ASSESSMENT OF THE QUALITY OF LIFE OF CHILDREN AFTER PARATHYROIDECTOMY WITH PRIMARY HYPERPARATHYROIDSIS ACCORDING TO THE PAS TABLE (PARATHYROID ASSESSMENT OF SYMPTOMS SCORE) AND SF-36 QUESTIONNAIRE

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Abstract*. The article presents literature data on the frequency and structure of the causes of primary hyperparathyroidism. It is known that PHPT manifests itself in a multisymptomatic clinical picture, involving various organs and systems in the pathological process, which leads to a significant decrease in the quality of life, disability of patients, and an increased risk of premature death. This article highlights the value of the PAS chart and SF-36 questionnaire not only in terms of assessing long-term results of surgery, but also in terms of diagnosing early stages of PHPT.*

Keywords*: primary hyperparathyroidism; parathyroidectomy; table PAS; SF-36 questionnaire.*

Primary hyperparathyroidism is one of the most common diseases of the parathyroid gland. According to the World Health Organization (WHO), primary hyperparathyroidism is the third most common endocrine disease in the world after diabetes and thyroid disease." The incidence of primary hyperparathyroidism is observed in 1% of the adult population and 2% of the population over 55 years of age. In recent years, the incidence of primary hyperparathyroidism worldwide has increased 5-fold. According to medical statistics, in 30% of cases in families with primary hyperparathyroidism, the disease manifests itself in children. Epidemiological studies have shown that the rate of progression of primary hyperparathyroidism in children has increased from 23% to 62% over the past 10 years. Involvement of many organs and systems in the pathological process, a high risk of early death and disability in the pediatric population, regardless of the form of the disease, leads to a decrease in the quality of life. The main goal of treatment of primary hyperparathyroidism is to bring the quality of life of patients to the level of the healthy population. In this regard, the use of effective treatment methods and studying the quality of life of patients with primary hyperparathyroidism is relevant [1,2,3,7,9,10].

To date, a number of studies are being conducted aimed at early detection of the disease in children with primary hyperparathyroidism, prevention of complications and quality of life of patients. In particular, the quality of life of patients was studied in a number of international studies devoted to the problem of this disease in children, which made it possible to clearly describe and evaluate the serious impairments caused by the disease during the development of the disease and during the rehabilitation period. In studies by many scientists on primary hyperparathyroidism, the effectiveness of treatment was assessed by biochemical parameters and bone mineral density. However, the success of therapy and the speed of recovery of patients should be focused on eliminating the symptoms of the disease that worsened the patient's condition before parathyroidectomy. Therefore, monitoring indicators of the quality of life of patients in the

immediate and long-term period after treatment of primary hyperparathyroidism in children is of particular importance in a comprehensive assessment of treatment results [1,4, 8,11,12,13,18].

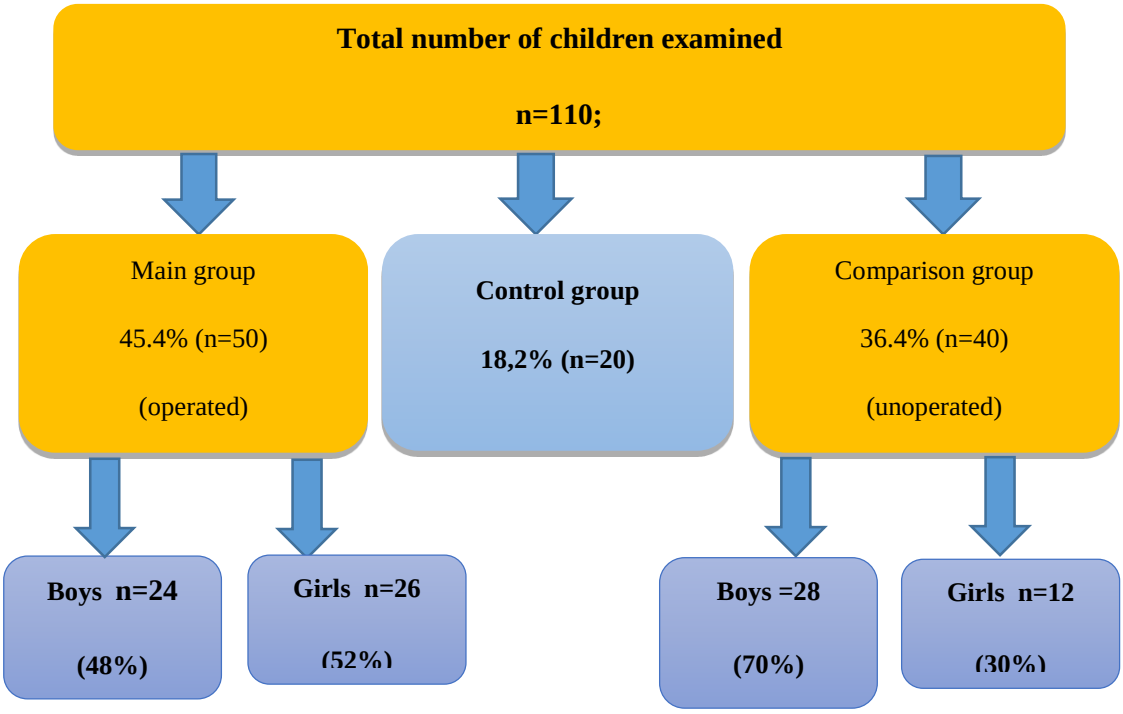
Various studies have been conducted on the diagnosis and treatment of primary hyperparathyroidism in children. According to the Russian community of endocrinologists and endocrine surgeons, surgical treatment of primary hyperparathyroidism in children is the only radical and effective method. The benefits of radical treatment of primary hyperparathyroidism have been proven - normalization of calcium levels in the blood, elimination of symptoms associated with hypercalcemia, restoration of renal and bone tissue. (Troshina V.V. et al., 2019). However, in many cases, the quality of life associated with the health of patients: physical, mental, emotional, social status remains without the attention of the doctor. For example, according to A.A. Novik, Watt Torquil (2006), when assessing the quality of life of patients, its discrepancy was 20-60% [5,6,14,15,25].

In studies conducted in children, after parathyroidectomy performed by an experienced surgeon, the success of treatment is 95-98%, complications after surgery occur in 1-2% (Demidova T.Yu., 2019). In studies by C. Harman et al (2017), despite successful parathyroidectomy in children, the development of relapse with pronounced clinical manifestations of the disease was noted; persistence and relapses of the disease were observed in 2-7% of cases. Therefore, the authors emphasize the need for long-term follow-up in primary hyperparathyroidism observed in children [16,17,19,20,21,22,28]. Other studies (Mihai R., 2008) have proven that after parathyroidectomy in patients, a number of symptoms described as parathyroid syndrome resolve. This prospective study examined the quality of life of 166 patients 12 months after parathyroidectomy. In a study examining the physical and mental functioning of operated patients based on the SF-36 questionnaire, positive results on quality of life were obtained. After parathyroidectomy, mental disorders are eliminated (Adler Yu.T., 2017), brain functions are restored, and symptoms such as depression and anxiety are eliminated (Pokhozhay V.V., 2018). However, most studies have been conducted in adult populations, and few studies have been conducted in children and adolescents.

In 1995 J.L. Pasieka and L.L. Parsons [8,23,24,27] were the first to propose a method for assessing the results of surgical treatment of PHPT using a visual analogue scale (VAS) from 0 to 100 (0 - no symptoms, 100 - severe symptoms) to measure 13 symptoms, specific for a given disease (weakness, bone pain, memory loss, etc.), and in 1998 the technique was validated. [18,22,25]. Later, as a result of a large multicenter study, the same specialists, based on the average VAS score, developed a scale for assessing symptoms for PHPT (Parathyroid Assessment of Symptoms score, PAS). According to the works of J.L. Pasieka and L.L. Parsons, the PAS scale allows you to obtain a reliable and valid assessment of symptoms characteristic of PTG pathology; this scale includes a number of indicators specific to PHPT: physical complaints (thirst, weakness, difficulty getting out of a chair or getting out of a car); emotional characteristics (mood lability, depression and irritability); pain syndrome (arthralgia, abdominal pain and headache); fatigue and memory loss (forgetfulness) [3,12,13,26]. Purpose of the study: to assess the quality of life of children after parathyroidectomy for PHPT using the PAS table and the SF-36 questionnaire.

Materials and methods: the source of the study were 90 sick children who applied to the RSNPMCE clinic in 2001-2016, who, based on the diagnosis of primary hyperparathyroidism, were treated in an inpatient setting and were under outpatient observation. At the first stage of the study, in order to study the frequency of occurrence of clinical forms and clinical manifestations

of primary hyperparathyroidism by appeal, a questionnaire was filled out for each examined child, which recorded anamnesis data, as well as clinical, laboratory and instrumental data. Surgical treatment (parathyroidectomy) was performed in 50 patients (main group), 40 patients (comparison group) were under outpatient observation (had contraindications to surgery, refused surgery). Patients in this group were recommended to reduce foods rich in calcium in their diet, drink 1.5-2 liters of fluid per day, and take vitamin D supplements in the required dose. The control group consisted of 20 healthy children without pathology of the thyroid and parathyroid glands. Inclusion criteria: children aged 3 to 15 years with a confirmed diagnosis of primary hyperparathyroidism. Exclusion criteria: children with severe somatic diseases, children under 3 years of age and over 15 years of age, patients with diabetes mellitus and severe renal failure. The duration of the study was 1-3-6 months in the near future and 1-5-10 years in the long term (Fig.-1).

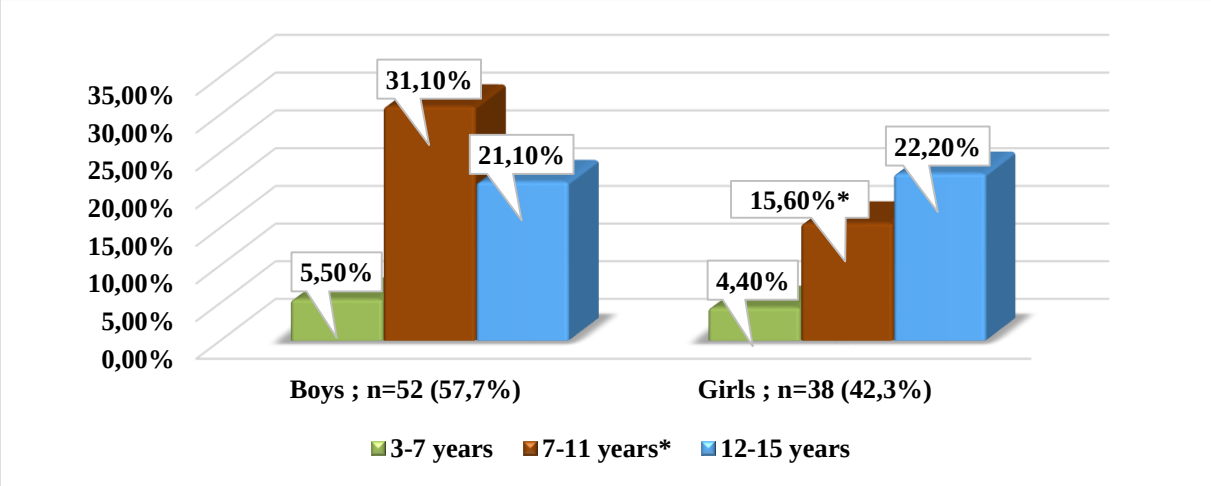


Rice. 1. Study design.

At the second stage of the study, all patients underwent ultrasound examination of the thyroid gland, parathyroid glands, and kidneys. The level of parathyroid hormone in the blood, vitamin 25(OH)-D, total and ionized calcium, phosphorus, alkaline phosphatase, and the level of calcium and phosphorus in the urine were determined. To study bone mineral density, radiography, echo-osteometry and X-ray densitometry were performed, parathyroid gland scintigraphy was performed to identify adenoma, and PAS and SF-36 questionnaires were used to assess parathyroid symptoms and quality of life.

Statistical analysis. The results obtained during the research were calculated on the basis of “Exel” arithmetic functions in the WINDOWS XP “Pentium-IV” Microsoft systems window.

Research results. All patients (n-90) were divided into age groups and the incidence of primary hyperparathyroidism among children of different ages was studied according to presentation. Primary hyperparathyroidism was reported in 57.7% (52) of boys and 42.3% (38) of girls. The ratio between boys and girls was 1.3:1 (Fig. 2.).



Note: * - p < 0.05 - the difference between the indicators of both groups is significant.

Rice. 2. Incidence of primary hyperparathyroidism among different age groups.

It was noted that primary hyperparathyroidism develops more often in boys (31.1%) than in girls (15.6%) of primary school age (7-11 years).

The duration of the disease was several years from the first clinical symptoms of hyperparathyroidism to diagnosis in the examined patients. One of the reasons for the underestimation of primary hyperparathyroidism is the lack of a system for its detection. In our study, the duration of the disease was 4-5 years in 53.3% of patients (Table 1).

Table No. 1.

Distribution of patients with primary hyperparathyroidism by disease duration

Duration of disease, years	Boys n=52	Girls n=38	Total
0-1	19	14	33
2-3	5	4	9
4-5	28	20	48

During the study, we identified a group of symptoms characteristic of the disease in children with primary hyperparathyroidism and analyzed the frequency of occurrence of clinical signs. Children with manifest primary hyperparathyroidism (87 patients) had delayed physical development in 72.4% (63), nephrolithiasis - 24.1% (21), bone deformation - 45.9% (40), pathological bone fractures - 28, 7% (25), pain in bones and joints – 71.2% (62); 47.1% (41) of patients had hair loss and 44.8% had brittle nails (39) (Table 2).

Table No. 2.

Frequency of clinical signs of primary hyperparathyroidism in children

Clinical signs	Nosological forms of primary hyperparathyroidism					
	Kidney form n=35		Bone form n=30		Mixed form n=22	
	abc	%	abc	%	abc	%
Polydipsia	26	74,2	11	36,3	9	40,2
Polyuria	24	68,5	13	43,3	8	36,3

Nephrolithiasis	16	45,7	-	-	5	22,7
Attacks of renal colic	31	88,5	-	-	6	27,3
Hair loss	13	37,1	19	63,3	9	40,9
Pain in bones and joints	25	71,4	26	86,6	11	50,1
Bone fractures	1	2,8	17	56,6	7	31,8
Bone deformity	1	2,8	27	90	12	54,5
Delayed physical development	24	68,5	25	83,3	14	63,6
Loose teeth	11	31,4	13	43,3	7	31,8
Brittle nails	7	20	23	76,6	9	45,4

In 26 patients with renal and mixed forms of the disease, the main and comparative groups revealed severe pathologies in renal function, including kidney anomalies in 5 (19.2%) patients, a “dry” kidney in 2 (7.6%), non-functioning kidney - in 2 (7.6%), single kidney (after nephrectomy) - in 3 (11.5%), nephrostomy was found in 3 (11.5%) patients. Chronic renal failure was registered in 11 (42.3%) patients. This, in turn, confirms the late diagnosis of the disease and the development of severe complications of urolithiasis in patients. The dynamics of symptoms of the disease according to the PAS questionnaire in primary hyperparathyroidism was analyzed. Clinical symptoms of the disease were determined on a scale from 0 to 100 (0 – absence, 100 – maximum level of disease symptoms). A value of 40–100 reflects a clear, strong expression of clinical signs. In patients of the main group, before parathyroidectomy, pronounced clinical signs were observed on almost all points. After the operation, a significant decrease in the clinical symptoms of the disease was found (fatigue, mood swings, joint pain, difficulty moving, weakness, headache, depression, bone pain). The stable effect persisted for 10 years (Table 3).

Table No. 3.

Indicators of parathyroid symptoms according to the PAS questionnaire before and after surgery in patients of the main group

Symptoms	Preoperative assessment n=50	After 3 months. after operation n=50	After 6 months. after operation n=50	After 12 months. after surgery n=50	10 years after surgery n=50
Bone pain	93,4±3,4	52,3±1,8 *	31,3±1,1 *	9,7±0,32 *	2,2±0,08 *
Fast fatiguability	98,7±1,8	45,7±1,5 *	28,7±0,92 *	11,3±0,38 *	0,8±0,03 *
Change of mood	95,3±3,3	37,2±1,3 *	20,2±0,69*	10,7±0,34*	1,9±0,06*

Depression	90,4±3,2	34,8±1,1*	19,8±0,62*	14,8±0,47*	0,9±0,04*
Stomach ache	87,2±2,9	42,2±1,4*	21,2±0,74*	15,4±0,51*	1,2±0,05*
Weakness	92,5±3,3	23,8±0,82*	12,6±0,42*	6,8±0,22*	1,9±0,07*
Irritable	78,3±2,6	31,3±1,0*	19,9±0,65*	12,9±0,42*	0,2±0,01*
Joint pain	94,8±3,5*	22,8±0,75*	10,2±0,36*	6,9±0,24*	0,9±0,03*
Memory loss	86,8±2,7	33,9±1,2 *	24,4±0,81*	9,8±0,33*	2,6±0,09*
Difficulty moving	94,8±3,2	23,8±0,94*	17,4±0,57*	10,9±0,36*	1,6±0,06*
Headache	96,3±3,6	34,7±1,2*	16,2±0,53*	10,1±0,33*	1,6±0,05*
Itchy skin	47,3±1,6	10,5±0,35*	7,3±0,24*	5,2±0,17*	1,3±0,04*
Thirst	66,7±2,3	23,8±0,83*	15,3±0,48*	10,7±0,35*	1,5±0,05*

Note: * - reliability of values compared with preoperative assessment (*** - P < 0.001).

In patients in the comparison group in the long-term period (10 years), there was a significant increase (p <0.05) in the average indicators of a number of symptoms of primary hyperparathyroidism (irritability, joint pain, difficulty moving, thirst, itching, headaches) (Table 4).

Table No. 4.

Indicators of parathyroid symptoms according to the PAS questionnaire in patients of the comparative group

Symptoms	During initial examination n=40	After 3 months. n=40	After 6 months. n=40	After 12 months. n=40	After 10 years n=40
Bone pain	96,5±1,7	97,7±1,4	95,7±1,8	98,4±1,1	97,6±1, 2
Fast fatiguability	97,2±1,6	98,5±0,9	97,7±1,2	98,3±1,4	97,5±1,3
Change of mood	98,4±1,7	97,8±0,8	97,2±0,1	96,8±1,2	97,1±1,5
Depression	97,6±1,2	98,3±0,9	96,8±1,8	96,6±1,6	97,5±1,8
Stomach ache	89,6±2,4	88,9±1,6	86,6±1,8	88,8±1,1	89,6±8,4
Weakness	91,5±2,3	93,7±0,8	92,6±1,3	91,6±5,3	92,2±7,8
Irritable	88,9±4,8	88,8±1,4	87,6±1,5	90,2±2,3	96,9±1,4*
Joint pain	91,2±1,3	96,4±0,8	96,4±1,7	97,9±1,4	98,1±1,3
Memory loss	89,8±3,8	91,2±2,9	90,4±2,4	93,5±3,2	96,8±1,8*
Difficulty moving	92,4±4,9	93,7±1,8	92,5±1,4	92,5±1,2	96,8±1,9*
Headache	92,7±3,2	94,3±1,8	93,5±6,2	94,7±1,3	98,3±1,4*
Itchy skin	65,8±5,3	66,8±4,8	65,7±4,3	72,8±3,8	81,3±4,3 *
Thirst	87,7±3,3	88,8±2,4	88,2±9,6	95,6±1,8	98,8±1,1*

Note: *- reliability of values compared to the assessment before the initial examination - *-p <0.05, **- p<0.005, ^ - p>0.05

The quality of life of patients in the main group was studied using the SF-36 questionnaire before and after treatment, in comparison with healthy respondents (control group) of the same age without parathyroid pathology and with normal phosphorus-calcium metabolism.

Table No. 5

Dynamics of quality of life indicators before and after treatment in patients of the main group

SF-36 Criteria	Control n=20	Before surgery n=50	After 3 months. after surgery n=50	After 6 months. after surgery n=50	After 12 months. after surgery n=50	10 years after surgery n=50
General health (General Health) Physical activity (Physical Functioning) Physical functioning (Role-Physical) Emotional activity (Role-Emotional) Social functioning (Social Functioning) Pain intensity (Bodily Pain)	98,4±3,4	16,8±0,54***	35,6±1,2***^^^	66,9±2,1***^^^	80,9±2,6***^^^	93,1±3,0^^^
	97,8±3,2	32,6±1,1***	47,8±1,5***^^^	69,7±2,3***^^^	80,3±2,5***^^^	93,7±3,1^^^
	96,3±3,1	30,1±0,95***	42,3±1,3***^^^	67,8±2,2***^^^	79,1±2,4***^^^	89,9±2,8^^^
	94,6±3,0	27,9±0,91***	44,7±1,4***^^^	58,6±1,8***^^^	61,6±1,9***^^^	79,8±2,6**^^^
	93,9±2,9	18,8±0,62***	36,7±1,1***^^^	59,1±1,9***^^^	68,5±2,3***^^^	78,9±2,5**^^^
	0,48±0,02	91,53±2,9***	26,4±0,86***^^^	11,2±0,36***^^^	5,22±0,17***^^^	0,45±0,01^^^
Viability	98,9±3,3	23,1±0,77***	46,7±1,6***^^^	61,8±1,9***^^^	79,9±2,5***^^^	95,7±3,1^^^
Mental health	99,2±3,4	66,3±2,2***	72,9±2,4***^	81,4±2,7***^^^	91,7±3,0***^^^	96,5±3,2^^^

Note: *-significance of differences compared to the control group (*-P<0.05; **-P<0.01; ***-P<0.001).

^- significance of differences compared with the indicators before surgery (^-P<0.05; ^^-P<0.01; ^^^-P<0.001)

Before treatment, it was noted that quality of life indicators (physical activity, general well-being, social functioning, vitality, mental health components) in the main group were lower compared to the control group. After 3 months, these indicators increased significantly, and by 10 years they were close to control. (Table 5). Patients in the comparison group had lower overall quality of life scores in all domains compared to the control group. A further decrease in quality of life indicators was observed in the immediate and long-term follow-up periods (Table 6). Thus, successful surgical treatment, along with normalization of the level of metabolism of the parathyroid glands, helps improve the quality of life of patients.

Table No. 6.

Dynamics of quality of life indicators in patients of the comparative group

SF-36 Criteria	Control n=20	At the initial examination; n=40	After 3 months. after treatment n=40	After 6 months. after treatment n=40	After 12 months. after treatment n=40	10 years after treatment n=40
General Health	98,4	17,8*	18,8*	17,6*	14,1*	11,1*
Physical Functioning	97,8	31,3*	32,3*	31,2*	30,8*	23,7*
Role-Physical	96,3	30,1*	33,1*	29,1*	28,7*	24,9*
Role-Emotional	94,6	28,9*	30,1*	27,9*	27,6*	25,8*
Social Functioning	93,9	19,8*	20,8*	19,7*	18,1*	13,9*
Bodily Pain	0,48	90,1*	89,1*	90,1*	93,2*	96,1*
Vitality	98,9	22,1*	23,3*	22,4*	20,1*	17,3*
Mental Health	99,2	64,3*	66,2*	64,7*	60,8*	56,8*

Note: *-significance of differences compared to the control group (*-P<0.05;

-P<0.01; *-P<0.001); reliability of the values compared to the assessment before the initial examination - (^-P<0.05; ^^-P<0.01; ^^-P<0.001).

CONCLUSIONS:

1. It has been established that the incidence of primary hyperparathyroidism in children according to referral rates is 57.7% in boys and 42.3% in girls. It was noted that primary hyperparathyroidism develops more in boys (31.1%) than in girls (15.6%) of primary school age (7-11 years). Late diagnosis led to an increase in the duration of the disease (4-5 years) in 53.3% of patients.

2. Clinical signs of PHPT in children are polysymptomatic, delayed physical development was noted in 72.4%, kidney stones in 24.1%, bone deformation in 45.9%, pathological bone fractures in 28.7%, pain in bones and joints in 71.2%, hair loss in 47.1%, brittle nails in 44.8% of patients.

3. Successful surgical treatment, along with normalization of the level of metabolism of the parathyroid glands, led to a positive increase in the quality of life of patients. The PAS and SF-36 questionnaires have shown their effectiveness as a reliable tool for the dynamic assessment of

patients with this disease, since they allow you to observe the actual symptoms of primary hyperparathyroidism after treatment, as well as carry out simple and rapid analysis.

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