusion criteria for the main group were:

1. Exogenous-constitutional obesity

2. Children aged from 7 to 18 years inclusive

3. Absence of the signs of disease, corresponding to acute or exacerbation of chronic disease at the time of inclusion of the patient in the study.

4. Absence of vitamin D medication for at least one month prior to inclusion in the study

Exclusion criteria for the study were:

1. Obesity due to endocrine pathology (hypothyroidism, hypopituitarism, hypercorticism, etc.)

2. “Central” genesis obesity (as a result of brain injuries)

3. Obesity due to a number of genetic and chromosomal diseases (Biedl-Bardet syndrome, Down syndrome, Prader-Willi syndrome, etc.)

The control group consisted of 30 children of similar age (mean 12.00±0.34 years) with normal body weight (BMI less than +1 SDS for the given sex and age), where boys were 14 children (46.7%) and girls 16 (53.3%).

The main group of overweight and obese children and the control group were comparable in age ($p>0.05$) and gender ($p>0.05$). The characteristics of the compared groups are summarized in Table 1.

Table 1

Comparative characteristics of children of the main group and the control group

Factors	Main group N=106	Control group N=30	P
Age, years; M±m	11.20± 0.25	12.00±0.34	>0.05
Boys, n, %	59 (55.6)	14 (46.7)	>0.05
Girls, n, %	47 (44.4)	16 (53.3)	>0.05
BMI; M±m	25.57±0.53	19.18±0.34	<0.001
SDS BMI; M±m	0.96±0.00	0.81±0.00	<0.001
Tanner 0-I, n, %	57 (54)	10 (33.3)	<0.05
Tanner II-V, n, %	49 (46)	20 (66.7)	<0.05

To analyze the role of puberty, the studied children of the main and control groups were divided by the presence of the start of pubertal development into pre-pubertal groups (Tapper I) and groups with the start and progression of puberty (Tapper II-IV).

All children of the main group were divided into 3 groups in accordance with the set tasks: Group I - 39 children had BMI +1,0 to +2,0 SDS, i.e. children had BMI characterizing excessive body weight, average BMI was 21,97±0,40 ($p<0,01$ compared to the control group), and mean figures of standard deviation of SDS were within 1,72±0,04, which was also significantly different from the control group ($p<0,01$) (Table 2.1.2).

Group II - 41 children included children with BMI >+2<+3 SDS, which was correspondingly I-II group of obesity, the average BMI in children of this group (26,92±0,51) significantly exceeded both the indicators of the control group ($p<0,01$) and the BMI of children of group I ($p<0,01$).

The standard deviation (SDS) of BMI in this group corresponded to the selected range with an average of 2.58±0.04, which was higher than the standard deviation of the control group ($p<0.01$) and the group of overweight children ($p<0.01$).

Group III - 26 children with BMI ≥+3 SDS, which corresponded to the III degree of obesity and higher, with a mean BMI of 33.00±0.93, which had a significant difference compared to group I ($p<0.01$) and group II ($p<0.01$), and the standard deviation of BMI was higher compared to group I ($p<0.01$) and group II ($p<0.01$).

The presented data characterize reliable differences in body weight in the studied groups, while age, gender separation, had no statistical differences (Table 2).

The study design included several phases

Stage I: anthropometric measurements of obese and overweight children and randomization of children by degree of obesity into groups.

Stage II: clinical and laboratory studies with determination of carbohydrate, lipid metabolism, 25(OH) D level, phosphorus-calcium metabolism indicators.

Stage III: conducting a comparative characterization of metabolic disorders according to vitamin D levels.

Table 2.

Comparative characteristics of children of the main groups distributed according to body weight

Factors	Group I SDS +1.0 to +2.0 n= 39	Group II >+2<+3 SDS n= 41	Group III ≥+3 SDS n= 26	Control group <+1 SDS n= 30
BMI; M±m	21.97±0.40*	26.92±0.51*^	33.00±0.93*°	19.18±0.37
SDS BMI; M±m	1.72±0.04*	2.58±0.04*^	3.37±0.04*°	0.35±0.04
Age; M±m	11.64±0.37	11.49±0.43	11.57±0.50	12.2±0.34
Boys; n, %	20 (51.3)	19 (46.4)	18 (69.2)	14 (46.7)
Girls; n, %	19 (48.7)	22 (53.6)	8 (26.8)	16 (53.3)
Body weight; M±m	46.61±2.21	60.80±2.80*^	77.5±4.27*°	46.46±2.40
Height; M±m	143.63±2.10*	148.91±2.33	151.46±2.70	153.6±2.82
WC; M±m	80.85±0.17	89.62±1.57	100.15±2.64	64.66±0.76
HW; M±m	81.35±2.21	94.52±1.60	99.30±2.38	79.50±1.34
WC/HW; M±m	0.96±0.05	0.94±0.00	1.00±0.00	0.81±0.00

Note: * $p<0.01$ compared to the control group

^ $p<0.01$ reliability of difference between group 1 and 2

° $p<0.01$ reliability of difference between group 2 and 3

Research Methods

Anthropometric and clinical research

Vitamin D supply was assessed by determination of 25(OH)D content in blood serum by the chemiluminescence method using standardized kits from "Roche Diagnostics" (Germany) on an Abbott Architect 8000 analyzer (USA). The results were evaluated taking into account the recommendations of the European Society of Endocrinologists (2011) [114]: Vitamin D deficiency - at 25(OH)D level less than 20 ng/mL (less than 50 nmol/L); Vitamin D insufficiency - at 25(OH)D level 20-29 ng/mL (51-75 nmol/L); normal Vitamin D content - at 25(OH)D level 30-100 ng/mL (76 - 250 nmol/L). A 25(OH)D content greater than 100 ng/mL (greater than 250 nmol/L) was evaluated as hypervitaminosis D.

Determination of 25(OH)D and parathyroid hormone content in serum was carried out in the spring-summer period, when vitamin D levels were maximal and parathyroid hormone levels were minimal.

The glycated hemoglobin (HbA1c) level with a reference interval of 4.0-6.0% was determined on a Bio Rad d10 liquid chromatograph (USA) in unfrozen whole blood, with the addition of the anticoagulant EDTA-K2. Glucose content in blood plasma was determined by glucose oxidase method, GLUCL reagent kit for Abbott Architect 8000 analyzer was used (reference interval 3.89-5.5 mmol/l). Serum insulin levels were measured on an enzyme immunoassay analyzer, using a set of reagents and calibrators produced by "Roche Diagnostics" ELECSYS Insulin (Germany) (normal range 17.8-173.0 pmol/l). All subjects underwent a standardized examination - oral glucose tolerance test (OGTT, glucose load 1.75 g/kg, not more than 75 g) and measurement of fasting glucose levels (glucose 0') and 120 min after glucose load (glucose 120'). A fasting glycemia above 5.6 mmol/L was diagnosed as impaired fasting glycemia (IFG); a glycemia level after 120 min above 7.8 mmol/L was diagnosed as impaired tolerance to carbohydrates (ITC). The insulin resistance index ($HOMA_R$) was calculated according to the formula: fasting insulin (pmol/L) × fasting glucose (mMol/L)/155 (normal is 3.2 and lower) [5].

Biochemical analysis of blood, in particular measurement of total cholesterol (TC) (normal range 0.00-5.17 mmol/l), triglycerides (TG) (normal range 0.00-1.69 mmol/l), high-density lipoproteins (HDL) (normal range 1, 04-1,55 mmol/l) and low density lipoproteins (LDL) (normal range 2,59-4,11 mmol/l) was performed on immunoenzyme analyzer Cobas Integra 400 (USA) using a set of reagents and other accessories from Roche Diagnostics (Germany).

Determination of the content of total and ionized calcium, inorganic phosphorus in blood serum, calcium and phosphorus levels in urine on a biochemical analyzer Beckman Coulter AU 480 (USA) (the norm of total calcium for children under 12 years - 2.2 - 2.7 mmol / l, over 12 years - 2.1- 2.55 mmol / l; ionized calcium for children over 1 year - 1.15 - 1.27 mmol / l. ; norms of inorganic phosphorus in serum for children older than 1 year - 1,45-1,48 mmol/l.; normal values in the morning portion - urine calcium - 0,07-0,3 mmol/mmol, creatinine.

The parathyroid hormone level in serum was determined on an Immulite 2000XPi Siemmens (Germany) immunochemiluminescence analyzer.

Statistical methods

The material was statistically processed using the application software package STATISTICA for Windows (version 7, StatSoft, Inc.) - and Excel 2016 for Windows. Methods of variation parametric and nonparametric statistics with determination of arithmetic mean (M), mean square deviation (σ), traditional mean error (m), relative values, Correlation analysis by Pearson method (r) were applied. Qualitative values by $\chi 2$ method, in case of small group sizes by Fisher's precise two-sided criterion for four-field tables. The statistical significance of measurements was determined by Student's criterion (t) with calculation of the probability of error (P).

Chapter III. CHARACTERIZATION OF METABOLIC STATUS AND LIFESTYLE OF OBESE CHILDREN

Characterization of heritability, anamnesis and lifestyle of obese children.

Childhood obesity is associated with hereditary influences in addition to lifestyle characteristics. Despite the familiarity of this fact, the latest literature data for the last decades do not have an unambiguously unified opinion on the significance of the aggravation of the development of obesity at different degrees of severity of this pathological process and indicate a different approach to understanding this problem [52: p. 17].

Heritability is primarily affected by the presence of obesity in first cousin relatives, as shown in Table 3. The frequency of obese parents was progressively related to the degree of childhood obesity, with the number of obese parents in children with grade III obesity being 2/3 each (16 mothers - 61.5% and 15 fathers - 57.7%), and the frequency of both obese parents being ½ - 13 pairs (50%).

Diabetes as one of the components of the metabolic syndrome developing on the influence of obesity was found with a significant frequency in fathers of both children with obesity of I-II grade (8-22%) and fathers of children with obesity of III grade (7-26.9%), in the group with BMI ≥+3 SDS carbohydrate metabolism disorder was found in both parents (3-11.5%).

In case of obesity concomitant pathology such as arterial hypertension, coronary heart disease in relatives of the I and II degree of kinship no significant difference by groups was revealed (Table 3.1.1).

At present, the risk factor for obesity development is the birth weight of the child, so a special group consisted of children with III grade of obesity, in which children born with body weight more than 4000 g - 13 children (50%; $p<0.05$) and 11 children (42.3%%; $p<0.05$) with reliable frequency in ½ of cases, i.e. in almost half of cases low birth weight children (less than 2500 g) were born, while in other groups there were no reliable differences between them.

Table 3.

Frequency of some diseases in genealogical anamnesis of children of the compared groups (n (%).

Diseases and degree of kinship	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Maternal obesity	13 (33.3)	21 (51.2)	16 (61.5)*	2 (6.6)
Father obesity	10 (25.6)	15 (36.5)	15 (57.7)*	1 (3.3)
Both parents obesity	8 (20.5)	14 (34.1)	13 (50)*	-
Relatives obesity II degree of kinship	15 (38.4)	18 (44)	14 (53.8)	7 (23.3)
Maternal type 2 CD	2 (5.1)	5 (12.2)	5 (19.2)	-
Father type 2 CD		8 (22)	7 (26.9)*	-
Both parents type 2 CD.	-	-	3 (11.5)	-
Type 2 CD in relatives of the II degree of kinship	4 (10.2)	6 (14.6)	7 (26.9)	3 (10)
Maternal GB	1 (2.6)	3 (7.3)	3 (11.5)	
Father GB	3 (7.7)	4 (9.7)	3 (11.5)	
Both parents GB	-	2 (4.9)	3 (11.5)	
GB in relatives of the II degree of kinship	9 (23.0)	12 (29.2)	8 (30.8)	6 (20)
Maternal IHD	-	-	-	-
Father IHD	-	-	1 (3.8)	-
Both parents IHD	-	-	-	-

IHD in relatives of the II degree of kinship	4 (10.2)	4 (9.7)	4 (15.3)	2 (6.6)

Note: * - reliability of data of group III to control P<0.05

However, we did not identify children born with a birth weight of more than 4000 g in the group of children with normal body weight (Table 4).

We were interested in studying the life history of children on vitamin D intake in the first and subsequent years of life. Questioning parents of obese children and processing data from children's outpatient records revealed that the frequency of continuous vitamin D intake during the first year of life in the preventive dose was very low in both the control group and the main group of children, only 2 children (7.7%) in the group with BMI ≥+3 SDS took vitamin D for more than 6 months, which was significantly less compared to the control group (p<0.02) and group II (p<0.05), while no differences were observed compared to group I (p>0.05).

Table 4.

Birth weight of children from the compared groups (n (%)

	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Normal birth weight	18 (46.1)	18 (44)	2 (7.7)*	22 (73.3)
Birth weight less than 2500 g	10 (25.6)	10 (24.3)	11 (42.3)	8 (26.7)
Birth weight more than 4000 g	11 (28.2%)	13 (31.7%)	13 (50)*	0

Note: * - reliability of data of group III to control P<0.05

The highest frequency of children not taking vitamin D in the first year was observed in children with III grade of obesity - 9 children (34.6%), while no significant differences were observed in comparison with other groups. The data show that in all groups, regardless of body weight, there were cases of insufficient

vitamin D intake, short duration of vitamin D intake or no vitamin D intake, including in the control group.

According to parents 1/5 children in the group of children with III grade of obesity were diagnosed with rickets (6 children 23%), the main symptoms of which were baldness of the back of the head, softening of the edges of the fontanel (4 children 15,4%), in rare cases, according to the mother, "valgus" or "varus" curvature of limbs was observed (2 children - 7,7%), all of them were treated with therapeutic dose of this vitamin. It should be noted that the frequency of appearance of these phenomena did not differ significantly between the comparison groups and the control and amounted to 1/5 to 1/6 cases in each group.

Anamnesis analysis of children with overweight and obesity, as well as in the control group, showed that the frequency of vitamin D intake after one year of life was low in all observation groups (Table 5), while the frequency of calcium medications was also not statistically different between the comparison and control groups, ranging from 1/5 to 1/6 cases.

Table 5.

Anamnesis data on vitamin D intake, calcium medications and signs of rickets in children of the compared groups (n (%))

Factors	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Vitamin D intake for 6 months or more	10 (25.6)	9 (22)*	2 (7.7)**	9 (30)
Vitamin D intake for 1 month	13 (33.3)	15 (36.6)	9 (34.6)	8 (26.7)
Did not take vitamin D	8 (20.5)	10 (24.3)	9 (34.6)	8 (26.7)
Diagnosis of rickets in the first year of life	8 (20.5)	7 (17.0)	6 (23.0)	5 (16.7)

Baldness of the back of the head, softening of the edges of the fontanel	5 (12.8)	6 (14.6)	4 (15.4)	4 (13.3)
"valgus" or "varus" curvature of the limbs	3 (7.7)	1 (2.4)	2 (7.7)	1 (3.33)
Vitamin D intake after 1 year of life	3 (7.74)	2 (4.9)	1 (3.8)	2 (6.7)
Use of calcium medications before 1 year of life	6 (15.4)	7 (17.0)	4 (15.4)	6 (20)

Note: * - reliability of data of group III to group II P<0.05

** - reliability of data of group III to control P<0.02

According to various authors, the age of childhood obesity appearance is of particular importance, with its ability to influence the development of early complications and its importance in weight gain in later years. In our study, the average age of onset of weight gain in children with III grade obesity was up to 3 years of life, i.e. during early childhood, and this indicator was observed in ¾ of cases (19 children -73.0%; p<0.001 compared with group I and p<0.001 compared with group II).

In the groups with overweight and obesity of I-II grade, obesity manifestation of half of the children started from 3 to 6 years of age (18 children 46.1% in group 1 and 18 children 44% in group 2), only a small proportion of children started to gain body weight after 6 years of age, the highest frequency of observation was in the group of overweight children (11 children 28.2%), which was significantly different from the group with obesity degree III (Table 6), where no cases of obesity with manifestation after 6 years of age were observed (p<0.001).

Table 6.

Time to manifestation of overweight and obesity in children of the compared groups (n (%))

Factors	Group I n= 39	Group II n= 41	Group III n= 26
Start of weight gain before 3 years of age	10 (25.6)*	15 (36.6)**	19 (73.0)
Weight gain 3-6 years of age	18 (46.1)	18 (44)	7 (27.0)
Weight gain after 6 years of age	11 (28.2)*	8 (19.5)**	0 (0)

Note: * - reliability of data of group I to group III; P<0.001

** - reliability of data of group II to group III P<0.001

One important factor in the development of obesity is the presence and duration of breastfeeding. Examination of children's anamnesis revealed that the frequency of children exclusively breastfed for up to 6 months, which is recommended by WHO, was different in all observation groups. Meanwhile, in children with III grade of obesity, it occurred with the lowest frequency in only 4 children 15, 4%, which was 1/6th ($p<0.05$ compared to control), in other observation groups, the frequency of exclusive breastfeeding was about 1/3, and did not statistically differ in themselves (Table 7).

The group of children with III grade of obesity was artificially fed and received unadapted milk mixtures from 3 months of life (18 children 69,2%), this fact was significantly higher both compared to the control group ($p<0,01$) and compared to children with overweight ($p<0,01$) and obesity I-II grade ($p<0,01$), which suggests a significant role of artificial feeding and giving unadapted mixtures in the development of severe obesity in children.

Table 7.

Comparative characteristics of feeding at 1 year of life of children of the compared groups (n (%)

Feeding peculiarities	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Exclusive breastfeeding until 6 months of age	12 (30.8)	12 (29.2)	4 (15.4)*	13 (43.3)
Mixed feeding	15 (38.5)^	16 (39.0)°	4 (15.4)*	12 (40.0)
Artificial feeding	12 (30.8)^^	13 (31.7)°°	18 (69.2)**	5 (16.7)
Early complementary feeding	15 (38.5)	14 (34)	10 (38.4)	8 (26.7)
Predominantly carbohydrate diet	8 (20.5)	11 (26.8)	9 (34.6)*	4 (13.3)
Feeding whole milk up to 6 months of age	5 (12.8)^^	5 (12.2)°°	11 (42.3)**	2 (6.7)

Note: * - reliability of control group to group III (* - P<0.05; ** - P<0.01)

^ - reliability of data from group I to group III (^ - P<0.05; ^^ - P<0.01)

° - reliability of data of group II to group III (° - P<0.05; °° - P<0.01)

In groups with overweight and obesity of I-II degree, the frequency of mixed and artificial feeding was almost evenly distributed in 1/3 of cases (Table 7).

Given the undoubted role of alimentary causes in the development of obesity and vitamin D deficiency states, we evaluated the nature of children's nutrition. According to our data, the diets of the examined children contained sweets consumed in high frequency by 34 children (87.1%), 37 children (90.2%) and 23 (88.5%) of groups I, II and III, correspondingly, which was statistically significant

compared to the control ($p<0.001$) but was not significant between the comparison groups (Table 8).

The same situation was observed with the consumption of excessive amounts of flour products, potatoes (Table 8), consumption of fried fatty dishes of local cuisine (fatty pilaf, kazon kebab, etc.), and it should be noted that this indicator in absolute number was present in children with 3 degrees of obesity 26 children (100%; $p < 0.001$ compared to control).

With great frequency in the interviewed children there were cases of drinking traditional drinks (tea, coffee) with added sugar (up to 6 and more teaspoons), as well as the use of sweet carbonated drinks and juices without controlling their volume, with children drinking them up to 1-3 liters a day.

At the same time, the frequency of low-calorie vegetables in the diets of children of the compared groups was only 1/5 in the overweight and obese groups and 1/3 in the control group, and fruit consumption was 1/3 each in the comparison and control groups. It should be noted that the difference between the main groups and the control group was not significant, indicating that obese children and children with normal body weight had a deficit in regular intake of fresh fruits and vegetables.

Since the goals of our study include the study of vitamin D levels and phosphorus-calcium metabolism, we evaluated the frequency of consumption of milk and milk products (cheese, brynza, fermented milk products), which are the main sources of calcium for children, so a total of 9 children (23.0%) in group I, 10 children (24.3% in group II and 7 children (27.0%) in group III received milk products daily, the rest several times a week or a month.

Table 8.

Comparative characterization of nutritional features in the comparison groups (n (%)

Nutritional Features	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30

Consumption of large quantities of sweets	34 (87.1)	37 (90.2)	23 (88.5)*	4 (13.3)
Excessive consumption of flour products and potatoes	30 (76.9)	38 (92.7)	24 (92.3)*	3 (10)
Regular consumption of sweet carbonated drinks	29 (74.3)	40 (97.5)	26 (100)*	2 (6.7)
Fried fatty traditional dishes	30 (76.9)	37 (90.2)	26 (100)*	8 (26.7)
Regular consumption of vegetables	9 (23.0)	8 (19.5)	5 (19.2)	9 (30)
Regular consumption of fruits	11 (28.2)	11 (26.8)	7 (27.0)	12 (40.0)
Regular consumption of milk and milk products	9 (23.0)	10 (24.3)	7 (27.0)	11 (36.7)
Use of vitamin and mineral complexes	4 (10.2)	5 (12.2)	4 (15.4)	6 (20)

Note: * - reliability of control group to group III (* - P<0.001)

It was found that obese children from 7 to 17 years old consumed on average only 160.12±13.07 ml of milk and/or milk products per day, which is insufficient to obtain the daily dose of calcium. Only 4 children (10.2%) in group I, 5 children (12.2%) and 4 children (15.4) in group III of school children had additional calcium supplementation with prophylactic purpose as a part of vitamin-mineral complexes, the dose of which did not exceed 150 mg/day, and these indicators were not statistically different from the indicators of children with normal body weight, i.e. there was a deficit of calcium preparations regardless of body weight.

Overweight and obese children presented a variety of complaints (Table 9). The main complaint was increased appetite: 31 children (79.5%), 35 children (85.4%) and 20 children (76.9%) in groups I, II and III, respectively, and the frequency of this complaint was statistically different from the control group ($p<0.001$), but did not differ between the main groups.

Table 9.

Comparative characteristics of children's complaints in comparison groups (n (%)

Complaints	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Increased appetite	31 (79.5)	35 (85.4)	20 (76.9)*	8 (26.7)
Headache	28 (71.8)	25 (61.0)	21 (80.8)*	5 (16.7)
Heartache	8 (20.5)	8 (19.5)	10 (38.4)*	
Epigastric and abdominal pain	27 (69.2)	30 (73.1)	22 (84.6)*	5 (16.7)
Breathlessness	12 (30.8)^	34 (83.0)	26 (100)*	
Hyperhydrosis	19 (48.7)^	23 (56.0)°	22 (84.6)*	3 (10)
Linear atrophy	3 (7.7)^	24 (58.5)°	23 (88.5)*	
Hyperpigmentation	8 (20.5)^	18 (44.0)°	19 (73.0)*	
Increase in arterial pressure	2 (5.1)^	6 (14.6)°	8 (30.8)*	

Note: * - reliability of control group to group III (* - P<0.001)

^ - reliability of data from group I to group III (^ - P<0.01)

° - reliability of data of group II to group III (° - P<0.01)

The complaint of headache was encountered with high frequency and was observed in 21 children (80.8%) of group III children, which was significant in relation to controls (p<0.001), but did not differ between the main groups.

The majority of children who complained of headache noted its occurrence affected by nervous tension, mainly in the evening. 8 children (30.8%) had headache with BP increases. BP increase in the group of children with III grade of obesity and above was statistically significant in relation to the group of overweight children (p<0.01) and children with I-II grade of obesity (p<0.01). This fact once again confirms the theory of AD development as a component of metabolic syndrome affected by obesity.

Children of the compared groups complained of episodes of stabbing pain in the heart area, which, according to the children, occurred both during physical activity and at rest; this indicator was also noted with high frequency in the group of children with a high degree of obesity - 10 children (38.4%; $p<0.001$ compared with control), but also occurred in children of other groups.

Children complaining of abdominal pain mostly reported pain in the epigastrium, umbilical region, and right subcostal region, and this complaint was common in children in all comparison groups, including the control group (Table 9).

It should be noted that breathlessness in children with III grade of obesity occurred even with minor physical activity and in an absolute number of children 26 (100%). It was also significantly greater in comparison with overweight children, as this symptom was observed in children of this group in only 12 patients (30.8%).

About 2/3 of group III, ½ of group I and group II obese patients reported increased sweating, and the rates were statistically different from each other, suggesting that sweating depended on the body weight of the children.

On examination of children, red or purple-blue, pink colored linear atrophy was most often located on the skin of the chest, shoulders and thighs of 23 children (88.5%) with III grade of obesity. Hyperpigmentation was also noted in natural folds of children in the neck, axillae, and groin areas - 19 children (73.0) in this group. This indicator was statistically different in children with overweight and I-II obesity grade, indicating the correlation between the frequency of occurrence of these indicators and body weight.

During the study, we were interested in examining the frequency of comorbid pathology. The most common pathology was GIT pathology in the form of chronic gastritis, which was observed in children of all the compared groups: 26 children (66.7%) in group I, 25 children (61.0%) in group II, and highest frequency in group III children - 21 children (80.8%; $p<0.001$ vs. control) (Table 10).

Cases of fatty hepatosis, with a quite high frequency were found in obese children - 11 children (26.8%) with I-II grade of obesity and 12 children (46.1%) with III grade of obesity, which was statistically higher compared to overweight

children, in whom signs of fatty hepatosis were observed in only 2 children (5.1%). Thus, biliary dysfunction was noted in all groups, including children in the control group (Table 10).

Table 10.

Comparative characterization of the frequency of somatic pathology in the comparison groups (n (%))

Somatic pathology	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Postural disorder	10 (25.6)	9 (22)	7 (27.0)	3 (10)
Platypodia	6 (15.4)	9 (22)	6 (23.0)*	1 (3.33)
Caries	12 (30.8)	16 (39.0)	13 (50)**	5 (16.7)
Bone cracks and fractures	1 (2.56)	5 (12.2)	4 (15.3)	2 (6.7)
Repeated cracks and fractures	-	2 (4.8)	2 (7.6)	
Vegetative-vascular dystonia	19 (48.7)	28 (68.3)	18 (69.2)**	2 (6.7)
Fatty hepatosis	2 (5.1)^^	11 (26.8)	12 (46.1)***	
Chronic gastritis	26 (66.7)	25 (61.0)	21 (80.8)***	3 (10)
Biliary dysfunction	10 (25.6)^	13 (31.7)	13 (50)**	2 (6.7)

Note: * - reliability of control group to group III (* - P<0.05; ** - P<0.001;

*** P<0,0001)

^ - reliability of data from group I to group III (^ - P<0.05; ^^ - P<0.01)

The second disorder - vegeto-vascular dystonia - was equally common in all observation groups, as in overweight 19 children (48.7%), children with I-II grade

obesity - 28 children (68.3%) and children with III grade of obesity - 18 children (69.2%; $p<0.001$ compared to control).

Significant prevalence of musculoskeletal pathology, mainly in the form of posture disorders and flat feet, was observed, with the frequency of these pathologies evenly distributed in the children of the compared groups, statistically differing only from the control group ($p<0.05$).

The somatoscopic assessment of the musculoskeletal system of school children revealed that obese children had pathologic types of posture, mainly slouching, combined disorders and scoliotic posture, in the presence of which the diagnosis of “Scoliosis” was made. Plantogram analysis revealed Platypodia in 1/3 of children in all observed groups.

Thus, clinical and anamnestic analysis showed that the majority of children aged 7 to 17 years, being in the period of intensive growth due to improper nutrition, dietary calcium deficiency, and adynamia, already had clinical signs of changes in the musculoskeletal system.

In addition, it was found that 1/10 obese patients had bone fractures (12.2% and 15.3% in group II and III, correspondingly) of which recurrent fractures occurred in 4.8% and 7.6%, respectively. There were also cases of fractures in children with normal body weight in 2 children (6.7%).

Thus, the presence of obesity in first cousin relatives, especially mothers, and the high prevalence of both parents being obese plays a major role in the heritability of obese children. Diabetes was more prevalent in fathers of obese children.

in obese children, a high prevalence of children born with a high body weight of more than 4000 g was detected, while in the group of children with III grade of obesity in half of the cases low birth weight babies were also born, indicating the possible development of the "economical type" of fat deposition in the following years.

The vitamin D intake analysis at 1 year and in the subsequent periods of life showed that in all groups, regardless of body weight, there were cases of insufficient vitamin D intake, short duration of vitamin D intake or absence of its intake,

including low frequency of calcium preparations intake, including in the control group, while in group III children there was a significant decrease in the frequency of intake in the first 6 months of life.

Children with obesity in groups II and III had early manifestation of obesity up to 3 years of life, and a correlation was found with the III grade of obesity and artificial feeding with non-adapted formula, giving whole milk up to 6 months of age. Sweets, sweet carbonated drinks, and carbohydrate-containing foods were present in the diets of the examined obese children with high frequency. At the same time in all groups, including the control group, there was a low frequency of consumption of milk products, the main sources of calcium.

From the concomitant pathology prevailed GIT damage and vegetovascular dystonia, as well as musculoskeletal system damage in the form of flat feet and scoliosis.

All the above-mentioned circumstances make it possible to include the above facts in the predictors or complications of childhood obesity.

Characterization of metabolic status of obese children

In determining the metabolic status of the children, carbohydrate metabolism was assessed first. The comparative evaluation of this type of metabolism depending on BMI revealed that the degree of frequency of carbohydrate metabolism disorders had a close correlation with it. At the same time in the general structure of examined children pathology of carbohydrate metabolism in the general group of children with overweight and obesity occurred in 50 children (47,16%), with one variant of carbohydrate metabolism disorders occurring in 1/8 of the whole sample of children with high body weight: 14 children and adolescents (13.2%), two variants in 6 (5.6%), three variants in 18 children and adolescents (17%), and 1/10 children of the main group (12 children, 11.3%) had pathology in four parameters of carbohydrate metabolism, which constituted a risk group for the development of type II diabetes in this group of children (Fig. 4.).

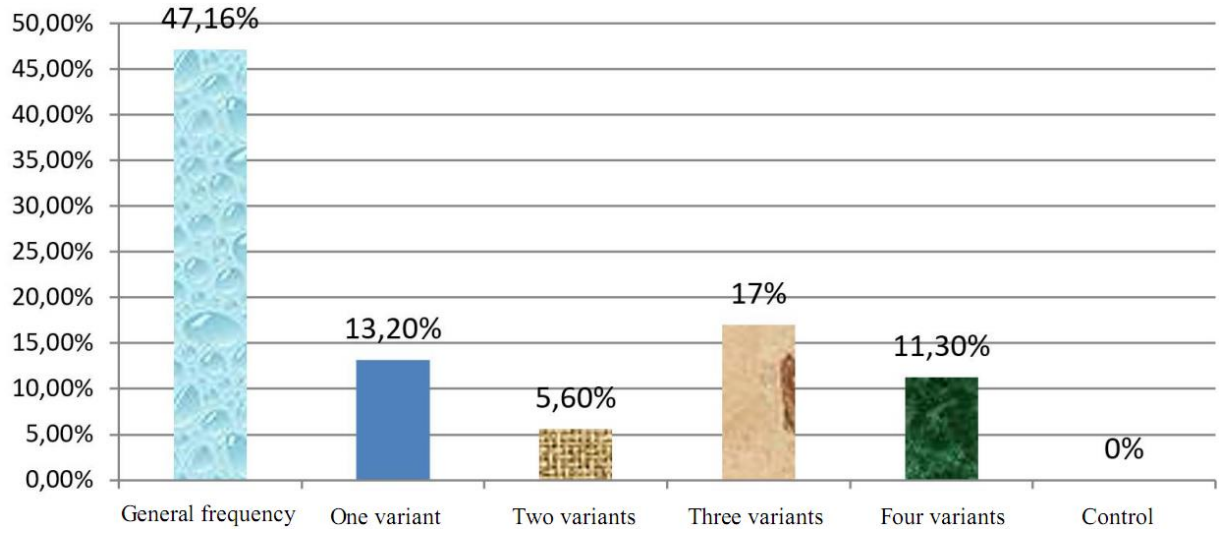


Fig. 4. Frequency of carbohydrate metabolism pathology in obese, overweight children and in the control group

As can be seen from the data presented in Table 11, disorders of carbohydrate metabolism occurred in all groups with body weight exceeding the normative values, with a significant, reliable frequency in the group with BMI ≥+3 SDS.

Thus, during the standard glucose tolerance test, disorders of carbohydrate metabolism were detected with the highest frequency in the group with III grade of obesity (BMI ≥+3 SDS), where, along with fasting hyperglycemia found in almost half of the children in this group 12 (46. 1%), 1%), impaired glucose tolerance was detected in 15 (57.7%), which spoke about the hidden nature of carbohydrate metabolism disorders in children, with some patients having both fasting hyperglycemia and glycemia above 7.9 mmol 2 hours after glucose load. The obtained data were significant in comparison with overweight children (BMI +1.0 to +2.0 SDS) both in terms of fasting hyperglycemia (5 children -12.8%; $p<0.01$) and impaired glucose tolerance (8 children - 20.5%); $p<0.001$), whereas in comparison with the results of the group of children with I-II degree of obesity (BMI >+2<+3 SDS), confidence limits were observed when compared with positive glucose tolerance test (13 children - 31.7%; $p<0.05$).

In children of this group (BMI ≥+3 SDS), high glycated hemoglobin was also detected in 11 (42.3%), and in part of children (2 children; 7.7%) it was the only lesion of carbohydrate metabolism, which is evidence of carbohydrate metabolism

disorders not detected by glucose tolerance test. The frequency of increased glycated hemoglobin levels was significantly higher in overweight children (5 children, 12.8%; p<0.01) and not significantly different from group 2 children (BMI >+2<+3 SDS) (10 children, 24.3%; p>0.1).

Table 11.

Comparative analysis of the frequency of carbohydrate metabolism pathology in comparison groups (n (%))

Factors	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Fasting hyperglycemia;	5 (12.8)^	11 (26.8)	12 (46.1)*	-
Impaired glucose tolerance	8 (20.5)^^	13 (31.7)°	15 (57.7)*	-
High levels of glycated hemoglobin (>7.5%)	5 (12.8)^	10 (24.3)	11 (42.3)*	-
Hyperinsulinemia (immunoreactive insulin)	9 (23.0)^	15 (36.6)°	16 (61.5)*	-
High IR HOMA $_{R}$	4 (10.2)^^	10 (24.3)°	13 (50.0)*	-

Note: * - reliability of control group to group III (* - P<0.001)

^ - reliability of data from group I to group III (^ - P<0.01; ^^ - P<0.001)

° - reliability of data of group II to group III (° - P<0.05)

In children of this group there was a greater frequency of children with high levels of immunoreactive insulin, the level of which did not exceed reference values, but was significantly higher compared to the indicators of other sick children. We

considered a level above 70 pmol/L as the threshold for high immunoreactive insulin level.

Thus, high immunoreactive insulin levels were found in more than half of group III children - 16 (61.5%; $p<0.001$ vs. control), while the IR HOMA $_R$ in 50% of cases (13 children; $p<0.001$ compared to control) had values exceeding the threshold value of 3.2, which indicates that despite the fact that the level of immunoreactive insulin was within the normal range, in combination with a high level of fasting glucose, insulin resistance was formed in this category of patients.

It should be noted that in group 3 children both the frequency of hyperinsulinemia and the frequency of high IR NOMA R were significantly higher both compared to group I (9 children 23.%; $p<0.01$ and 4 children 10.2%;. $p<0.001$, correspondingly) and compared to group II with I-II degree of obesity (15 children 36.6%; $p<0.05$ and 10 children 24.3%; $p<0.05$, correspondingly).

The comparative characterization of the level of the main indicators of carbohydrate metabolism revealed that all average indicators of carbohydrate metabolism did not exceed the limits (Table 12.). Children and adolescents with III grade of obesity or higher (BMI ≥+3 SDS) had significantly higher rates than other groups.

At the same time, the main indicator of carbohydrate metabolism fasting glucose in all three groups having values reference values (4,94±0,11; 4,98±0,15; 5,3±0,18 mmol/l) did not significantly differ from each other ($p>0,05$), only in comparison with the control group the indicator of fasting glucose level had significantly low indices (4,01±0,11; $p>0,0001$).

Table 12.

Average values of carbohydrate metabolism in the comparison groups

Factors	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Fasting glucose; mmol/L	4.94±0.11	4.98±0.15	5.3±0.18*	4.01±0.11
Глюкоза через 120' после нагрузки	7.28±0.18^	7.41±0.12	7.87±0.21*	6.34±0.08
Glycated hemoglobin (HbA1c ;%)	5.00±0.15^^	5.14±0.14°°	6.00±0.16*	4.50±0.09
Insulin (pmol/L)	39.21±4.67^^	48.21±5.17°	65.46±6.35*	17.47±0.81
IR HOMA $_R$ (RU)	1.34±0.19^^	1.6±0.21°	2.34±0.26*	0.46±0.02

Note: * - reliability of control group to group III (* - P<0.0001)

^ - reliability of data from group I to group III (^ - P<0.05; ^^ - P<0.01)

° - reliability of data of group II to group III (° - P<0.05; °° - P<0.01)

In a comparative analysis of fasting glycemic levels 120 minutes after glucose loading, the mean glycemic levels were within the normal range in all study groups: 7.28±0.18; 7.41±0.12; 7.87±0.21 mmol/l, in groups I, II and III, correspondingly, with only glucose levels in the group of children with III grade of obesity significantly higher than in overweight children (p<0.05) and normal weight children (p<0.0001).

The level of glycated hemoglobin being within the normal range in all three groups of the study (5.00±0.15; 5.14±0.14; 6.00±0.16% in group I, II and III, respectively) significantly differed from each other (p0.0001-III group to control; p<0.01-III group to group I; p<0.01-III group to group II), which indicates a close

correlation between the increase in body fat mass and the pathology of carbohydrate metabolism.

Similarly to the level of glycated hemoglobin, the values of immunoreactive insulin and insulin resistance index HOMA $_{R,}$ statistically significantly differed depending on the degree of weight gain, the higher the degree of obesity, the greater the deviation of indicators from the variant of the norm was observed (Table 12).

We also analyzed the state of carbohydrate metabolism according to gender differences. It was found that in boys there was a predominance of the frequency of cases of all types of disorders of carbohydrate metabolism, with the highest frequency of hyperinsulinemia 26 (44.06%) and impaired glucose tolerance 23 (38.9%), in girls there were also cases of impaired glucose tolerance 14 (29, 8%) and high insulin 14 (29, 85%), with the highest frequency compared to other types of carbohydrate metabolism disorders, but it should be noted that the entire difference between boys and girls, for all types of carbohydrate metabolism pathology was not statistically significant (Table 13.).

Table 13.

Frequency of carbohydrate metabolism disorders in children in the comparison group depending on gender

Factors	Main group children n=106		P
	Boys n=59	Girls n=47	
Fasting hyperglycemia;	19 (32.2)	9 (19.4)	>0,1
Impaired glucose tolerance	23 (38.9)	14 (29.8)	>0,2
High level of glycated hemoglobin	17 (28.81)	10 (21.3)	>0,5
Hyperinsulinemia	26 (44.06)	14 (29.8)	>0,1
High IR HOMA $_{R}$	18 (30.5)	10 (21.3)	>0,2

A study of the frequency of observations of pathology of carbohydrate metabolism depending on the stage of pubertal period in children revealed that high

fasting glucose 20(48%), hyperinsulinemia 23 (46.9%), and especially impaired glucose tolerance 25 (53.06%) were diagnosed significantly more frequently in pubertal children compared with prepubertal children (8 children 14.3%; 17 children 29.8%, and 11 children 19.3%, respectively) (Table 14). And the difference was significant between the level of fasting hyperglycemia ($p<0.001$), impaired glucose tolerance ($p<0.001$), and high IR HOMA $_R$ ($p<0.001$).

Table 14.

Frequency of carbohydrate metabolism disorders in children of comparison groups depending on the period of sexual maturation

Factors	Main group children n=106		P
	Prepuberty n=57	Puberty n=49	
Fasting hyperglycemia;	8 (14.03)	20 (40.8)	<0.001
Impaired glucose tolerance	11 (19.3)	26 (53.06)	<0.001
High level of glycated hemoglobin	10 (17.5)	16 (32.6)	>0,1
Hyperinsulinemia	17 (29.8)	23 (46.9)	>0,1
High IR HOMA $_R$	8 (14.03)	20 (40.8)	<0.001

Analyzing the state of fat metabolism in children and adolescents depending on SDS BMI revealed that lipid metabolism disorders occurred in 41 (38.6%) patients in the total sample of overweight and obese patients. At the same time, 1/8 children (16 children - 15%) had 1 indicator of lipid metabolism pathology, 1/10 children (12 children - 11.3%) had 2 indicators and 12.3% had abnormalities in 3 or more indicators of lipid metabolism (Fig. 5).

Among the most frequent disorders of lipid metabolism there was a decrease in the high-density lipoprotein cholesterol fraction (HDL-C). It was found that the most frequent decrease in this index was observed in children with a significant excess of body weight from normal values (BMI ≥+3 SDS), being observed in

almost half of the children in this group - 12 children (46.1%), with a significant predominance of the frequency of occurrence compared to children with excess body weight (4 children - 10.2%; $p<0.01$) and compared to children with body weight corresponding to the I-II degree of obesity (8 children 19.5%; $p<0.02$); These indicators are shown in Table 15.

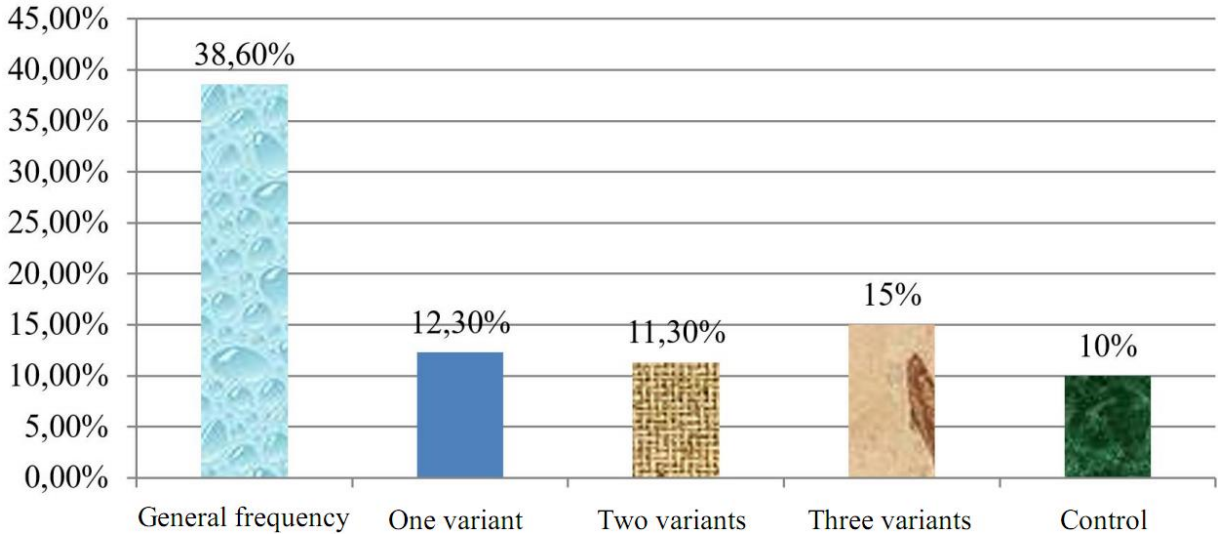


Fig. 5. Frequency of lipid metabolism pathology in children of comparison groups

Hypertriglyceridemia was the second type of pathology in terms of frequency of occurrence. Similar to the lowering of HDL-C levels, the prevalence of this index depended on body weight, being most frequent in group III 10 (38.4%), which was significantly higher compared with group I (5 children 12.8%; $p<0.05$) and compared with group II (5 children -12.8%; $p<0.05$). This index was also observed in the group of children with normal body weight (in 2 children - 6.7%), which is probably an early sign of hypercholesterolemia development in the adult period, even in persons with normal body weight.

The frequency of total cholesterol (3 children 7.7%, 5 children 12.2%; 7 children 27%) and low-density lipoprotein cholesterol fractions (4 children 10.2%, 8 children 19.5%; 12 children 46.1%) increased according to body weight gain, with total cholesterol levels not significantly different in the obese groups, whereas low-density lipoprotein cholesterol had a significant frequency, being significantly higher in both group I children ($p<0.01$) and group II children ($p<0.05$).

Table 15.

Comparative analysis of the frequency of lipid metabolism pathology in children of comparison groups

	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Hypertriglyceridemia	5 (12.8)^	7 (17.0)°	10 (38.4)*	2 (6.7)
Hypercholesteremia	3 (7.7)^	5 (12.2)	7 (27.0)**	0
Low HDL-C	4 (10.2)^^	8 (19.5)°°	12 (46.1)**	1 (3.33)
High LDL-C	3 (7.7)^^	7 (17.0)°	10 (38.4)*	0

Note: * - reliability of control group to group III (* - P<0.01; ** - P<0.001;

^ - reliability of data from group I to group III (^ - P<0.05; ^^ - P<0.01)

° - reliability of data of group II to group III (° - P<0.05; °° - P<0.02)

Characterization of the mean blood lipid levels, in all study groups showed that all values were within the reference values. Table 16 shows that triglyceride levels ranged from 0.94±0.08 mmol/L in group I to 1.50±0.10 mmol/L in group III (with normal TG >1.7 mmol/L), although all levels were within normal limits, they were statistically different from each other and increased with increasing body weight.

The same characteristic was observed for all lipid metabolism values. The high-density lipid fraction was slightly lower than normal (HDL-C < 1.03 mmol/L) in group III children (1.00±0.02 mmol/L) and significantly different from both overweight children (1.23±0.03 mmol/L; p<0.001) and children with grade I-II obesity (1.15±0.02 mmol/L; p<0.001).

The mean levels of total cholesterol and LDL-C had the highest value of reference values, but remained within the normal range in all groups (Table 16).

Table 16.

Average values of lipid metabolism in the comparison groups

	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Triglyceride; mmol/L	0.94±0.08^	1.04±0.07°°	1.50±0.10*	0.74±0.06
Total cholesterol; mmol/L	3.50±0.20^	3.96±0.18°	4.97±0.26*	2.89±0.14
HDL-C; mmol/L	1.23±0.03^	1.15±0.02°°	1.00±0.02*	1.32±0.02
LDL-C; mmol/L	3.02±0.13^	3.25±0.18°	4.44±0.30*	2.36±0.09

Note: * - reliability of control group to group III (* - P<0.001)

^ - reliability of data from group I to group III (^ - P<0.001)

° - reliability of data of group II to group III (° - P<0.01; °° - P<0.001)

Therefore, in children of group III, changes in serum lipid profile had a more pronounced atherogenic character in comparison with other groups, where statistically significant differences in the impairment of lipid metabolism parameters were revealed.

Analyzing the quantitative values of metabolic parameters that characterize comorbidity of childhood and adolescent obesity in correlation with the degree of obesity severity, the data on statistically correct growth of the median of all

parameters that characterize lipid metabolism in accordance with the growth of body weight were obtained.

Identification of gender differences in the level of lipid metabolism revealed that boys regardless of the observation group had more significant changes in lipid metabolism values, which is evidence of a high risk of atherogenic disorders in males compared to females. Combinations of several types of fat metabolism disorders were also more common in boys. Therefore, a higher frequency of impairments was noted for all types of pathologic indicators of hypertriglyceridemia lipid metabolism - 18 children (30.5%) p<0.01; low level of HDL-C - 16 children (27.1%) p>0.2; high level of LDL-C - 16 children (27.1%) p<0.05.

Table 17

Frequency of lipid metabolism disorders in the compared groups depending on gender

Factors	Main group children n=106		P
	Boys n=59	Girls n=47	
Hypertriglyceridemia	18 (30.5)	5 (10.6)	<0.01
Hypercholesteremia	9 (15.2)	6 (12.7)	>0,5
Low HDL-C	16 (27.1)	8 (17.0)	>0,2
High HDL-C	16 (27.1)	6 (12.7)	<0.05

Analyzing the level of lipid metabolism values depending on sexual development revealed that already in the prepubertal stage there were significant changes in lipid metabolism values: hypertriglyceridemia, 8 children (14.0%; p<0.05); hypercholestrinemia, 6 children (10.5%); low HDL-C, 7 children (12.3%; p<0.01); and high LDL-C, 8 children (14.0%; p<0.02) (Table 18).

Table 18.

Frequency of lipid metabolism disorders in children of the compared groups depending on the period of sexual maturation

Factors	Main group children n=106		P
	Prepuberty n=57	Puberty n=49	
Hypertriglyceridemia	8 (14.0)	15 (30.61)	<0.05
Hypercholesteremia	6 (10.5)	9 (18.4)	>0.2
Low HDL-C	7 (12.3)	17 (34.7)	<0.01
High LDL-C	8 (14.0)	13 (32.6)	<0.02

This indicates the formation of lipid metabolism disorders at an early age and before the clinical manifestation of obesity complications, while at the pubertal stage, the frequency of lipid metabolism pathology statistically exceeded the indicators of children in puberty, which should be alarming with regard to the development of early atherosclerotic changes in children in this category.

Therefore, childhood and adolescent obesity is accompanied by characteristic metabolic abnormalities. Analyzing the level of carbohydrate and lipid metabolism, it was found that in overweight and obese children and adolescents, the frequency of pathology of carbohydrate and lipid metabolism depended on the degree of fat mass in the child's body, with the highest frequency of glycated hemoglobin, hyperinsulinemia, insulin resistance, as well as all indicators of lipid metabolism. Children with III grade of obesity, as well as boys during puberty, had the most severe disorders.

Chapter IV. DETERMINATION OF VITAMIN D STATUS AND OSTEOPENIC CONDITIONS

Determination of vitamin D status and bone tissue metabolism in correlation with parameters of carbohydrate and lipid metabolism

The next stage of our study was to determine the status of vitamin D supply in obese children and its correlation with metabolic parameters.

The level of vitamin D 25(OH)D supply in 106 children and adolescents with overweight and obesity was determined, and for comparison studies were conducted in 30 healthy children with body weight in the range of SDS BMI <+1, all children and adolescents were residents of Samarkand region.

Table 19.

Average vitamin D level in the study groups

Research groups	Vitamin D level ng/mL
Total patient group (+1.0 to ≥+3 SDS); n=106	19.80±0.98*
Group I (+1.0 to +2.0 SDS); n= 39	22.19±1.60
Group II (>+2<+3 SDS); n= 41	19.34±1.40
Group III (≥ +3 +3 SDS); n= 26	15,28±1,32*
Control group (<+1 SDS); n= 30	23.29±1.47

Note: * - reliability of the control group to the total patient group (* - P<0.02)

** - reliability of control group to group III (* - P<0.02)

Comparative characterization of vitamin D levels in the study and control groups revealed widespread vitamin D insufficiency and deficiency in children of all ages, and the frequency of these pathological conditions was dependent on body weight.

Thus, in the groups of children and adolescents of the main groups with overweight and obesity (106 patients) the serum 25(OH)D content was 19.80±0.98 ng/mL, which was the upper limit of vitamin D deficiency, and in the control group

a slightly higher 23.29±1.47 ng/mL, which was the lower limit of 25(OH)D insufficiency, but the difference was statistically significant (p<0.02) (Table 19).

The distribution of vitamin D levels in children of the main and control groups was also almost identical and revealed only a small number of children with vitamin D reference values, both in the group of children with overweight and obesity and with normal body weight according to age and sex (Table 20).

Table 20.

Vitamin D supply in groups of overweight and obese children and children with normal body weight

	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Vitamin D - 30 ng/mL.	7 (15.4)^	3 (7.3)	0 (0)**	8 (26.7)
Vitamin D - 21-30 ng/mL	8 (23.0)	13 (31.7)	6 (23.0)	9 (30)
Vitamin D - <20 ng/mL	24 (61.5)	25 (61.0)	20 (76.9)*	13 (43.3)

Note: * - reliability of control group to group III (* - P<0.01; ** - P<0.001)

^ - reliability of data from group I to group III (^ - P<0.01)

Comparative analysis revealed that in the groups of children with overweight and obesity of varying severity there was a predominance of patients with vitamin D deficiency. Thus in the group of children with BMI ≥+ 3 SDS vitamin D deficiency accounted for ¾ of cases where 20 children (76.9%) had Vitamin D - <20 ng/mL, then the remaining ¼ were children with vitamin D insufficiency (21-30 ng/mL) 6 children 23.%, with no cases of vitamin D levels within the normal range (≥30 ng/mL).

In the second group of children with BMI >+2<+3 SDS the status of vitamin D deficiency amounted to 2/3 of the number of observations (25 children -61%), while the children of this group had cases of vitamin D levels within the reference

values, which amounted to only 7.3% (3 children), with the frequency of deficiency in 13 children (31.7%).

In the first observation group of overweight children (BMI +1.0 to +2.0 SDS), the frequency distribution of occurrence of different vitamin D levels was similar to group 2: 24 children - 61.5% (Vitamin D <20 ng/mL), 9 children - 23%; (Vitamin D 21-30 ng/mL), but the frequency of observations of normal vitamin D levels was significantly higher compared to the group of children with III grade of obesity: 6 children - 15.4% (Vitamin D≥30 ng/mL) ($p<0.01$).

In the control group, the frequency of children with vitamin D deficiency was 1/3 (13 children 43.3%), and in children with III grade of obesity, compared to children in the control group, there was a significant difference in the frequency of vitamin D deficiency ($p<0.01$), and with the indicators of children in group II ($p<0.05$), while with the group of overweight children no confidence limits were found ($p>0.1$).

The frequency of insufficient and normal vitamin D levels was almost equally distributed, each accounting for 1/3 of the total number of children in the control group: 9 children (30%) with Vitamin D 21-30 ng/mL and 8 children (26.7%) with Vitamin D ≥30 ng/mL. It should be noted that the index of the frequency of vitamin D deficiency, reliably differed only from the frequency of manifestations of vitamin D deficient state in group III ($p<0.01$), while with the other groups it did not differ significantly ($p>0.2$).

This fact indicates that in the group of children with normal body weight, who are also in health groups I and II, vitamin D deficiency and insufficiency are also found at a high level, which requires the application of therapeutic and preventive measures even in the group of conditionally healthy children.

Therefore, the obtained results indicate that the predominant number of examined children living in Samarkand region had vitamin D insufficiency and deficiency. However, in the group of children with vitamin D deficiency and III grade of obesity (BMI ≥+ 3 SDS), the quantitative values of median Vitamin D were statistically significantly lower (12.19±0.84 ng/mL) than in the group of children

with deficiency and overweight (15.87±0.51 ng/mL; p<0.001), and with the group of children with vitamin D deficiency and normal body weight (15.83±0.84 ng/mL; p<0.001) (Table 21).

Comparative analysis of the average level of vitamin D in the group with insufficiency of this indicator showed statistically insignificant level in all groups with different body weight.

Thus, the average level of 25(OH)D in its deficiency in the group of children with BMI ≥+2<+3 SDS was 25.96±0.59 ng/mL, in the group of children with more marked obesity (BMI ≥+3 SDS) 25.58±1.05 ng/mL and almost the same value in the group with overweight 25.15±0.94 ng/mL (p>0.05).

In children with normal vitamin D supply, average vitamin D values were also not statistically different (Table 21).

Table 21.

25(OH)D values in the study groups according to the degree of its supply.

	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
Vitamin D ≥30 ng/mL.	40.5±2.51	41.2±4.84	-	35.33±1.45
Vitamin D 21-30 ng/mL	25.15±0.94	25.96±0.59	25.58±1.05	25.54±073
Vitamin D <20 ng/mL	15.87±0.51^	13.76±0.63°	12,19±0,84*	15.83±0.84

Note: * - reliability of control group to group III (* - P<0.001)

° - reliability of control group to group II (° - P<0.01)

^ - reliability of data from group I to group III (^ - P<0.001)

Analyzing the vitamin D content, we obtained some differences according to gender. Thus, vitamin D deficiency was observed in 38(64.4%) boys and 31(66.0%) girls of the main group, and 7(5%) boys and 6(37.5%) girls of the control group, vitamin D insufficiency was observed in 14(23.7%) boys and 9(19.14%) girls of the main group of children with overweight and obesity and 5(35.7%) boys and 6(37.5%) girls of the control group, 5%) girls of the control group, normal vitamin

D levels were observed in 7(11.9%) boys and 7(15%) girls of the main group, and it should be noted that there were no children from group 3, in which normal vitamin D levels were not observed (Table 22).

Table 22.

Frequency of occurrence of different degrees of vitamin D sufficiency in children of the compared groups depending on gender

	Main groups children n=106		Control group n=30	
	Boys n=59	Girls n=47	Boys n=14	Girls n=16
Vitamin D ≥30 ng/mL.	7 (11.9)	7 (15.0)	2 (14.3)	4 (25.0)
Vitamin D 21-30 ng/mL	14 (23.7)	9 (19.14)	5 (35.7)	6 (37.5)
Vitamin D <20 ng/mL	38 (64.4)	31 (66.0)*	7 (50)	6 (37.5)

Note: * - reliability between girls of the main and control groups (*- P<0.05)

It should be noted that all differences regarding boys to girls, boys to boys and girls to girls from the main and control groups were not statistically different. Thus, vitamin D deficiency was observed more in boys in the main study group, whereas no gender differences were found in the control group.

Studying vitamin D status depending on the stage of pubertal development revealed that the number of children with different variants of vitamin D status was statistically significantly different between the group of children and adolescents with obesity and overweight and prepubertal development (Tanner 0-I) and the group of children with the same weight pathology in whom puberty has started (Tanner II-V) (Table 23).

It was determined that significant Vitamin D deficiency was predominantly in pubertal age children - 38 children (77.5%) and only 32 (56.14%) pre-pubertal children and adolescents had significant Vitamin D deficiency, which was statistically significantly true (p<0.05). Vitamin D insufficiency was found

statistically significantly more often in the group of prepubertal children in 17 children (29.8%) and 7 adolescents (14.3%), correspondingly in children in puberty ($p<0.05$), and normal vitamin D supply occurred mainly in 8 (14.3%) prepubertal children (4 adolescents 8.16%; $p>0.05$).

Table 23.

Frequency of occurrence of different degrees of vitamin D sufficiency in children of the main groups and control groups depending on the stage of pubertal development

Vitamin D level	Main groups children n=106		Control group n=30	
	Prepuberty n=57	Puberty n=49	Prepuberty n=10	Puberty n=20
Vitamin D ≥30 ng/mL.	8 (14.03)	4 (8.16)	3 (30)	3 (15)
Vitamin D 21-30 ng/mL	17 (29.8)*	7 (14.3)	5 (50)	7 (35)
Vitamin D <20 ng/mL	32 (56.14)^	38 (77.5)*°	2 (20)	10 (50)

Note: * - reliability between subgroups of the main group (* - $P<0.05$)

^ - reliability of prepubertal stage of the main and control groups (° - $P<0.05$)

° - reliability of puberty of the main and control groups (^ - $P<0.05$)

Determination of serum PTH levels in children of the studied groups revealed that the level of this hormone varied widely both in the main group and in the control group. At the same time, the average level of this hormone did not exceed the reference values in all study groups.

Thus, the average PTH level in the group of children and adolescents with III degree obesity was 47.00±1.95 pg/mL, which was statistically significantly higher compared with all groups: with the group of children with obesity I-II degree (36.36±2.1; $p<0.0001$), with the group of overweight children (36.00±2.40; $p<0.0001$), and the control group (28.9±2.75; $p<0.0001$) this fact indicates the

predominance of the main body of children with vitamin D deficiency in this group (Table 24)

Studying the state of phosphorus-calcium metabolism revealed that the level of total Ca in serum remained within the reference values in all observation groups (2.17±0.04 mmol/l in group I; 2.16±0.03 mmol/l in group II; 2.18±0.05 mmol/l in group III) and in control (2.11±0.04), i.e. no significant differences depending on BMI were found (p>0.05).

Table 24

Biochemical indexes of blood and urine, PTH level in children of the compared groups

	Group I n= 39	Group II n= 41	Group III n= 26	Control group n= 30
PTH; pg/mL	36.00±2.40^	36.36±2.14°	46.98±1.95*	28.73±2.67
Serum Ca; mmol/L	2.17±0.04	2.16±0.03	2.18±0.05	2.11±0.04
Serum P; mmol/L	1.04±0.04	1.06±0.04	0.95±0.04*	1.14±0.05
Serum alkaline phosphatase; U/L	216.65±12.9	204.51±11.82	196.33±13.9	197.57±11.80
Morning urine Ca; mmol/L	1.88±0.10^	2.27±0.13°	2.98±0.06*	1.54±0.10
Morning urine P; mmol/L	38.74±3.38^	48.24±3.32	55.19±3.46*	32.5±3.51
Urine creatinine	67.43±4.06^	65.46±3.53°	90.7±4.19*	52.40±3.97
CCR	0.30±0.02	0.36±0.02	0.34±0.01	0.32±0.02

Note: * - reliability of control group to group III (* - P<0.0001)

^ - reliability of data from group I to group III (^ - P<0.0001)

° - reliability of data of group II to group III (° - P<0.0001)

The blood phosphorus index was also within the reference values (1.04±0.04 mmol/l in group I; 1.06±0.04 mmol/l in group II; 0.95±0.04 mmol/l in group 3), not

differing significantly from each other, with only the index of children with normal body weight (1.14±0.05 mmol/l) showing a significant difference in relation to children with III grade of obesity ($p<0.001$), plasma calcium and phosphorus values are presented in Table 24.

To accurately characterize phosphorus-calcium metabolism, we studied morning Ca excretion with urine in children and adolescents of the studied groups. At the same time, all groups had calcium levels within the normal range (with the norm of 1.2-6.25 mmol/L), but the highest values were observed in the group of BMI ≥+ 3 SDS to 2.98±0.06 mmol/L, which was significantly higher compared with the group of children with I and II degree of obesity (2.27±0.13 mmol/L; $p<0.000$), overweight 1.89±0.10 mmol/L; $p<0.000$, with the control group 1.54±0.10 mmol/L; $p<0.000$. This fact is associated with a higher activity of PTH stimulating bone resorption with Ca leaching into the general circulation with increased urinary calcium excretion.

Determining calcium in morning urine does not always give the most accurate result. To increase the reliability of the results, there is an analysis that examines the level of calcium in the urine but adjusted for the level of urine creatinine, the so-called calcium-creatinine ratio (CCR). The urine creatinine level is a relatively constant value, this allows to smooth out the errors detected by daily variations in the concentration of urine and trace elements in it.

When determining the CCR, it was revealed that in all groups it remained within the normal range (0.30±0.02 in group I; 0.36±0.02 in group II; 0.34±0.01 in group III), not significantly differing from each other ($p>0.05$), indicating that there was no calcium-phosphorus metabolism pathology. Therefore, the CCR index related to bone resorption indicators remained within the normal range in all observation groups.

The level of total alkaline phosphatase in the sampling of patients according to the study groups also did not exceed the reference values (216,65±12,9 U/L in group I; 204,51±11,82 U/L in group II; 196,33±13,9 U/L in group III), no special differences depending on the grade of obesity were determined. We associated

relatively high levels of alkaline phosphatase in serum with acceleration of bone tissue formation and activation of its resorption.

Table 25.

Biochemical indexes of blood and urine, PTH level in children of the main groups and control group depending on gender

Factors	Main groups children n=106		Control group n=30	
	Boys n=59	Girls n=47	Boys n=14	Girls n=16
PTH; pg/mL	39.45±1.80	38.42±2.13^	31.64±4.27	26.18±3.32
Serum Ca; mmol/L	2.17±0.03	2.17±0.03	2.05±0.07	2.15±0.06
Serum P; mmol/L	1.00±0.03	1.04±0.03	1.20±0.07	1.10±0.07
Serum alkaline phosphatase; U/L	209.58±9.90	205.22±11.09	214.32±15.11	182.90±17.35
Morning urine Ca; mmol/L	2.34±0.10*	2.27±0.11^	1.56±0.15	1.53±0.13
Morning urine P; mmol/L	44.28±2.59*	49.65±3.34^	33.14±4.92	31.93±5.12
Urine creatinine	72.54±3.30*	72.39±3.84^	51.80±6.48	52.93±5.02
CCR	0.342±0.01	0.326±0.021	0.335±0.04	0.308±0.03

Note:

- reliability between boys of the main and control groups (- $P<0.05$)

^ - reliability between girls of the main and control groups (^ - $P<0.05$)

According to the study design we analyzed the level of indicators of phosphorus-calcium metabolism depending on gender, as can be seen in Table 25, there were no significant differences in all biochemical indicators of blood and urine, as well as the level of PTH hormone, the only significant difference was the level of PTH between the girls of the main (38.42±2.13 pg/mL) and control groups

(26.18±3.32 pg/mL), and the level of this hormone in the group of girls with high body weight was statistically higher ($p<0.05$).

There were also differences between girls and boys of the main and control groups regarding urine calcium and creatinine, which were significantly higher in children and adolescents of the main group ($p<0.05$ and $p<0.05$), but the calcium-creatinine index characterizing true calcium excretion remained within the normal range and did not differ significantly from the control ($p>0.05$) (Table 26).

Table 26

Average biochemical indexes of blood and urine, PTH level in children of the main groups and controls depending on the stage of pubertal development

	Main groups children N=106		Control group N=30	
	Prepuberty N=57	Puberty N=49	Prepuberty N=10	Puberty N=20
PTH; pg/mL	36.45±1.90	42.0±1.90*	20.5±4.17	32.85±3.08*
Serum Ca; mmol/L	2.14±0.03	2.20±0.03	2.25±0.05	2.037±0.06
Serum P; mmol/L	1.10±0.03	0.93±0.03	1.27±0.06	1.08±0.07
Serum alkaline phosphatase; U/L	199.92±9.94	215.16±10.80	192.00±22.44	200.35±14.08
Morning urine Ca; mmol/L	2.15±0.10^	2.48±0.10°	1.33±0.16	1.64±0.12
Morning urine P; mmol/L	40.73±2.57	53.10±3.06	26.4±6.35	35.55±4.14
Urine creatinine	69.19±3.14	76.10±3.87	48.5±5.26	54.35±5.38
CCR	0.318±0.018	0.351±0.02	0.276±0.02	0.343±0.03

Note: * - reliability between subgroups of the main group (* - $P<0.05$)

^- reliability between prepuberty of the main and control groups (^ - $P<0.01$)

° - reliability between puberty of the main and control groups

(° - P<0.01)

Analyzing the dependence of the PTH index on the stage of puberty onset, it was revealed that in children in the prepubertal stage (Tanner 0-I) the level of PTH was 36.45±1.90 pg/mL, which was significantly higher than in the pubertal stage (Tanner II-V) - 42.0±1.90 pg/mL ($p<0.05$). In children of the control group, this parameter was distributed similarly, PTH level was significantly higher in puberty stage 32.85±3.08 pg/mL (20.5±4.17pg/mL in prepuberty stage ($p<0.05$) (Table 26).

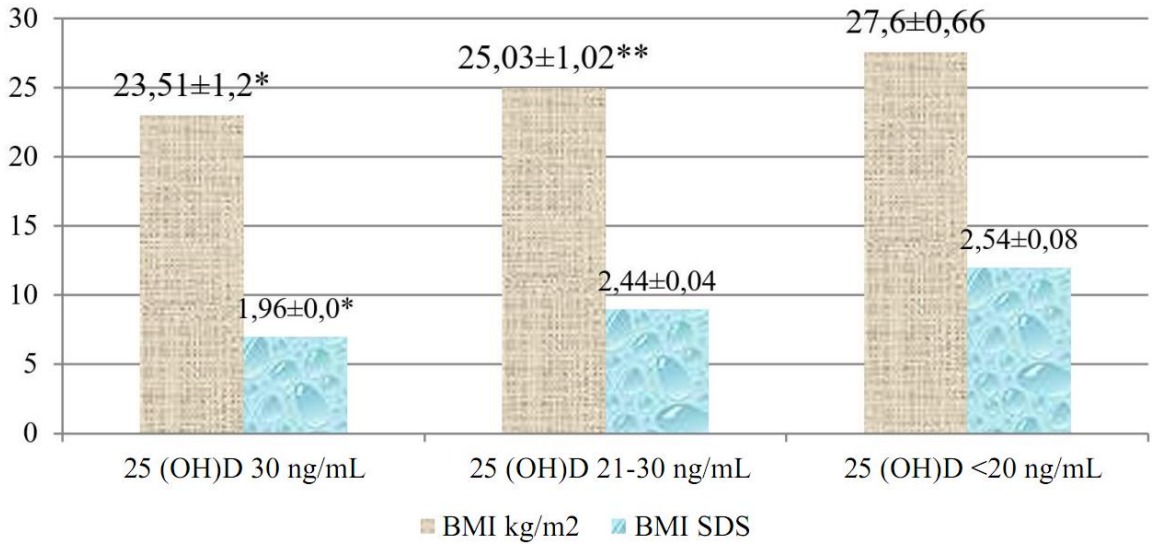
After assessment of vitamin D status, we analyzed the correlation of individual biochemical markers of carbohydrate and lipid metabolism, bone metabolism depending on the body's vitamin D supply, as well as the correlation with anthropometric data and peculiarities of anamnesis of obese children.

Comparing the median anthropometric, biochemical parameters, the following features were found (Table 27).

It was revealed that the group of children with vitamin D deficiency had the highest BMI (27.6±0.66), which was significantly increased in children of this group both in comparison with the group with normal vitamin D level (23.51±1.2; $p<0.001$) and with children with vitamin D deficiency (25.03±1.02; $p<0.05$). Correspondingly, the standard deviation of BMI scores (Z-score -SDS) also had statistically higher data in the group of children with vitamin D deficiency (2.54±0.08; $p<0.01$), compared to the group with normal micronutrient levels.

Among the indicators of carbohydrate metabolism, fasting glucose was of particular importance in statistical differences between groups with different vitamin D status, with increased levels corresponding to decreased vitamin D levels ($p<0.000$ compared with normal vitamin D levels, and $p<0.000$ compared with the vitamin D deficiency group) and the IR $HOMA_R$ ($p<0.001$ compared with normal vitamin D levels, and $p<0.05$ compared with the vitamin D deficiency group). Statistically significant differences were observed in measures of lipid metabolism, but the difference was observed only between deficient and normal vitamin D levels.

Almost all indexes of phosphorus-calcium metabolism showed a progressive deterioration of indicators depending on the level of vitamin D in serum.



(*p<0.001 between groups with deficient and normal 25(OH)D levels,
** p<0.05 between groups with deficient and normal 25(OH)D levels

Fig. 6. Average BMI and BMI SDS levels according to Vitamin D levels

The previous chapter showed that PTH levels in comparison group children were within the physiologic norm. Analysis of the results revealed statistically significant differences depending on BMI, higher levels of this hormone in the pubertal period were also revealed. Thus, PTH activity, despite the reference values of average values, statistically increased affected by decrease in the level of 25(OH)D. The highest activity of this hormone was observed in vitamin D deficiency (45.92±1.26 pg/mL), which was significantly higher than in children with normal vitamin D levels (22.00±3.51 pg/mL; p<0.000) and in children with vitamin D deficiency (27.11±1.9 pg/mL; p<0.000). No cases of increased PTH level in children affected by reduced vitamin D supply have been revealed.

Serum calcium and phosphorus levels, alkaline phosphatase excretion of urine calcium and phosphorus also had the highest statistically high levels in micronutrient deficiency.

Table 27.

Average levels of metabolic indexes depending on vitamin D status

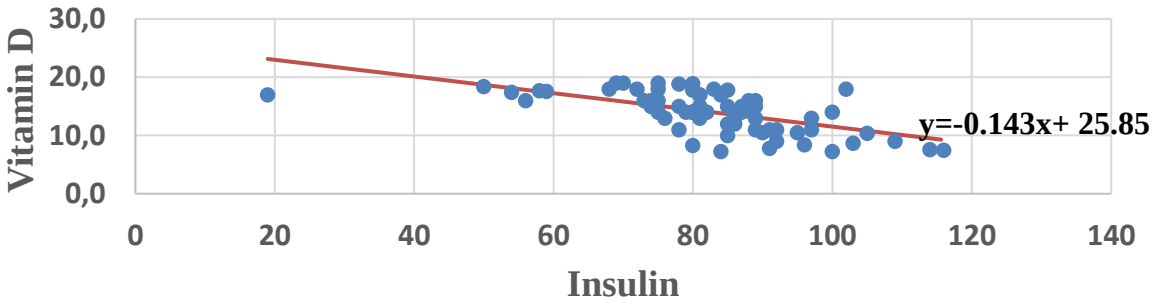
Factors	Vitamin D ≥30 ng/mL.	Vitamin D 21-30 ng/mL	Vitamin D <20 ng/mL
Fasting glucose; mmol/L	4.59±0.18***	4.61±0.11^^	5.28±0.10
Глюкоза через 120' после нагрузки	7.16±0.16	7.00±0.09	7.40±0.13
Glycated hemoglobin (HbA1c ;%)	4.72±0.27**	5.15±0.18	5.44±0.11
Insulin (pmol/L)	29.16±8.02**	45.07±5.48	53.80±4.1
IR HOMA $_R$ (RU)	0.91±0.31**	1.29±0.16^	1.96±0.17
Triglycerides; mmol/L	0.83±0.18*	0.98±0.07	1.21±0.06
Total cholesterol; mmol/L	3.43±0.30*	3.81±0.21	4.2±0.17
HDL-C; mmol/L	1.24±0.07	1.14±0.03	1.13±0.02
LDL-C; mmol/L	2.87±0.35*	3.18±0.21	3.64±0.16
PTH; pg/mL	22.00±3.51***	27.11±1.9^^	45.92±1.26
Serum Ca; mmol/L	2.17±0.08	1.99±0.04^^	2.24±0.03
Serum P; mmol/L	1.32±0.05***	1.25±0.04^^	0.89±0.02
Serum alkaline phosphatase; U/L	154.13±13.37***	163.37±10.02^^	230.71±9.07
Morning urine Ca; mmol/L	1.04±0.04***	1.7±0.16^^	2.71±0.04
Morning urine P; mmol/L	14.8±1.58***	29.03±2.5^^	57.44±1.85
Urine creatinine	45.9±5.9**	67.53±4.8	77.97±2.87
CCR	0.27±0.05	0.25±0.01	0.37±0.01

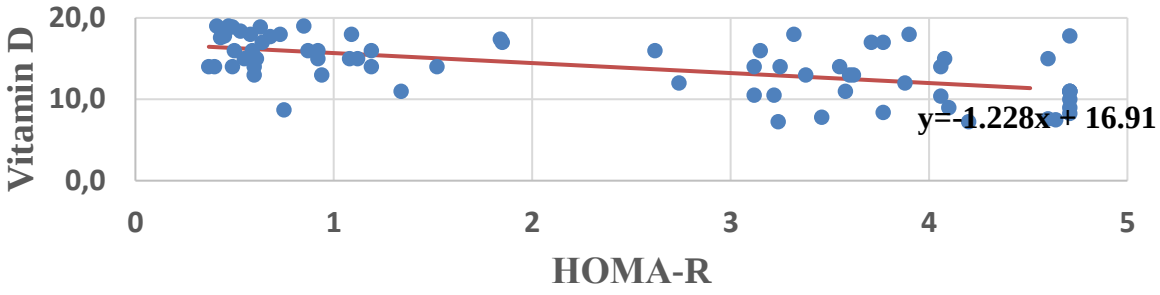
Note: * between vitamin D deficient and normal groups,

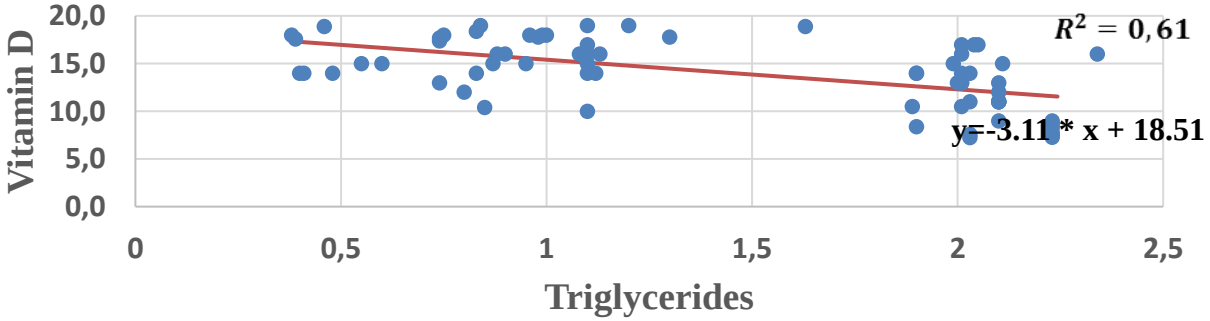
* p<0.05;** p<0.01; ***p<0.0000

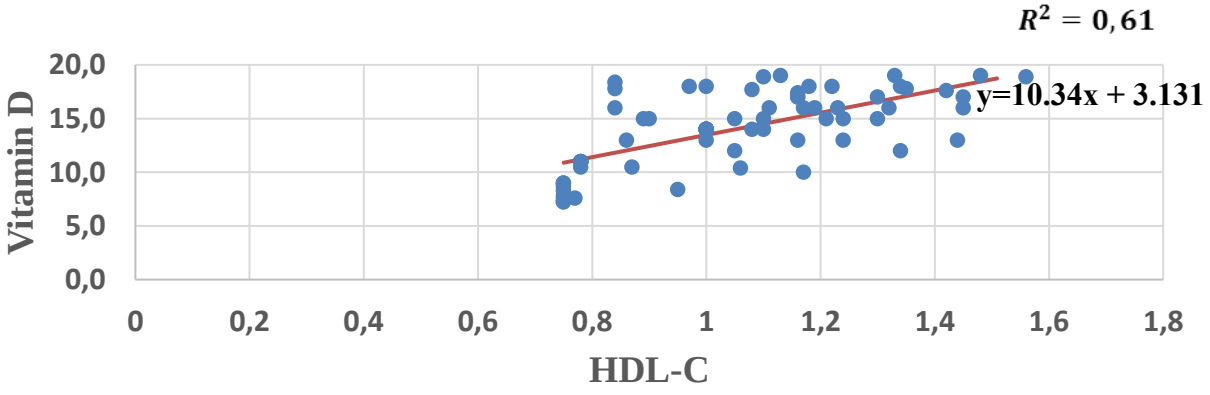
^ between vitamin D deficient and insufficient groups:

^ p<0.05;^^ p<0.0000









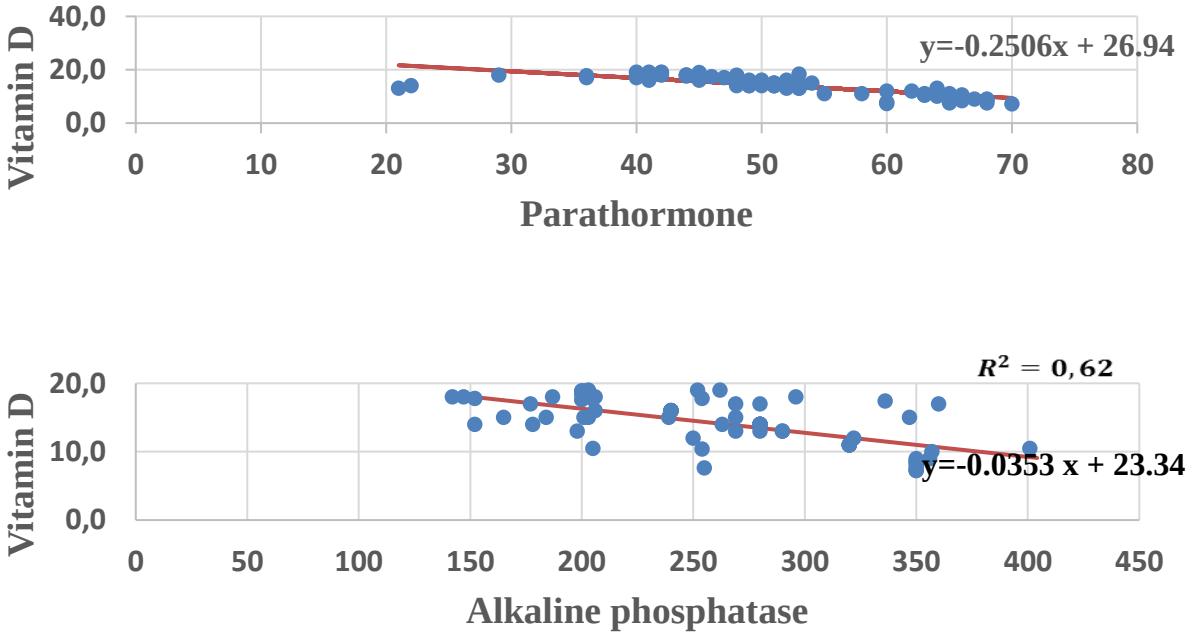
Note: R² - value of approximation reliability.

Fig. 7. Correlation graph between vitamin D level and carbohydrate and lipid metabolism indexes

Correlation analysis in the group of children with III grade of obesity revealed the closest correlations between vitamin D and with other metabolic indexes. Correlation interrelations with trend line construction, determination of reliability of vitamin D level approximation with lipid, carbohydrate and phosphorus-calcium metabolism indexes were revealed that the level of immunoreactive insulin (r=-0.6; R2=0.64) and IR HOMA $_R$ significantly increased with decreasing of 25(OH)D concentration in serum (r=-0.6; R2=0.63). (r=-0.6; R2=0.63), blood triglycerides (r=-0.6; R2=0.61), HDL-C level decreased (r=0.7; R2=0.64).

From indexes of phosphorus-calcium metabolism, the closest inverse relationship was between vitamin D and PTH activity (r=-0.8; R2=0.62), and alkaline phosphatase activity (r=-0.7; R2=0.62).

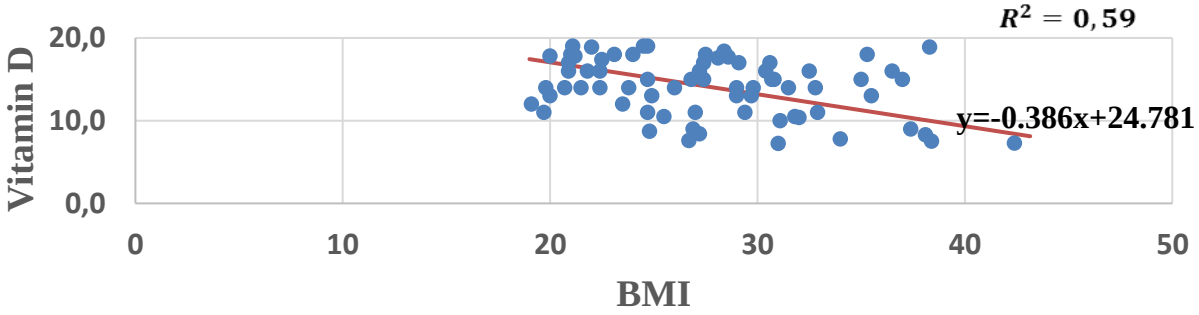
At the same time, the degree of 25(OH)D level reduction correlates with the severity of obesity; an inverse correlation between serum 25(OH)D level and BMI was found (r=-0.6; R2=0.59).



Note: R^2 - value of approximation reliability.

Fig. 8. Correlation graph between vitamin D level and PTH, alkaline phosphatase activity

Thus, when revealing interrelations with lipid, carbohydrate metabolism and phosphorus-calcium metabolism, it was revealed that with a decrease in serum 25(OH)D concentration, blood glucose, immunoreactive insulin and IR HOMA $_R$ increased significantly. Blood triglycerides were most closely correlated with lipid metabolism. From the indexes of phosphorus-calcium metabolism the closest high negative correlation was between vitamin D and PTH activity. These changes indicate that vitamin D deficiency in children 8-10 years of age is a risk factor for cardiometabolic disorders in older age.



Note: R² - value of approximation reliability.

Fig. 9. Correlation graph between vitamin D levels and BMI

Concluding this subchapter it should be noted that obese children have low vitamin D concentrations, corresponding predominantly to the deficiency level, which is consistent with the data of other studies [33: p. 57-64] and indicates the relevance of the problem of vitamin D deficiency in obesity. The degree of 25(OH)D level reduction correlates with the severity of obesity (the higher the degree of obesity, the lower the vitamin D level); a negative correlation between serum 25(OH)D level and BMI was found. The result confirmed the literature that the obesity increases the probability of developing vitamin D deficiency [33: p. 57-64].

CONCLUSION

Obese children represent a special risk group for vitamin D insufficiency and deficiency, which in recent years has been correlated with the same health risks corresponding to obesity. In turn, the pathogenetic role of vitamin D in the formation of obesity and the effect of adipose tissue on its metabolism are mutually determined processes It should be noted that there are no studies concerning the peculiarities of carbohydrate and lipid metabolism in correlation with phosphorus-calcium metabolism affected by disturbed vitamin D status in obese children, therefore the aim was set: to study the peculiarities of metabolic and osteopenic disorders formation at vitamin D deficiency affected by obesity in school-age children.

To achieve the goals and objectives set in the work 106 children with primary exogenous constitutional obesity and overweight (main group) living in Samarkand region at the age from 7 to 17 children (11,20± 0,25 years) were studied, with boys were 59 children (55,6%) and girls 47 children (44,4%).

The diagnosis of obesity was established according to WHO guidelines. If obesity was diagnosed, its degree was determined according to the classification of V.A. Peterkova et al. 2014.

The control group consisted of 30 children of similar age (mean 12.00±0.34 years) with normal body weight (BMI less than +1 SDS for the given sex and age), where boys were 14 children (46.7%) and girls 16 (53.3%).

The main group of overweight and obese children and the control group were comparable in age ($p>0.05$) and gender ($p>0.05$).

All children of the main group were divided into 3 groups in accordance with the set tasks: Group I - 39 children had BMI +1,0 to +2,0 SDS, i.e. children had BMI characterizing excessive body weight; Group II - 41 children included children with BMI >+2<+3 SDS, which corresponded to the I-II obesity group; Group III - 26 children with BMI ≥+3 SDS, which corresponded to the III obesity group and above. The presented data characterize reliable differences in body weight in the studied groups, while age, gender separation, had no statistical differences.

General clinical, instrumental, biochemical, immunoenzymometric and statistical methods were applied during the study.

Anamnestic data showed that the frequency of obese mothers and fathers was progressively related to the degree of obesity in the children, with the number of obese mothers and fathers in children with grade 3 obesity being 2/3 each, and the frequency of both obese parents being ½. Diabetes occurred with significant frequency in fathers of both children with grade I-II obesity and fathers of children with grade III obesity. There was no significant difference in obesity-related pathology such as hypertension, coronary heart disease in the first and second degree of kinship.

At present, the risk factor for the development of obesity is the state of health of the child in the fetal period, which is characterized by high plasticity of metabolism, the ability to adapt all metabolic systems of the body to environmental factors. In our study, in the group of children with severe obesity, both children born with body weight above 4000 g (50%) and children born with body weight less than 2500 g (42.3%) were observed.

We were interested in studying the life history of children on vitamin D intake in the first and subsequent years of life. Questioning parents of obese children and processing data from children's outpatient records revealed that both the control group and the main groups of children had a very low frequency of continuous vitamin D intake during the first year of life in the prophylactic dose, with only 7.7% of group III taking vitamin D for more than 6 months, which was significantly lower compared with the control ($p<0.02$) and group I ($p<0.05$). The data obtained indicated that in all groups with different body weight there were cases of insufficient vitamin D intake, short duration of vitamin D intake or no vitamin D intake including in the control group. According to parents, 1/5 children in the group with III grade of obesity were diagnosed with rickets with the main symptoms of baldness of the back of the head, softening of the edges of the fontanel, in rare cases, according to the mother, there was "valgus" or "varus" curvature of the limbs, all of them were treated with a therapeutic dose of this vitamin. It should be noted that the

frequency of appearance of these phenomena did not differ significantly between the comparison groups and the control and amounted from 1/5 to 1/6 cases in each group.

According to different researchers, the age of obesity manifestation is of great importance in the increase of body weight and the development of early complications of obesity. In our study, the average age of onset of weight gain in children with III grade of obesity was before 3 years of life, i.e. during early childhood, with this indicator accounting for ¾ of cases. Comparative analysis of the frequency of manifestation of obesity in the study groups at an early age indicates a high degree of reliability of this factor in the occurrence of this pathology. This also allows the inclusion of this fact in predictors of obesity.

Given the undoubted role of alimentary causes in the development of obesity and vitamin D deficiency states, the study evaluated the nature of nutrition. According to our data, in the diets of the examined children with high frequency were present sweets, excessive amount of flour products, potatoes, fried fatty dishes of local cuisine. At the same time, the frequency of low-calorie vegetables and fruits in the diets of children of the compared groups was only 1/5 in the overweight and obese groups and 1/3 in the control group, indicating a deficit in the regular intake of fresh vegetables and fruits. Consumption of milk and milk products (which are the main sources of calcium for children, was observed in only 23.0% in group I, 24.3% in group II and 27.0% in group III. It was found that obese children from 7 to 17 years old consumed on average only 160.12±13.07 ml of milk and/or milk products per day, which is insufficient to obtain the daily dose of calcium.

Clinical and anamnestic analysis showed that the majority of children aged 7 to 17 years, being in the period of intensive growth due to improper nutrition, dietary calcium deficiency, and adynamia, already had clinical signs of changes in the musculoskeletal system. In addition, it was found that 1/10 obese patients had bone fractures of which recurrent fractures occurred in 4.8% and 7.6%, respectively. There were also cases of fractures in children with normal body weight in 2 children (6.7%). The somatoscopic assessment of the musculoskeletal system of school

children revealed that obese children had pathologic types of posture, mainly slouching, combined disorders and scoliotic posture, in the presence of which the diagnosis of “Scoliosis” was made. Plantogram analysis revealed Platypodia in 1/3 of children in all observed groups.

In the determination of metabolic status of children, carbohydrate and lipid metabolism were evaluated. It was found that the degree of frequency of carbohydrate metabolism disorders had a close correlation with BMI. At the same time in the general structure of examined children carbohydrate metabolism disorders in the general group of children with overweight and obesity were found in 47,16%, in 1/10 children of the main group there was pathology in four parameters of carbohydrate metabolism, which formed a risk group for the development of type II diabetes in this group of children. Analyzing the state of fat metabolism in children and adolescents depending on SDS BMI revealed that lipid metabolism disorders occurred in 38.6% of patients.

Carbohydrate metabolism disorder was found in all groups with body weight exceeding the normative values, with a significant, reliable frequency in the group with III grade of obesity and higher, there was a higher frequency of fasting hyperglycemia ($P<0.001$), impaired glucose tolerance ($P<0.001$), high glycated hemoglobin (>7.5%) ($P<0.01$), hyperinsulinemia ($P<0.001$) and increased IR $HOMA_R$ ($P<0.001$) compared with group I and control group.

The frequency of triglyceridemia was correlated with body weight of obese children, progressively significantly increasing according to BMI ($P<0.01$-III group to I group; $P<0.05$ group III to group II), the same pattern was observed regarding high LDL-C levels ($P<0.01$-III group to group I; $P<0.05$ group III to group II), and decreasing HDL-C levels ($P<0.01$-III group to group I; $P<0.02$ group III to group II). Characterization of the average level of blood carbohydrate and lipid indexes in the observation groups showed that all values did not exceed the reference values but statistically differed from each other and increased with increasing body weight.

Identification of gender differences in the level of lipid metabolism revealed that boys, regardless of the observation group, had a higher frequency of pathology

compared to girls, hypertriglyceridemia ($p<0.01$ compared to girls); high level of LDL-C ($p<0.05$), which is evidence of a high risk of atherogenic disorders in males compared to females. At the same time, the indicators of carbohydrate metabolism were not statistically significantly different between the genders.

Analyzing the level of lipid metabolism indexes depending on sexual maturation revealed that in puberty stage there were significant changes in lipid metabolism indexes, which represented a higher frequency of observations compared to prepuberty: hypertriglyceridemia ($p<0.05$), increased LDL-C ($p<0.02$) and decreased HDL-C ($p<0.01$).

The frequency of carbohydrate metabolism disorders according to the stage of sexual maturation indicated that high fasting glucose (48%), hyperinsulinemia (46.9%) and especially impaired glucose tolerance (53.06%) were significantly more common in pubertal children compared to prepubertal children. And the difference was significant between the level of fasting hyperglycemia ($p<0.001$), impaired glucose tolerance ($p<0.001$), and high IR $HOMA_R$ ($p<0.001$).

Vitamin D status was studied in children with obesity of different degrees and children with normal body weight, all children were residents of Samarkand region. The results indicated that insufficiency and deficiency of vitamin D has a wide distribution among children of all ages, at the same time, this frequency of these pathological conditions was dependent on body weight.

Comparative analysis revealed that in the groups of children with overweight and obesity of varying severity there was a predominance of patients with vitamin D deficiency. Thus, in group 3 children vitamin D deficiency made up ¾ of cases (76.9%), the remaining ¼ of children - vitamin D insufficiency (23.%), while no cases of vitamin D levels within the normal range were observed. In the second group of children with obesity of 1-2 degree the state of vitamin D deficiency amounted to 2/3 of the number of observations (61%), while in children of this group there were cases of vitamin D level within reference values, which amounted to only 7.3%, with the frequency of deficiency in 31.7%. In the first observation group in overweight children the frequency distribution of occurrence of different vitamin D

levels were found with similarity to group 2: 61.5% deficiency, 23% insufficiency, 15.4% normal vitamin D levels ($p<0.01$). In the control group, the frequency of vitamin deficient children was more than 1/3 (43.3%), and this rate did not differ from the frequency of vitamin D deficient children in group 1, the confidence limits were only in comparison with obese children in group 2 ($p<0.05$) and group 3 ($p<0.01$). The frequency of vitamin D insufficiency (30%) and normal levels (26.7%) were almost equally distributed, each accounting for 1/3 of the total number of healthy children. The obtained data indicates that in the group of children with normal body weight who are in health group I-II, vitamin D deficiency and insufficiency are also found at a high level, which requires the application of therapeutic and prophylactic measures even in the group of healthy children.

Determining the average level of vitamin D, in children of the general group (n= 106) the median was 19.80±0.98 ng/ml, which characterized the deficiency of this indicator in the body, while in children with normal body weight (n= 30) the median values were slightly higher, within the lower limit of insufficiency 23.29±1.47 ng/ml was significantly lower compared with children of the main group ($P<0.02$). Determining the mean level of vitamin D in groups of obese and overweight children, depending on the degree of vitamin D deficiency revealed that the median vitamin D level in all groups was not statistically different, the confidence limits had a level of vitamin D deficiency in all groups of observation.

Therefore, comparing the obtained results it was revealed that the predominant number of examined children living in Samarkand region had vitamin D insufficiency and deficiency.

Determination of serum PTH levels in children of the studied groups revealed that the level of this hormone varied widely both in the main group and in the control group. At the same time, the average levels of this hormone did not exceed the reference values in all study groups. Thus, the mean PTH level in the group of children and adolescents with 3 degree obesity was 47.00±1.95pg/mL, which was statistically significantly higher compared to all the compared groups.

Studying the state of phosphorus-calcium metabolism revealed that the level of total Ca in blood serum remained within the reference values in all observation groups and in the control group, i.e. there were no significant differences depending on the degree of BMI ($p>0.05$). Also the blood phosphorus indexes were within the reference values, not significantly different from each other, with only the index of children with normal body weight showing a significant difference compared to children with III grade of obesity ($p<0.001$).

To accurately characterize phosphorus-calcium metabolism, we studied morning Ca excretion with urine in children of the studied groups. At the same time, calcium levels within the normal range were observed in all groups, but the highest values were observed in group III BMI, which was significantly higher compared to the group of children with III grade of obesity ($p<0.001$), overweight ($p<0.001$), and control group ($p<0.001$). This fact is associated with a higher activity of PTH stimulating bone resorption with Ca leaching into the general circulation with increased urinary calcium excretion.

Determining calcium in morning urine does not always give the most accurate result. To increase the reliability of the results, there is an analysis that examines the level of calcium in the urine but adjusted for the level of urine creatinine, the so-called CCR. Determination of CCR revealed that it remained within the normal range in all groups, not significantly differing from each other ($p>0.05$), indicating that bone resorption indexes remained within the normal range in all observation groups. The level of total alkaline phosphatase in the sampling of patients according to the study groups also did not exceed the reference values, no special differences depending on the grade of obesity were determined. We associated relatively high levels of alkaline phosphatase in serum with acceleration of bone tissue formation and activation of its resorption.

Correlation interrelations with trend line construction, determination of reliability of vitamin D level approximation with lipid, carbohydrate and phosphorus-calcium metabolism indexes were revealed that the level of immunoreactive insulin ($r=-0.6$; $R2=0.64$) and IR HOMA $_R$ significantly increased

with decreasing of 25(OH)D concentration in serum (r=-0.6; R2=0.63). (r=-0.6; R2=0.63), blood triglycerides (r=-0.6; R2=0.61), HDL-C level decreased (r=0.7; R2=0.64). These changes indicate that vitamin D deficiency in children 7-17 years of age is a risk factor for cardiometabolic disorders in older age. From indexes of phosphorus-calcium metabolism, the closest inverse relationship was between vitamin D and PTH activity (r=-0.8; R2=0.62), and alkaline phosphatase activity (r=-0.7; R2=0.62

At the same time, the degree of 25(OH)D level reduction correlates with the severity of obesity; an inverse correlation between serum 25(OH)D level and BMI was found (r=-0.6; R2=0.59). The obtained result confirms the literature data that the obesity increases the probability of developing vitamin D deficiency. Therefore, obese children have a low concentration of vitamin D, corresponding predominantly to the level of deficiency, which is consistent with the data of other studies [33:p.57-64] and indicates the relevance of the problem of vitamin D deficiency in obesity.

Therefore, this work presents the substantiation and a new solution to the recent problem of modern pediatrics, which consists in studying the features of carbohydrate and lipid metabolism in correlation with phosphorus-calcium metabolism, related to impaired vitamin D status in obese children. As a result of the conducted research the following conclusions and practical recommendations were presented

CONCLUSIONS

1. In children with severe obesity there was a high frequency of musculoskeletal system damage in the form of posture disorders (27.0%) and flat feet (23.0%) affected by dietary calcium deficiency, with a low frequency of vitamin D intake during the first 6 months of life (7.7%) and early manifestation of obesity (73.0%) according to anamnesis.

2. In 47.16% of obese children there was observed pathology of carbohydrate metabolism and in 38.6% pathology of lipid metabolism, the frequency

and degree of disorders of which increased with increasing body weight, prevailed in boys, affected by puberty.

3. Low vitamin D sufficiency of school-age children regardless of body mass index was revealed, vitamin D levels depending on the degree of weight gain, the highest frequency of vitamin D deficiency (76.9%), changes in PTH activity and pathology of phosphorus-calcium metabolism in children with severe obesity.

4. There was determined a close inverse correlation between serum vitamin D level and immunoreactive insulin level (r=-0.6; R2=0.64), IR HOMAR (r=-0.6; R2=0.63), blood triglycerides (r=-0.6; R2=0.61), body mass index (r=-0.6; R2=0.59), PTH activity (r=-0.8; R2=0.62), alkaline phosphatase (r=-0.7; R2=0.62) and direct correlation with HDL-C (r=0.7; R2=0.64).

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