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PECULIARITIES OF PHYSICAL AND SEXUAL DEVELOPMENT OF GIRLS WITH AUTOIMMUNE HEPATITIS IN PUBERTY PERIOD

E. F. Chaykivska

Danylo Halytsky Lviv National Medical University, Ukraine

Abstract

Autoimmune hepatitis (AIH) is a rare immune-mediated chronic disease that, when inadequately treated, leads to progressive liver damage, which in turn leads to cirrhosis, liver failure, or death. Features of physical and sexual development of girls with AIH at puberty are little studied. **The objective:** to determine the characteristics of physical and sexual development of girls with autoimmune hepatitis in puberty period. **Materials and methods**. A comprehensive clinical and paraclinical examination of 66 adolescent girls of the group AIH with autoimmune hepatitis and 180 conditionally somatically healthy girls of the control group aged 12-17 years was performed. The examination included clinical and anamnestic data, anthropometry, biochemical examination of liver function, determination of serum autoantibodies, markers of viral hepatitis, ultrasound and elastography of the hepatobiliary system, liver biopsy followed by histological examination of biopsy, assessment. **Results.** Age-related changes in body length and body weight, chest circumference, waist and hips among girls with AIH were characterized by a significant lag at all stages of pubertal development. In patients with AIH, the onset of pubertal development was manifested by the development of mammary glands to the stage of Mal in 43.94% of girls, the previous appearance of puberty to thelarchein 34.85% of patients, and in 21.21% of patients noted simultaneous puberty and thelarche. Delayed development of sexual characteristics was manifested in 12-, 13- 14-, 15-, 16- and 17-year-old girls with AIH by a decrease in the score

of sexual development in all age categories compared to the same indicator in the respective age control groups: respectively 3.21 ± 0.40 **vs** 4.94 ± 0.37 points, 3.46 ± 1.00 **vs** 7.91 ± 0.58, 7.03 ± 1.44 **vs** 11.08 ± 0.25, 7.80 ± 0, 65 **vs** 11.86, 10.65 ± 0.79 **vs** 11.98. In the examined girls with AIH during puberty, such disorders of menstrual function were noted as: primary amenorrhea in 7.58% of cases, secondary amenorrhea – in 6.06%, oligomenorrhea – in 27.27%, opsomenorrhea– in 27.27%, juvenile uterine bleeding – in 9.09%, dysmenorrhea – in 31.82%, a combination of various disorders – in 18.18%. **Conclusions.** The presence of antinuclear antibodies, antibodies to microsomes of the liver and kidneys type 1, antibodies to smooth muscle, disorders of enzymatic, protein-forming, antitoxic, cytolytic activity of the liver in girls with autoimmune hepatitis is accompanied during puberty by a high frequency of abnormalities. formation of inverted puberty, delayed sexual development and delayed onset of menarche for 10-11 months, frequent menstrual disorders.

Key words: girls, puberty; autoimmune hepatitis; physical development; sexual development; menstrual disorders.

The reproductive system is the only system that begins to function actively not from the fetal period (such as the cardiovascular system) or from the birth of a child (as a respiratory system), but after reaching certain physical and mental parameters of a girl's development or a certain calendar age. Puberty is a period of transition from childhood to adulthood, characterized by the development of secondary sexual characteristics, maturation of the gonads and the achievement of reproductive capacity [1, 6]. By the end of puberty, even with a regular menstrual cycle, in contrast to the reproductive period, the reproductive system has significant lability and is particularly sensitive to the effects of adverse exogenous and endogenous factors [8].

The liver is the main organ of metabolism in the body, plays the role of an important hormonal secretory gland and functions to maintain hormonal balance and homeostasis [5]. Diseases of this organ can significantly affect a woman's endocrine status, especially during periods of endocrine transitions (puberty, pregnancy, menopausal transition) [7]. One such liver disease is autoimmune hepatitis (AIH), a rare immune-mediated chronic disease that, when left untreated, leads to progressive liver damage, which in turn leads to cirrhosis, liver failure, or death[14]. AIH remains a diagnostic and therapeutic problem: at least one-third of patients have cirrhosis of the liver, one-fifth have recurrent disease, and one-third of cases develop cirrhosis despite treatment [9]. Girls and women make up 75% of AIH patients. The peak incidence of AIH occurs in childhood, when the disease is called juvenile AIH [10, 11].

Juvenile AIH can occur at any age from childhood to adolescence with a frequency of 0.4 and 3.0 per 100,000 children, respectively [10]. AIH is characterized by a sharp increase in recurrence during perimenarche and the peak incidence - after menarche [7]. Features of physical and sexual development of girls with AIH at puberty are little studied.

Therefore, the aim of the study was to determine the characteristics of physical and sexual development of girls with autoimmune hepatitis during puberty.

Material and methods. During 2010-2020, 66 girls of the main group of AIH, patients with AIH, and 180 conditionally somatically and gynecologically healthy girls of the control group K aged 12-17 years were under observation. The age distribution of the examinedgirls is presented in table 1.

Table 1

Age distribution of examined patients

Age, in years	Number of patients	
	GroupAIH, n=66	Group K, n=180
12	11	30
13	11	30
14	11	30
15	11	30
16	11	30
17	11	30

The diagnosis of AIH was established in accordance with the International Recommendations of the European Association for the Study of Liver Diseases (EASL, 2015) [9] on the basis of complaints, clinical and laboratory examination, ultrasound and liver biopsy. The level of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), bilirubin and its fractions, creatinine, urea was determined by the kinetic method; γ-glutamate transferase (γ-GT), triglycerides, cholesterol (CS), alkaline phosphatase (AF) activity, uric acid, albumin, total protein content - colorimetric method on a Cobas 6000 analyzer, Roche Diagnostics GmbH (Switzerland); prothrombin time and International Normalized Ratio (INR) – coagulometric method using the analyzer and test systems Sysmex CA 1500 (Japan), Siemens (Germany); thymol test – by sediment sample followed by photometry using an analyzer and test systems Mefan 8001, Phyllis-Diagnostics (UIS); serum IgG, IgM – by immunoturbidimetric method on the analyzer Cobas 6000, Roche Diagnostics GmbH (Switzerland). The level of circulating immune complexes was determined by the method of

Yu. A. Grinevich, A. N. Alferov (1981). AIH activity was assessed by the results of liver tests by V. F.Uchaikin (1998).

Serum autoantibodies were determined in all girls with AIH by immunofluorescence using a Eurostar III Plus fluorescence microscope and EUROIMMUN test systems (Germany): ANA (antinuclear antibodies) Anti-LKM-1 (antibodies to liver and kidney microsomes type 1), anti-SM (antibodies to smooth muscle), anti-LC1 (antibodies to cytosolic antibodies type 1). To exclude the viral nature of the disease, markers of hepatitis viruses were determined: anti-HAV IgM, HBsAg, anti-HBsIgM, anti-HBsIgG, HBV DNA PCR, anti-HCV IgG and HCV RNA PCR. All girls with AIH underwent a puncture biopsy of the liver with morphological and immunohistochemical examination of the biopsy on a microscope OLYMPUS BX-51 (Japan). The activity of the inflammatory process was characterized by the index of histological activity by R. G. Knodell et al. (1981).

Anthropometric surveys included the measurement of height, body weight and calculation of the body mass index (BMI) by the formula [weight (kg) / height (m^2)]. Measurements of the circumference of the chest (CC), waist (CW), thighs (CT) were performed with a tensile-resistant centimeter tape in accordance with WHO recommendations.

The degree of sexual development was determined by the generally accepted method of the development of secondary sexual characteristics: pubic hair and in the axillary region, the development of the mammary glands and the formation of menstruation by J. M. Tanner (1962) and L. G.Tumilovich (1975) [12]. The corresponding feature was evaluated by the stage of its development (0, 1, 2 and 3), which was expressed in points.

The development of the breast (Mammae - Ma) was evaluated as follows: Ma0– the breast is not issued, the nipple rises above the nipple circle; Ma1– the gland gives out a little, forms with a nipple a cone – "bud stage"; Ma2– the gland is significantly issued together with the nipple, has the shape of a cone; Ma3– the gland has a rounded shape, on a wide base, the nipple rises above the nipple circle.

When assessing the development of pubic hair (Pubis - P) was considered P0 as a lack of hair growth; P1– as a single straight hair in the center of the pubis and on the labia majora; P2– as hair that curls on the pubis and labia majora; P3– like thick hair that curls along the entire plane of the pubis, on the labia.

Hair growth in the inguinal areas (Axillaris - Ax) was evaluated as follows: Ax0– no hair growth; Ax1– single hair; Ax2– hair thicker in the central part of the axilla; Ah3– thick hair all over the armpit.

The formation of menstrual function (Menstruation– Me) was characterized as: Me0– no menstruation; Me1– the presence of 1-2 menstruation before the examination; Me2– erratic menstrual cycle (irregular menstruation, is a variant of the norm 1 year after the onset of menarche); Me3– regular menstruation.

For a comprehensive assessment of sexual development used the method of summation of points by L. G.Tumilovich et al. (1975) [13], which takes into account the degree of development of each of the secondary sexual characteristics. Accordingly, the above characteristics were evaluated taking into account the correction factor. The coefficient for mammary glands was 1.2, for the degree of pubic hair – 0.3, for axillary hair – 0.4, to assess menstrual function – 2.1. The score of the development of each individual trait was calculated as the product of the average quantitative assessment of the secondary sexual trait or menstruation on the degree of development of each trait in a given patient [13]. The sum of the scores of the development of each individual trait was the score of sexual development (SSD). This score was compared with the score of the degree of sexual development of adolescent girls according to existing guidelines and determined the degree of sexual development taking into account the age of menarche.

The obtained data were statistically processed using the Excel software package 10. Calculated the mean value (M), standard deviation error (SE). Student's t-test, Wilcoxson-Mann-Whitney U test, Fisher's φ test, and χ^2 test were used to identify differences between comparative indicators. Pearson's linear correlation index or Kendall's rank correlation index was calculated to determine the relationship between the parameters.

Results and discussion. Among the surveyed girls with AIH, the age of onset of the disease was 11.74 ± 0.42 years. 83.33% of girls have type AIH, 4.55% have type II AIH, and 12.12% have seronegative AIH. The presence of autoimmune antibodies to the structural elements of hepatocytes was found in 81, 82% of girls, including: ANA autoantibodies were detected in 27.27% of patients, SMA– in 78.79%, ANA + SMA– in 19.70%, LKM– in 4.55%.

In 31.82% of patients AIH is established at the stage of liver cirrhosis. 63.64% of girls with AIH had an acute onset of the disease with a clinical picture of acute hepatitis, 36.36% – subacute onset. All patients had manifestations of astheno-vegetative syndrome. Dyspeptic disorders were registered in 50.00% of patients; increase in body temperature to 37–39 ° C – by 36.36%; palmar erythema – in 63.64%; telangiectasia – in 77.27%; small-spotted-papular rash – 4.55%; icteric skin and sclera – 80.30%; hepatomegaly – in 71.21%; splenomegaly – in 63.64%.

45.45% of the surveyed had transaminase activity with 2-5-fold excess of the upper limit of normal (ULN), and 54.55% of girls had 6-20 normal. The average multiplicity of excess ULN for ALT was 17.15 ± 0.39; for AST – 21.24 ± 0.70; for γ-GT– 1.84 ± 0.06. In 4.55% of children in the period of incomplete clinical and laboratory remission, transaminases were within the normative values. The average multiplicity of excess ULN for AF was 1.70 ± 0.04. Hyperbilirubinemia mainly due to the direct fraction was observed in 57.58% of girls with AIH (mean total bilirubin was 47.96 ± 1.06 vs. 11.95 ± 0.32 μmol / l in the control).

Girls with AIH had a probable increase in the level of γ-globulins (28.55 ± 1.12 vs. 15.03 ± 0.23% in the control), Ig M (5.90 ± 0.40 vs. 1.09 ± 0.05 g / l), Ig G (12.60 ± 0.34 vs. 10.60 ± 0.23 g / l), thymol test (5.22 ± 0.12 vs. 2.03 ± 0.07 U / l), EOM (1.36 ± 0.08 vs. 0.99 ± 0.01), urea (6.82 ± 0.28 vs. 5.12 ± 0.07 mmol / L), creatinine (82.87 ± 2.66) vs. 57.45 ± 0.78 μmol / l), circulating immune complexes (106.00 ± 3.91 vs. 53.36 ± 1.68 conventional units) against a background of decreased albumin levels (21.26 ± 0.20 vs. 40,64 ± 0.29%), prothrombin index (69.26 ± 0.76 vs. 87.03 ± 0.36%). When assessing the R. G.Knodell index in the group of patients with AIH, the minimum degree of clinical and biochemical activity was determined in 21.21% of girls, low – in 24.24%, moderate – in 34.85%, high – in 19.70% (13) patients.

Histological examination of liver biopsies in girls with AIH showed a morphological picture from periportal to panacinar hepatitis, bridging and multiacinar necrosis with cirrhosis, penetration of inflammatory cells into hepatocytes (emperipolosis), destruction of the original structure of the liver. cells in the follicles in the stroma of the portal tracts. When assessing the severity of histological activity by R. G. Knodell, mild liver fibrosis was detected in 28.79% of cases, moderate – in 43.94%, liver cirrhosis – in 28.79%.

Anthropometric studies showed that age-related changes in height and body weight, CC, CW and CT among girls with AIH were characterized by a significant lag at all stages of pubertal development, while BMI had no statistically significant differences compared with the control group (Table 2).

Throughout puberty, the body weight of girls with AIH and in control increased gradually and in moderation. Weight gain in these years was 2–4 kg per year, on average in the group AIH2.64 ± 0.45 kg / year vs. 2.94 ± 0.90 kg / year in group K ($p > 0.05$). A rapid jump in body weight was observed at 14 years of age and 17 years of age. At the age of 14, body weight gain in the group AIHwas 3–4 kg (with fluctuations in body weight from 43 to 47 kg) and averaged 3.56 ± 0.45 kg / year, whereas in group K at 14 years body weight ranged from 48 to 59 kg, weight gain was from 4 to 6 kg and averaged 5.23 ± 0.86 kg / year.

At the age of 17 in the control group there was again an increase in body weight by an average of 2.97 ± 0.55 kg / year (with fluctuations in body weight from 53 to 66 kg), then in patients with AIH– by 1.55 ± 0.56 kg / year (with fluctuations in body weight from 43 to 55 kg).

Table 2

Some parameters of physical development of the surveyed girls during puberty, M ± SE

Age, years	Gro-up	n	Height, m	Body weight,kg	BMI, kg / m^2	CC, sm	CW, sm	CT, sm
12	AIH	11	1.46± 0.01[k]	38,18± 0,80[k]	17,91± 0,59	68,53± 0,20[k]	55,85± 0,29[k]	81,64± 0,29[k]
	C	30	1.52± 0.01	42,40± 0,44	18,34± 0,26	70,07± 0,14	57,25± 0,32	88,00± 0,29
13	AIH	11	1.48± 0.01[k]	41,63± 0,51[k]	18,93± 0,24[k]	69,60± 0,32[k]	56,98± 0,37[k]	83,18± 0,37[k]
	C	30	1.55± 0.01	46,53± 0,33	19,34± 0,15	77,03± 0,24	58,03± 0,24	89,03± 0,24
14	AIH	11	1.49± 0.01[k]	45,18± 0.41[k]	20,27± 0,24	70,80± 0,21[k]	58,62± 0,25[k]	85,82± 0,25[k]
	C	30	1.59± 0.01	51,77± 0,48	20,42± 0,20	78,47± 0,34	60,17± 0,17	92,10± 0,18
15	AIH	11	1.52± 0.01[k]	47,89± 0,85[k]	20,81± 0,41	70,86± 0,29[k]	60,12± 0,35[k]	87,82± 0,35[k]
	C	30	1.63± 0.01	53,13± 0,34	19,95± 0,18	80,63± 0,20	61,63± 0,20	94,13± 0,20
16	AIH	11	1.58± 0.01[k]	49,82± 1,01[k]	20,03± 0,53	80,44± 0,57	59,94± 0,62[k]	87,77± 0,70[k]
	C	30	1.64± 0.01	54,13± 0,69	20, 09± 0,24	80,80± 0,36	61,87± 0,36	94,38± 0,37
17	AIH	11	1.61± 0.01[k]	51,36± 1,01[k]	19,92± 0,25	80,59± 0,25	62,75± 0,56	92,95± 0,56[k]
	C	30	1.65± 0.01	57,10± 1,36	20,97± 0,17	81,23± 0,28	63,95± 0,29	95,72± 0,96
Note. [k]– the statistical probability with the index of group K ($p<0.05$).								

Age-related changes in body length (growth gain) among the AIH group were characterized by lag in stages P1 and P2 of pubertal development, while in stages P2 and RH there is a jump in growth, but its magnitude is also lower compared to the control group. The jump in growth in control was observed at 14-15 years – by 0.04 m / year, and in the group with AIH with a delay – at 16 years by 0.06 m / year. At other stages, girls with AIH showed a smaller increase in body length compared to the control, which was reflected in the final growth – 1.61 ± 0.01 vs. 1.65 ± 0.01 m ($p <0.01$). The annual increase in body length in both groups from 12 to 17 years averaged 0.03 ± 0.01 m / year and probably did not differ.

The increase in CC among girls occurred before the age of 17, with the largest increase in control observed at the age of 10-14 years, which corresponded to the transition P2-R3 and R3-P4. In the groupAIH, the largest increase in CC occurred later – at the age of 16, which corresponded to stage P4.

As can be seen from table. 2, the increase in CW and CT also occurred before the age of 17, but in the group with AIH it was slower and the size of CW and CTwas probably smaller than in group K.

Analysis of the appearance of secondary sexual characteristics showed that in 95.56% (172) cases in the control group the onset of pubertal development was manifested by the development of the mammary glands to the Mal stage, in 1.11% (2) children – pubic hair, and then began the development of the mammary glands, in 3.33% (6) girls the simultaneous beginning of development of mammary glands and sexual hair growth was registered. In patients with AIH, the onset of pubertal development was manifested by the development of the mammary glands to the stage of Mal in 43.94% (29) girls, the previous appearance of puberty to thelarchehad 34.85% (23) patients, and 21.21% (14) patients noted simultaneous pubarche and thelarche. This development of secondary sexual characteristics is proposed in the literature to be called "inverted" or unconventional. Accordingly, the mean age of thelarche in girls with AIH was 10.59 ± 0.09 years ($p<0.01$) vs. 10.37 ± 0.04 years in group K, pubarche 10.72 ± 0.11 vs. 11.12 ± 0.04 years (Table 3).

Table 3

Age of signs of sexual development, in years, M ± SE

Age, years	Gro-up	n	Age of thelarhe	Age of pubarche	Age of axillary	Age of menarche
12	AIH	11	10.45±0.17 к	10.55±0.17 к	12.00±0.01 к	11.67±0.16 к
	C	30	10.00±0.09	10.43±0.07	10.83±0.06	12.24±0.08
13	AIH	11	10.45±0.41	10.23±0.20 к	10.64±0.16 к	12.03±0.30 к
	C	30	10.23±0.07	10.95±0.06	11.47±0.06	12.29±0.08
14	AIH	11	10.73±0.21к	12.27±0.15 к	13.09±0.23 к	13.00±0.01 к
	C	30	10.60±0.09	11.45±0.08	11.63±0.36	12.47±0.10
15	AIH	11	10.55±0.17 к	11.27±0.15	11.55±0.17	12.91±0.33 к
	C	30	10.33±0.09	11.15±0.08	11.79±0.08	12.47±0.11
16	AIH	11	10.73±0.25 к	11.82±0.24 к	12.91±0.22 к	13.09±0.36 к
	C	30	10.39±0.10	11.15±0.09	11.63±0.09	12.44±0.10
17	AIH	11	10.64±0.21	11.91±0.22	12.59±0.18	11.94±0.21 к
	C	30	10.63±0.14	11.47±0.14	12.18±0.15	12.56±0.11
Note. к – the statistical probability with the index of group K ($p<0.05$).						

In girls of the control group, breast growth began earlier and was more intense than in the group of patients with AIH. Thus, among girls 12 years old in group K Ma1 was noted in 43.33% (13), Ma2– in 40.00% (12), Ma3– in 16.67% (5); in the group of 13 years: Ma1– in 13.33% (4), Ma2– in 60.00% (18), Ma3– in 26.67% (8); in the group of 14 years: Ma1– in 6.67% (2), Ma2– in 50.00% (15), Ma3– in 43.33% (13); in the group of 15 years: Ma1– in 3.33% (1), Ma2– in 36.67% (11) and Ma3– in 60.00% (18); at the age of 16-17 – all girls had Ma3 (Table 4).

Table 4

The severity of signs and score of sexual development (SSD) in the dynamics of puberty in the study groups, in points, M ± SE

Age, years	Gro-up	n	Ma	Ax	P	Me	SSD
12	AIH	11	1.20± 0.01 к	0.40± 0.01 к	0.46± 0.05	1.15± 0.35	3.21± 0.40 к
	C	30	2.64± 0.09	0.69± 0.04	0.49± 0.03	1.12± 0.28	4.94± 0.37
13	AIH	11	1.31± 0.27 к	0.33± 0.11 к	0.30± 0.09 к	1.53± 0.60 к	3.46± 1.00 к
	C	30	3.08± 0.11	0.96± 0.04	0.72± 0.04	3.15± 0.47	7.91± 0.58
14	AIH	11	2.51± 0.40 к	0.84± 0.13 к	0.63± 0.10 к	3.05± 0.83 к	7.03± 1.44 к
	C	30	3.52± 0.06	1.16± 0.02	0.87± 0.02	5.53± 0.21	11.08± 0.25
15	AIH	11	2.62± 0.15 к	0.98± 0.07 к	0.76± 0.05 к	4.20± 0.00 к	8.56± 0.23 к
	C	30	3.60± 0.01	1.17± 0.02	0.88± 0.01	5.60± 0.18	11.25± 0.20
16	AIH	11	2.62± 0.28 к	0.65± 0.17 к	0.60± 0.10 к	3.93± 0.29 к	7.80± 0.65 к
	C	30	3.60± 0.01	1.20± 0.01	0.90± 0.01	6.16± 0.10	11.86± 0.10
17	AIH	11	3.49± 0.11	1.02± 0.12	0.79± 0.06	5.35± 0.62	10.65± 0.79
	C	30	3.60± 0.01	1.19± 0.01	0.89± 0.01	6.30± 0.01	11.98± 0.02
Note. к– the statistical probability with the index of group K (p<0.05).							

Among girls with AIH 12 years Ma1 was noted in 100% (11), Ma2– in 0.00% (0), Ma3– in 0.00% (0); 13 years: Ma0– in 18.18% (2), Ma1– in 54.55% (6), Ma2– in 27.27% (3), Ma3– 0.00% (0); 14 years: Ma1– in 45.45% (5), Ma2– in 0.00% (0), Ma3– in 54.55% (6); 15 years: Ma1– 0.00% (0), Ma2– in 81.82% (9) and Ma3– in 18.18% (2); 16 years: Ma1– in

18.18% (2), Ma2– in 45.45% (5) and Ma3– in 36.36% (4); 17 years: Ma1– in 0.00% (0), Ma2– in 9.09% (1) and Ma3– in 90.91% (10) girls.

The mean value of Ma according to J. M. Tanner, which characterizes the development of the mammary glands, in 12-, 13-, 14-, 15-, 16- and 17-year-old girls was equal, respectively, in the AIH group 1.20 ± 0.01 vs. 2.64 ± 0.09 points in group K; 1.31 ± 0.27 vs. 3.08 ± 0.11 points; 2.51 ± 0.40 vs. 3.52 ± 0.06 points; 2.62 ± 0.15 vs. 3.60 ± 0.01 points; 2.62 ± 0.28 vs. 3.60 ± 0.01 points; 3.49 ± 0.11 against 3.60 ± 0.01 points (see Table 4), which indicates a slower development of the mammary glands in girls on the background of AIH. Ma3 was registered only in 36.36% (4/11) cases in the age group of 16 years, and in 90.91% (10/11) – in the age group of 17 years.

Pubic hair in girls of group K was developed to the degree of R3 in the age group of 13 years in 96.67% (29/30) cases and at 14 years – in 93, 33% (28/30), in the age groups from 15 years – in 100% of cases. Among girls with AIHP3 observed for the first time in the age group of 14 and 15 years – in 54.55% (6/11) cases, at the age of 17 years – only in 72.73% (8/11). The mean value of P according to J.M. Tanner, which characterizes the development of pubic hair, in 12-, 13-, 14-, 15-, 16- and 17-year-old girls was respectively in the group AIH 0.46 ± 0.05 vs. 0.49 ± 0.03 points in group K; 0.30 ± 0.09 vs. 0.72 ± 0.04 points; 0.63 ± 0.10 vs. 0.87 ± 0.02 points; 0.76 ± 0.05 vs. 0.88 ± 0.01 points; 0.60 ± 0.10 vs. 0.90 ± 0.01 points; 0.79 ± 0.06 versus 0.89 ± 0.01 points (Table 4).

Auxiliary hair growth in group K corresponded to Ax3 at 14 years in 90.00% (27/30) of girls, at 15 years – in 93.33% (28/30), at 16 and 17 years it was in all girls. Among girls with AIHAx3, 54.55% (6/11) were registered for the first time in the age group of 14 and 15 years, in the age group of 17 years, as in the control, it was present in 72.73% (8/11) cases, but at the same time, 36.36% (4/11) of girls in the age group of 16 years and 9.09% (1/11) ones in the age group of 17 years were at the stage of Ax0. The mean value of Ax according to J. M. Tanner, which characterizes the development of auxiliary hair growth, in 12-, 13-, 14-, 15-, 16- and 17-year-old girls was, respectively, in the AIH group 0.40 ± 0.01 vs. 0.69 ± 0.04 points in group K; 0.33 ± 0.11 vs. 0.96 ± 0.04 points; 0.84 ± 0.13 vs. 1.16 ± 0.02 points; 0.98 ± 0.07 vs. 1.17 ± 0.02 points; 0.65 ± 0.17 vs. 1.20 ± 0.01 points; 1.02 ± 0.12 versus 1.19 ± 0.01 points (see Table 4).

According to various authors, the average age of menarche in the world today ranges from 12.9 to 13.3 years. For example, in the United States, the average age of menarche is 12.4 (11.3; 13.5) years [6]. The age interval for the onset of menarche in Ukraine is between 10 years and 3 months and up to 14 years and 6 months, and is a constant value [5].

According to the study, the average age of menarche in group K was 12.43 ± 0.04 years, in the group AIH– 13.33 ± 0.11 years ($p<0.01$), that is 10-11 months later than in almost healthy peers.

Among conditionally healthy girls in the age group of 12 years Me1 was noted in 26.67% (8) cases, Me2– in 13.33% (4); in the group of 13 years Me1 was registered in 10.00% (3) of patients, Me2– in 30.00% (9), Me3– in 26.67% (8); in the group of 14 years Me1 was not observed, Me2 was in 30.00% (10) cases, Me3– in 66.67% (20); at the age of 15 the sign of Me2 was noted in 6.67% (2) of girls, Me3– in 93.33% (28). In all age groups of 16- and 17-year-old girls of group K in all cases Me3 was registered.

Among girls with AIH in the age group of 12 years Me1 was registered in 54.55% (6), in 45.45% (5) patients there were no menstruation; in the age group of 13 years: Me0 was in 54.55% (6), Me1– in 18.18% (2); Me2– in 27.27% (3); in the age group of 14 years Me0 was observed in 27.27% (3) of patients, Me1– in 9.09% (1), Me2– in 27.27% (3), Me3– in 27.27% (3); in the age group of 15 years, all girls had Me2; in the group of 16 years: Me1– in 9.09% (1), Me2– in 90.91% (10) girls; in the age group of 17 years: Me0– in 9.09% (1), Me2– in 18.18% (2), Me3– in 81.82% (9) people. The mean value of Me according to JM Tanner, which reflects the formation of menstrual function, in 12-, 13-, 14-, 15-, 16- and 17-year-old girls was respectively in the group AIH 1.15 ± 0.28 vs. 1.12 ± 0.28 points in group K; 1.53 ± 0.60 vs. 3.15 ± 0.47 points; 3.05 ± 0.83 vs. 5.53 ± 0.21 points; 4.20 ± 0.01 vs. 5.60 ± 0.18 points; 3.93 ± 0.29 vs. 6.16 ± 0.10 points; 5.35 ± 0.62 vs. 6.30 ± 0.01 points (see Table 4). The rate of development of menstrual function in group K in the period from 12 years to 15 years gradually increased, reaching a maximum at 14 years (after menarche), while in the AIH group reached a maximum at 17 years.

Delayed development of sexual characteristics was manifested in 12-, 13-, 14-,15-, 16- and 17-year-old girls with AIH with a decrease in SSD in all age categories compared to the same indicator in the respective age groups of control: respectively 3.21 ± 0, 40 vs. 4.94 ± 0.37, 3.46 ± 1.00 vs. 7.91 ± 0.58, 7.03 ± 1.44 vs. 11.08 ± 0.25, 7.80 ± 0.65 vs. 11.86, 10.65 ± 0.79 vs. 11.98 points.

In the examined girls with AIH during puberty, such disorders of menstrual function were noted as: primary amenorrhea in 7.58% (5) cases, secondary amenorrhea – in 6.06% (4), oligomenorrhea – in 27.27% (18), opsomenorrhea– in 27.27% (18), juvenile uterine bleeding – in 9.09% (6) dysmenorrhea – in 31.82% (21), a combination of various disorders – in 18.18% (12).

Conclusions

The presence of antinuclear antibodies, antibodies to microsomes of the liver and kidneys type 1, antibodies to smooth muscle, disorders of enzymatic, protein-forming, antitoxic, cytolytic activity of the liver in girls with AIH is accompanied during puberty by a high frequency of abnormalities. formation of inverted puberty, delayed sexual development and delayed onset of menarche for 10-11 months, frequent menstrual disorders.

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