



## Various Developmental Disorders in Adolescents in the Pilot Regions of the Republic of Uzbekistan, Identified by the Screening Method (Namangan, Jizzakh, Surkhandarya Regions and RKK)

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**Abstract:** The purpose of the study is to study the characteristics of hormonal disorders in adolescents with impaired development of pilot regions of the Republic of Uzbekistan, identified by the screening method (Namangan, Dzizak, Surkhandarya regions and RKK).

**Material and research methods.** We examined 188 teenagers from three regions of the RUZ: 78 in the Namangan region, 20 in the Jizak region and 45 in the Surkhandarya region and 45- in RKK.

**Research results.** Among the developmental disorders, the most commonly found the delay growth and puberty in 203 teenagers (48.5%), as well as a weight deficiency - 263 cases (62.9%). An isolated growth retardation (GR) was detected in 187 adolescents (44.7%). In addition, various developmental disorders as a delay in psycho-motor development were observed-in 23 (5.5%), a delay in physical, sexual and mental development-in 18 (4.3%), and a delay in speech development-in 16 (3.8 (3.8%), a delay in physical and mental development-in 16 (3.8%), a delay in psycho-motor and speech development-in 11 (2.6%), family lowness in 10 (2.4%).

**Conclusions.** Among the 2123 adolescents examined during the screening process, the delay puberty was identified in 418 (19.6%), while in 168 (17.3%) boys and 250 (21.6%) girls.

**Key words:** teenagers, puberty, hormones.

**Background.** The pathogenesis of delayed puberty includes several conditions, but most often it is associated with constitutional growth and puberty retardation (CGRP). There are three main groups of differential diagnoses of delayed puberty and growth (RGR): functional hypogonadism, disorders

causing primary hypogonadism, and GnRH deficiency leading to hypogonadotropic hypogonadism (HH), although up to 30 different etiologies underlying delayed puberty have been identified [12].

Puberty is a transitional period during adolescence leading to the achievement of reproductive capacity. The ongoing physical, psychological and emotional changes are a consequence of the synthesis of sex hormones by the gonads under the control of the hypothalamic-pituitary axis. Activation of pulsatile secretion of gonadotropin-releasing hormone (GnRH) by the hypothalamus is an endocrine sign of the onset of puberty. The development of this hypothalamic-pituitary axis begins in utero with an increase in the concentration of gonadotropin from the end of the first trimester, although in men it is lower than in women and decreases by birth in both sexes.<sup>1</sup>The axis reactivates in early infancy, a period called "mini-puberty", with a peak between 1 week and 3 months of age in both sexes, but with a later peak and longer tail in female infants. Young children then have a long period of dormancy between the ages of about 2 and 8–9 years.[3,4].

Delayed puberty is usually defined in girls by the absence of Tanner stage 2 breast development by age 13 or the absence of menarche at age 15, and in boys by the absence of Tanner stage 2 genital development (testicular volume) above 3 ml) at the age of 14 years. In adolescents with delayed puberty, the main differential diagnosis is between a central or gonadal cause [5].

Using the interpretation of reproductive hormones in late childhood and adolescence to distinguish healthy puberty from abnormal puberty is not easy. Biochemical parameters should be taken in the context of clinical signs, imaging and radiographic studies, and observation of puberty [6, 7].Diagnosis may require more advanced or resource-intensive studies, such as measurement of gonadotropin response to stimulation with gonadotropin-releasing hormone or, more recently, kisspeptin, as well as genetic analysis with whole exome or panel testing.The competence of the clinical team that puts these pieces of the puzzle together is key to delivering the right treatment within the limited time window, minimizing negative outcomes, and optimizing therapeutic care for our patients [8-10].

All of the above motivated the present study.

The purpose of the study is to studyhormonal characteristics of adolescents in the pilot regions of the Republic of Uzbekistan.

**Material and research methods.** We examined and examined as part of the screening in total for the period from January 1, 2020 to December 31, 2022 - 2123 adolescent boys and girls in 4 different regions of the Republic of Uzbekistan. In the Jizzakh region, 523 adolescents were examined, in the Namangan region - 500 adolescents aged 11 to 15 years. In the Surkhandarya region, 600 teenagers were examined, in the RKK - 500, in the city at the age of 11 to 15 years. The main contingent was students of colleges and schools.

Of the 2123 examined boys and girls, 1023 (19.6%) adolescents were selected and examined further with suspicion of various developmental disorders. Of these, 418 (19.6%) were diagnosed with mental retardation, of which 168 (17.3%) were boys and 250 (21.6%) were girls. Subsequently, delayed puberty (DP) was detected in 188 (8.8%) of the total number of examined 2123 adolescents.

Thus,among the selected 188 adolescents with mental retardation were patients from four regions of Ruz to perform hormonal studies: 78 in Namangan region, 20 in Jizzakh region and 45 in RKK and 45 in Surkhandarya region.

All data were recorded in a questionnaire specially developed by us for each patient with all clinical, anamnestic, objective and instrumental studies, which was subsequently entered into the database we created.

All selected 188 patients underwent a general clinical study, which included:

1) General clinical, biochemical and genetic studies - complete blood count, urine, ALT, AST, inflammatory tests (seromuroid, CRP), karyotyping and sex chromatin, glucose tolerance test (in obese patients).

- 2) Hormonal blood tests (STH, IGF-1, TSH, prolactin, LH, FSH, free testosterone, DHEA, cortisol - in blood serum were carried out in the laboratory of RSNPMC Endocrinology of the Ministry of Health of the Republic of Uzbekistan).
- 3) Anthropometric and genitometric studies
- 4) ECG, ultrasound of the genital organs (if necessary)
- 5) X-ray of the Turkish saddle (sighting image), CT or MRI of the Turkish saddle - in order to exclude volumetric formations of the hypothalamic-pituitary region.
- 6) X-ray of the hand with the definition of growth zones and bone age
- 7) X-ray of the lungs was carried out in order to exclude somatic pathology of the chest organs.

Statistical calculations were carried out in the Microsoft Windows software environment using the Microsoft Excel-2003 and Statistica version 6.0, 2003 software packages. The data obtained are reflected in the dissertation as  $M \pm m$ , where  $M$  is the mean value of the variation series,  $m$  is the standard error of the mean value.

**Research results.** Examination of adolescents in 4 pilot regions contributed to the diagnosis of various forms of delay and disorders of sexual development. Table 1 shows the distribution of examined adolescents by age - stages of J. Tanner's puberty.

**Table 1. Distribution of patients by sex and age (according to 5 stages of J. Tanner's puberty) by region.**

Tanner stages of puberty	Age, years, by stages of puberty according to Tanner	Total n=2123							
		A		B		C		D	
		n	DP	n	DP	n	DP	n	DP
I	prepubertal	10/11	-	23/26	-	-	-	-	-
II	11.7 ± 1.3 years	40/52	4/5	65/61	10/10	98/92	4/4	25/51	11/22
III	13.2 ± 0.8 years	80/91	8/13	43/40	20/22	47/67	8/13	43/74	17/21
IV	14.7 ± 1.1 years	36/40	6/2	38/42	9/11	46/65	6/12	38/56	10/20
V	15.5 ± 0.7 years	65/75	12/10	90/95	17/19	89/96	5/10	90/123	11/68
<b>Total - 2123</b>		<b>500</b>	<b>70</b>	<b>523</b>	<b>118</b>	<b>600</b>	<b>60</b>	<b>500</b>	<b>170</b>
		<b>231/269</b>	<b>40/30</b>	<b>259/264</b>	<b>56/62</b>	<b>280/320</b>	<b>23/39</b>	<b>196/304</b>	<b>49/121</b>

Note: A - Namangan region, B - Jizzakh region, C - Surkhandarya region, D - RKK, n - the total number of examined adolescents in the region, ZPR - the number of patients with delayed puberty and growth. Numerator - boys, denominator - girls

As can be seen from Table 1, a total of 966 boys and 1157 girls were examined in 4 pilot regions. Of these, 418 (19.6%) were diagnosed with mental retardation, of which 168 (17.3%) were boys and 250 (21.6%) were girls. A larger number of adolescents with ST were identified in the RRC - 170 out of 500 examined (34%).

Further, 188 representatives of 4 regions were selected from among 418 adolescents with mental retardation to perform hormonal studies. These results are shown in Table 2.

Table 2 gives the frequency of identified delays and various developmental disorders among 418 adolescents.

**Table2. The frequency of delay and various developmental disorders in adolescents by regions from among 418 selected adolescents.**

No.	Type of violation development	Regions				Total
		A	B	C	D	
1	RFP	70 (16.7%)	118 (28.2%)	60(14.3%)	170 (40.6%)	188 (44.9%)
2	growth retardation	24 (5.7%)	55 (13.1%)	20 (4.7%)	88 (21.0%)	187 (44.7%)
3	ZFPR	24(5.7%)	81 (19.3%)	22(5.3%)	76 (18.1%)	203 (48.5%)
4	MRT	4 (0.9%)	1 (0.2%)	8 (1.91%)	10 (2.4%)	23 (5.5%)
5	ZRR	1 (0.2%)	1 (0.2%)	5 (1.1%)	9 (2.2%)	16 (3.8%)
7	underweight	64 (15.3%)	88 (21.0%)	38(9.0%)	73 (17.4%)	263 (62.9%)
8	ZFPUR	2 (0.4%)	1 (0.2%)	8 (1.9%)	7 (1.7%)	18 (4.3%)
9	ZUFR	1 (0.2%)	3 (0.7%)	4 (0.9%)	8 (1.8%)	16 (3.8%)
10	ZPMRR	1 (0.3%)	-	5 (1.1%)	5 (1.1%)	11 (2.6%)
11	CH	-	-	4 (0.9%)	6 (1.4%)	10 (2.4%)
<b>Total</b>						

Note: A -Namangan region, B - Jizzakh region, C - Surkhandarya region, D - RKK,ZR - growth retardation, ZP - delayed puberty, ZFPR - physical and sexual developmental delay, ZPMR - psychomotor developmental delay, ZRR - speech developmental delay, ZFPUR - physical, sexual and mental developmental delay, ZUFR - physical and mental developmental delay, ZPMRR - delayed psycho-motor and speech development, HF - family short stature.

As can be seen from Table 2, among the developmental disorders, the most common Delay growth and puberty (DGP) was found in 203 adolescents (48.5%), as well as weight loss - 263 cases (62.9%). Isolated growth retardation (GR) was detected in 187 adolescents (44.7%). In addition, there were various developmental disorders such as MRT - in 23 (5.5%), ZFPUR - in 18 (4.3%), ZRR - in 16 (3.8%), ZUFR - in 16 (3.8%), ZPMRR - in 11 (2.6%), HF - in 10 (2.4%).

Of the 1023 examined, 418 patients with various developmental disorders were selected and examined in the future, among which delayed puberty (DP) was detected in 188 adolescents (8.8% of the total number of examined).

Table 3 gives the average values of various hormones in patients with DGP, which we compared with normal values for a given sex and age periods and with patients with somatotrophic insufficiency(1).

**Table 3. Average values of various hormones in patients with DGP and GR.**

Hormones	Control	GR n=25	DGP N=20
STH	2.9±0.2ng/ml	2.4 ± 0.6 P>0.5	0.7± 0.07* P<0.05
IGF-1	156.5±9.8 ng/ml	110.8±2.7 P <0.05	116.4±10.4 P<0.05
LH	5.2±0.3 IU/L	4.11±0.9 P > 0.05	1.99±0.8* P < 0.05
FSH	5.3±0.1 IU/L	3.8±0,9 P > 0.05	1.8±0,one* P < 0.05
TSH	2.5±0.2IU/L	2, 92±0.7 P>0.05	4.67±0,8* P < 0.05
Prolactin	5.7±0.3 ng/ml	6.7±0,9 P>0.05	7.±0.8 P>0.05
testosterone free	12.6 ±1.6 nmol/l	9.2±0.8 P > 0.05	4.12±0.9 P < 0.05

cortisol	norm morning 596.5 ± 11.7 nmol / l	334.25±9.3 P>0.05	400.2±8.2 P>0.05
free thyroxine	15, 8 ±0.9 pmol/l	13.2±1.3 P>0.05	8.9±1.3 P < 0.05

P-significance of differences compared with the control group ( $P < 0.05$ ). The table for comparison shows fluctuations in hormone levels from 11 to 16 years of age in the control group (healthy individuals)

As follows from Table 3, in patients with DGP, there was an unreliable decrease in basal values of LH, FSH ( $p > 0.05$ ) compared with the control group, as well as unreliably low levels of free testosterone (OT) in blood plasma ( $p > 0.05$ ) against the background of moderate hyperprolactinemia. While in patients with GR, the basal values of LH, FSH, STH, IGF-1 and free testosterone were significantly low ( $p < 0.05$ ).

**Conclusions.** 1) Out of 2123 adolescents screened 418 (19.6%) were diagnosed with mental retardation, of which 168 (17.3%) were boys and 250 (21.6%) were girls.

2) Among the developmental disorders, the most common was DGP in 203 adolescents (48.5%), as well as weight loss - 263 cases (62.9%). Isolated growth retardation (GR) was detected in 187 adolescents (44.7%). In addition, various developmental disorders were observed such as a delay in psychomotor development - in 23 (5.5%), a delay in physical, sexual and mental development - in 18 (4.3%), a delay in speech development - in 16 (3.8%) %, delayed physical and mental development - in 16 (3.8%), delayed psycho-motor and speech development - in 11 (2.6%), family short stature - in 10 (2.4%).

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