Serum hormone levels and anthropometric characteristics in girls with hyperandrogenism

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Key words: *hyperandrogenism, premature adrenarche, girls.*

Summary. *Polycystic ovary syndrome is considered to originate during puberty. The aim of this study was to investigate hormonal status in relationship to anthropometric data in girls with premature adrenarche and adolescent girls with hyperandrogenism, as these conditions are related to polycystic ovary syndrome in adulthood.*

Materials and methods. 20 girls with premature adrenarche (aged 4.9–10.2 years), 21 postmenarcheal girls with hirsutism (aged 13.3–17.8 years), 2 groups (n=13 in each) of healthy volunteers of similar age and body mass index participated in the study.

Results. Serum testosterone and dehydroepiandrosterone sulphate levels were significantly higher in all patients than in controls. Free androgen index and leptin levels were significantly higher, and sex-hormone-binding globulin lower in hirsute adolescents vs. controls. Birth weight standard deviation scores were comparable in all 4 groups. Serum dehydroepiandrosterone sulphate negatively correlated with birth weight standard deviation scores in the group of girls with premature adrenarche ($r=-0.57$, $p<0.001$). By linear regression, 76% in variation of serum leptin levels could be explained by subscapular skinfold thickness standard deviation scores, and by serum sex-hormone-binding globulin, insulin, and dehydroepiandrosterone sulphate levels in all participants. Mean age of onset of menarche was younger in hirsute girls vs. controls (12.1±1.3 vs. 13.5±1.3 years, $p=0.004$).

Conclusions. Inverse correlation of dehydroepiandrosterone sulphate levels and weight at birth indicates relationship between premature adrenarche in girls and fetal growth. Higher leptin levels in adolescents with hyperandrogenism than in healthy girls show possible involvement of leptin in pathogenesis of hyperandrogenism.

Introduction

Clinical features of hyperandrogenism (hirsutism, acne, and menstrual irregularity) are a common problem in women and have been linked to excessive androgen production from the ovaries or the adrenal glands or both (1). One of the most frequent causes of hyperandrogenism in adolescent girls and women is polycystic ovary syndrome (PCOS) (2). PCOS is a syndrome of ovarian dysfunction along with hyperandrogenism and polycystic ovary morphology (3). Insulin resistance and hyperinsulinemia are thought to be important factors in pathogenesis of PCOS (4). The fact that many of the endocrine changes occurring during puberty also occur, but to the greater degree, in PCOS, has led to the hypothesis that PCOS may originate from abnormal pubertal development (5). The hyperinsulinemia/insulin resistance and increased insulin-like growth factor's-I (IGF-I) activity during puberty have been proposed as inducing factors in the development of PCOS. However, whether hyperinsulinemia and insulin resistance may be primary in the development of ovarian hyperandrogenism is still unclear (6).

Term *premature adrenarche* (PA) applies to the appearance of pubic and/or axillary hair before the age of 8 years in girls and 9 years in boys, while puberty is otherwise normal (7). Adrenarche is the "puberty" of the adrenal gland. Biochemically adrenarche is characterized by increases in dehydroepiandrosterone (DHEA) and its sulfate (DHEAS), both products of the zona reticularis of the adrenal gland (6). Longitudinal observations suggest that girls with premature adrenarche are at high risk for hyperandrogenism and PCOS in adulthood (7). This asso-

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ciation is also consistent with the observed elevated production of DHEAS from adrenal glands of women with PCOS, such that both the adrenals and gonads contribute to elevated circulating testosterone (T) concentrations in women with this syndrome (8).

Recent studies have pointed out that there may be an association between intrauterine growth retardation and premature adrenarche, hyperinsulinemia and functional ovarian hyperandrogenism in girls (9, 10). There is currently no validated clinical test for detecting insulin resistance in the general population (3). In order to assess accurately insulin resistance, dynamic invasive tests, such as the intravenous euglycemic clamp technique, are recommended to use as the best methods (4), which are difficult to perform in routine practice, especially in pediatric settings. Insulin (in addition to androgens and thyroxin) is known to regulate sex hormone-binding globulin (SHBG) production by liver. Low circulating SHBG concentration is a marker for hyperinsulinemia/insulin resistance in childhood and adolescence, as well as in adulthood (6, 11).

Most of women with PCOS are obese, and the fat distribution is often abdominal/visceral, similar to that frequently associated with metabolic abnormalities (e.g., hypertension, dyslipidemia, insulin resistance, type 2 diabetes mellitus) (12). L. Ibanez *et al.* reported, that girls with premature adrenarche had excess of total body and central fat mass throughout all pubertal stages. Girls with premature adrenarche, having high body mass index (BMI) and abnormal waist-to-hip ratio, are prone to have higher postpubertal androgen levels (6). We aimed to investigate whether girls with premature adrenarche and adolescents with clinical and/or biochemical hyperandrogenism in our clinical practice had direct and indirect evidence for hyperinsulinemia, and how their weight at birth and current anthropometric parameters were related to hormonal status.

Materials and methods

Subjects

20 girls with premature adrenarche (age range 4.9–10.2 years), 21 adolescent girls with symptoms of hyperandrogenism (age range 13.3–17.8 years), and 26 healthy girls (age range 4.8–17.7 years) participated in this study. None of the girls had signs of systemic virilization or underlying other diseases. None of them was taking hormonal medications, including oral contraceptives. Patients were recruited in 2002–2004 from the Department of Children Endocrinology at Kaunas University of Medicine Hospital. About a half of the patients and 70% of healthy girls were living in Kaunas city or its region, and the rest were from different places of Lithuania. Informed and written consent to participate from the parents and assent from the children were obtained. The study was approved by the Ethics Committee for Biomedical Research of Kaunas Region.

Blood samples were obtained in the morning (08.00–09.00 h) by standard venepuncture technique; the serum was separated by centrifugation within one hour and stored at –30°C until assay. Oral glucose tolerance test was performed in all obese girls with PA and hyperandrogenism, and impairment of glucose tolerance was ruled out. There were no signs of true precocious puberty in girls with premature adrenarche at the time of diagnosis. Congenital adrenal hyperplasia was excluded by basal level of 17-hydroxyprogesterone (17-OHP) in patients and controls, and also by its stimulation with adrenocorticotropic hormone (ACTH, 0.25 mg i. v.) in 14 hirsute patients and 9 girls with PA.

Methods

Pubertal development was staged by the same person using the method of J. M. Tanner (13). Height (cm) and weight (kg) were recorded at examination and body mass index (kg/m^2) derived, using A. Quetelet's formula (1870): weight/height^2. Height was measured using Harpender stadiometer (Holtain LTH, Crymych, UK) to the nearest 0.1 cm, and weight was measured using Seca 700 (Germany) mechanical medical scales to the nearest 0.1 kg. Skinfold thickness (mm) was measured at subscapular (just bellow the angle of the left scapular, in the vertical line) and triceps (half-way down left arm between tip of acromion and the tip of the olecranon, of relaxed arm) sites using Holtain calipers (LTD, Crymych, UK). Hip and waist circumferences (cm) were recorded and the waist/hip ratio calculated. Daytime blood pressure (BP) was measured in mmHg using aneroid sphygmomanometer with appropriate cuff sizes. The bone age was assessed in all girls with premature adrenarche by Greulich-Pyle method (14). Anthropometric data were expressed as a mean and standard deviation (SD). As uniform Lithuanian standards from early childhood till 18 years of age for all anthropometric characteristics are not currently available, BMI, height, weight, and skinfold thickness at triceps and subscapular sites were expressed as standard deviation scores (SDSs) using 1996 Growth Reference Data of Dutch children (15) which allows comparisons at different ages. Blood pressure was also expressed as a SDS using data from the Second Task Force on Blood Pressure Control in Children (16). Birth weight SDSs were calculated according to Swedish infants data (17).

Hormone assays

Hormone levels for all participants were measured using the same kits. DHEAS, estradiol (E2), IGF-I, 17-OHP and T were measured by radioimmunoassays (RIAs) using kits by BioSource Europe S.A., Belgium, for E2, IGF-I, 17-OHP, T (with sensitivity 36.8 pmol/L, 0.13 nmol/L, 0.06 nmol/L, 0.17 nmol/L, respectively), and Immunotech S. A., France, for DHEAS (sensitivity 0.16 μmol/L). Insulin and SHBG levels were measured by immunoradiometric assay (IRMA) kits produced by BioSource Europe S. A., Belgium, with sensitivity 1 mIU/L, and by ZenTech S. A., Belgium, with sensitivity 0.3 nmol/L, respectively. Serum leptin was measured by solid phase Enzyme Amplified Sensitivity Immunoassay (EASIA, BioSource Europe S. A., Belgium), with sensitivity 0.1 μg/L. The maximal intra-assay coefficient of variation for all hormones did not exceed 7.5%.

Statistical analysis

The normality assumption of the variables was checked by Kolmogorov-Smirnov test. Associations between age, different anthropometric characteristics, and their SDS, as well as between serum hormone levels, were assessed by Pearson's and Spearman's correlation coefficients where appropriate. Anthropometric characteristics and hormone levels were compared between patients and age-matched controls by Student's t test. Differences between the groups of dichotomous variables (where symptom was absent or present, such as thelarche, *acanthosis nigricans*, etc.) were assessed by Chi-square test. Multivariate linear regression analysis was used to evaluate how other hormones and body composition can predict insulin, leptin and SHBG levels. Statistical significance was considered when $p<0.05$. Data analysis was performed using SPSS statistical package (Chicago, IL).

Results

Influence of age on anthropometric measures and hormone levels

A slight tendency to a decrease of weight SDS, BMI SDS and height SDS was observed in all girls ($r=-0.33$, $r=-0.31$, $r=-0.31$, respectively; $p<0.05$). Serum levels of E2, DHEAS, T, free androgen index (FAI, calculated by formula: Tx100/SHBG), 17-OHP, IGF-I were significantly positively, and SHBG negatively, correlating with age, analyzing all girls ($r=0.66$, $r=0.66$, $r=0.70$, $r=0.54$, $r=0.44$, $r=0.69$, $r=-0.51$, respectively; $p<0.001$). No dependency on age for leptin and insulin levels was found, however, there was a weak association between age and leptin levels in younger girls (PA group and their comparison girls were analyzed together, $r=0.34$; $p=0.057$). Anthropological parameters and serum hormone levels, and significant differences between groups of patients *vs.* controls are presented in Table.

Patients with premature adrenarche vs. age-matched controls

Mean bone age of girls with premature adrenarche was statistically higher than mean age (9.1±1.6 *vs.* 7.7±1.3 years; $p=0.004$). Their mean age of onset of pubic hair development was 5.8±1.9 years (range, 0.8–7.9 years). 7 (35.0%) girls with premature adrenarche *vs.* 2 (15.4%) of the comparison group were obese (BMI>2 SD), the difference was not significant (ns). One (5%) girl with PA, but no one from the control group had *acanthosis nigricans,* and acne was present also in one girl with PA (ns). More girls in the control group had breast development than in PA group (6 (46.2%) *vs.* 3 (15.0%); $p=0.05$) that would explain the significantly higher estradiol levels in controls.

Patients with clinical hyperandrogenism vs. age-matched controls

All patients had hirsutism score ≥6 according to Ferriman-Gallwey (range 6–21) (18), 15 hirsute girls had irregular periods, and those who recorded regular menses had at least one of the following data: elevated FAI, DHEAS, LH/FSH>1, obesity. The mean age of onset of menarche in patients was significantly younger than in controls (12.1±1.3 *vs.* 13.5±1.3, respectively; $p=0.004$). 5 (23.8%) of patients, and no one of the comparison adolescents were obese (BMI>2 SD; $p=0.055$). 8 (38.1%) patients and 2 (15.0%) controls had *acanthosis nigricans* (ns), acne was present in 13 (61.9%) patients and 6 (46.2%) controls (ns).

Five girls with hirsutism (23.8%) also had polycystic ovaries determined by transabdominal ultrasound examination (at least one ovary appeared enlarged and contained >10 cysts, each <10 mm in diameter scattered around or through an echodense thickened stroma (19)), therefore their symptoms were consistent with the classical PCOS diagnostic criteria.

Analyzing all girls, insulin levels were associated with: leptin ($r=0.54$; $p<0.001$), SHBG ($r=-0.36$; $p<0.005$), DHEAS ($r=0.33$; $p<0.01$), 17-OHP ($r=0.29$; $p<0.05$), FAI ($r=0.26$; $p<0.05$), and subscapular skinfold thickness SDS ($r=0.38$; $p<0.005$). Insulin levels correlated significantly positively with DHEAS in premature adrenarche patients ($r=0.50$; $p<0.05$), and with T and 17-OHP levels in girls with hirsutism ($r=0.46$, $p=0.05$ and $r=0.70$, $p=0.001$, respectively). Insulin levels inversely correlated with SHBG levels in patients

Table. **Anthropometric details and serum hormone levels of patients *vs.* controls**

	Premature adrenarche (n=20)	Controls-1 (n=13)	Adolescents with hyperandrogenism (n=21)	Controls-2 (n=13).
Age (years)	7.72 (1.3)	8.67 (2.1)	16.03 (1.3)	15.94 (1.1)
Birth weight (g)	3320.00 (264.7)	3301.17 (472.3)	3157.00 (479.4)	3354.17 (432.99)
Birth weight SDS	–0.36 (0.5)	–0.51 (1.1)	–0.54 (1.3)	–0.03 (0.8)
Height (cm)	132.57 (8.7)	133.67 (14.8)	165.45 (5.0)	167.69 (7.0)
Height SDS	0.52 (1.2)*	–0.42 (1.3)*	–0.59 (0.7)	–0.19 (1.1)
Weight (kg)	33.03 (9.1)	32.16 (11.2)	59.46 (8.2)	56.73 (9.8)
Weight SDS	1.75 (1.8)	0.49 (1.8)	0.40 (1.3)	0.01 (1.2)
BMI (kg/m^2)	18.65 (4.0)	17.58 (3.8)	21.75 (3.1)	20.06 (2.4)
BMI SDS	2.10 (2.5)	0.94 (2.2)	0.77 (1.5)	0.02 (1.0)
Waist:hip ratio	0.84 (0.04)	0.86 (0.06)	0.77 (0.1)**	0.72 (0.1)**
Subscapular skinfold SDS	2.51 (4.4)	0.71 (3.0)	3.05 (3.4)*	0.41 (1.2)*
Triceps skinfold SDS	2.12 (2.2)	1.31 (2.8)	0.60 (1.1)	0.32 (1.2)
Systolic BP (mmHg)	102.65 (9.0)	104.00 (8.9)	117.62 (7.4)	109.73 (14.0)
Systolic BP SDS	0.53 (0.9)	0.41 (0.9)	0.79 (0.6)	0.11 (1.2)
Diastolic BP (mmHg)	67.25 (8.2)	70.00 (10.0)	75.95 (5.6)*	70.00 (7.8)*
Diastolic BP SDS	0.72 (0.8)	0.80 (1.0)	0.85 (0.5)*	0.28 (0.7)*
Leptin (μg/L)	4.01 (5.8)	5.53 (6.8)	7.99 (6.3)*	3.6 (3.1)*
Insulin (mIU/L)	13.88 (3.9)	14.54 (7.5)	17.00 (9.8)	14.28 (3.7)
SHBG (nmol/L)	62.02 (22.8)	69.18 (20.0)	31.18 (13.2)**	56.15 (20.3)**
Estradiol (pmol/L)	90.33 (49.0)*	132.76 (66.1)*	370.48 (221.1)	358.51 (171.2)
Testosterone (nmol/L)	0.30 (0.1)*	0.21 (0.1)*	1.71 (0.7)**	1.00 (0.4)**
FAI	0.60 (0.4)	0.36 (0.3)	6.11 (3.9)**	2.06 (1.1)**
DHEAS (μmol/L)	3.2 (1.5)**	1.30 (1.2)**	6.95 (2.5)*	4.99 (2.3)*
17-OHP (nmol/L)	2.17 (1.2)	1.46 (0.98)	4.10 (2.4)	3.89 (2.4)
IGF-1 (nmol/L)	24.76 (5.6)	23.26 (6.5)	38.53 (8.2)	39.74 (7.0)

Comparison girls for premature adrenarche group are denoted as "controls-1", and for hirsutism group as "controls-2" (data are shown as a mean with SD in parenthesis. Significant differences between patients and controls are marked as * $p<0.05$, ** $p<0.005$). Abbreviations: SDS – standard deviation score; BP - blood pressure; SHBG - sex hormone-binding globulin; FAI – free androgen index; DHEAS - dehydroepiandrosterone sulfate; 17-OHP – 17-hydroxyprogesterone; IGF-I – insulin-like growth factor-I.

with hirsutism ($r=-0.46$; $p<0.05$).

Analyzing all girls, leptin levels significantly positively correlated with weight SDS, BMI SDS, skinfold thickness SDS at triceps and especially at subscapular sites ($r=0.48$, $r=0.49$, $r=0.57$, $r=0.78$, respectively; $p<0.001$). Correlations of leptin with insulin and SHBG levels are represented in Fig. 1 and Fig. 2. There was a weak positive relationship between leptin and serum E2, DHEAS and FAI levels ($r=0.25$, $r=0.26$, $r=0.27$, respectively; $p<0.05$). Interestingly, leptin levels correlated significantly with both skinfold thickness SDS in hirsute adolescents and girls with PA, and with triceps skinfold thickness SDS in younger controls. By multiply linear regression, 76.0% in variations of leptin levels could be explained by subscapular skinfold thickness SDS, SHBG, insulin, and DHEAS levels in all analyzed girls ($p<0.001$).

SHBG levels were also significantly ($p\leq0.001$) negatively correlated with subscapular skinfold thickness ($r=-0.57$), DHEAS ($r=-0.66$), T ($r=-0.54$), IGF-I ($r=-0.41$), E2 ($r=-0.39$) levels in all girls. Weaker correlations between SHBG and weight SDS, BMI SDS, triceps skinfold SDS and systolic BP SDS were found. By linear regression, 68.9% in variations of SHBG levels could be explained by leptin, T, and DHEAS levels in all analyzed girls ($p<0.001$).

Birth weight SDS did not show relationship with the investigated hormone levels in all children except in premature adrenarche group (Fig. 3), however there was no association between age and DHEAS in this

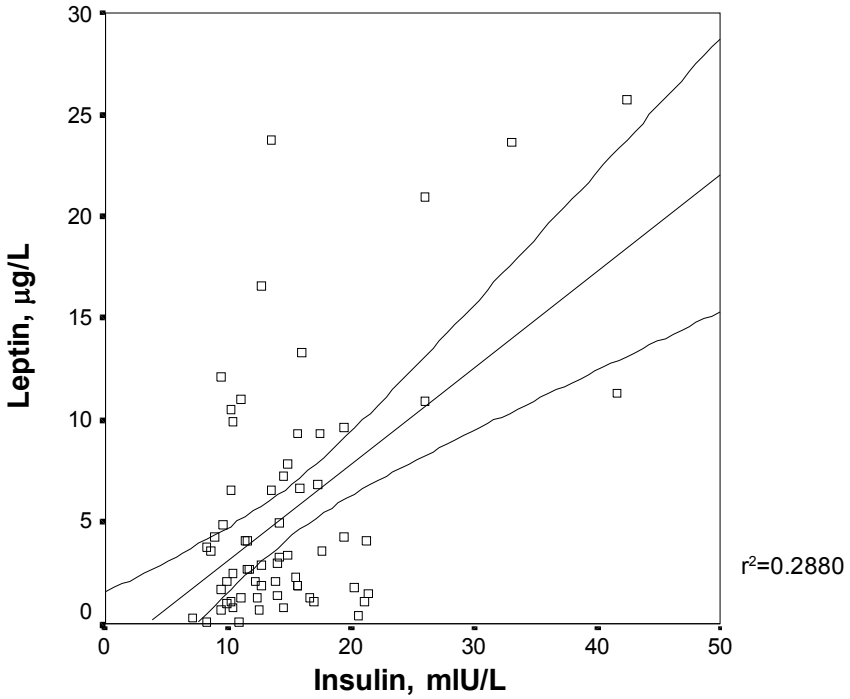

Fig. 1. **Correlation of leptin with insulin levels in all girls** (r=0.54, p<0.001)

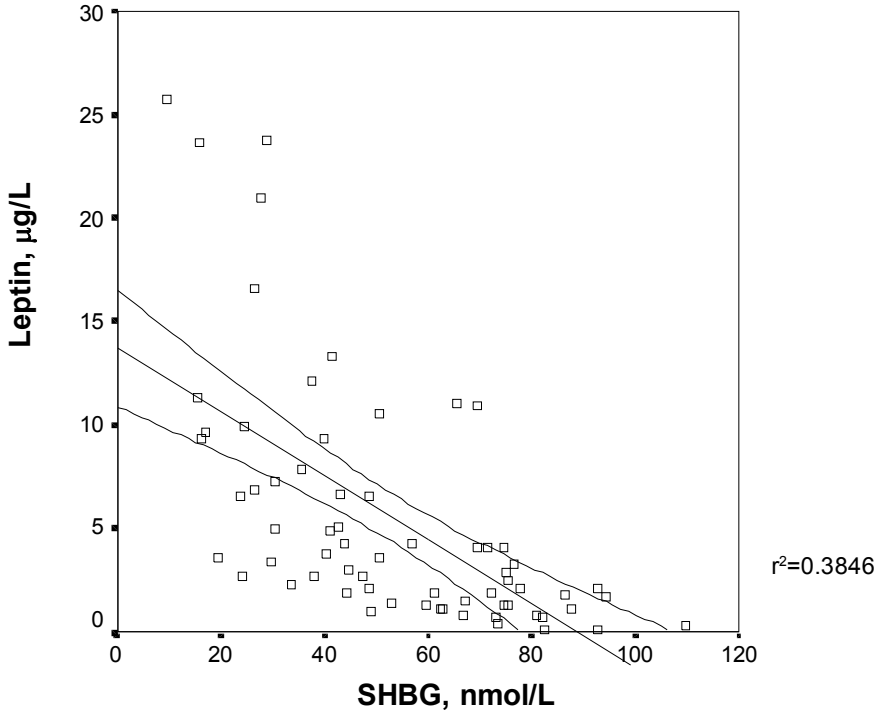

Fig. 2. **Correlations of leptin with sex hormone-binding globulin (SHBG) levels in all girls** (r=–0.62, p<0.001)

group. A positive relationship between birth weight SDS and weight SDS in controls (r=0.59 and r=0.75 in "group-1" and "group-2", respectively; p<0.05), and with height SDS in controls (r=0.59 and r=0.67 in "group-1" and "group-2", respectively; p≤0.05) was found.

Discussion

Fasting serum insulin levels were not different in any of the four groups. However, serum daytime insulin levels vary widely in humans. Chronic hyperinsulinemia can be represented by such symptoms as *acanthosis nigricans* (20), and decreased serum SHBG

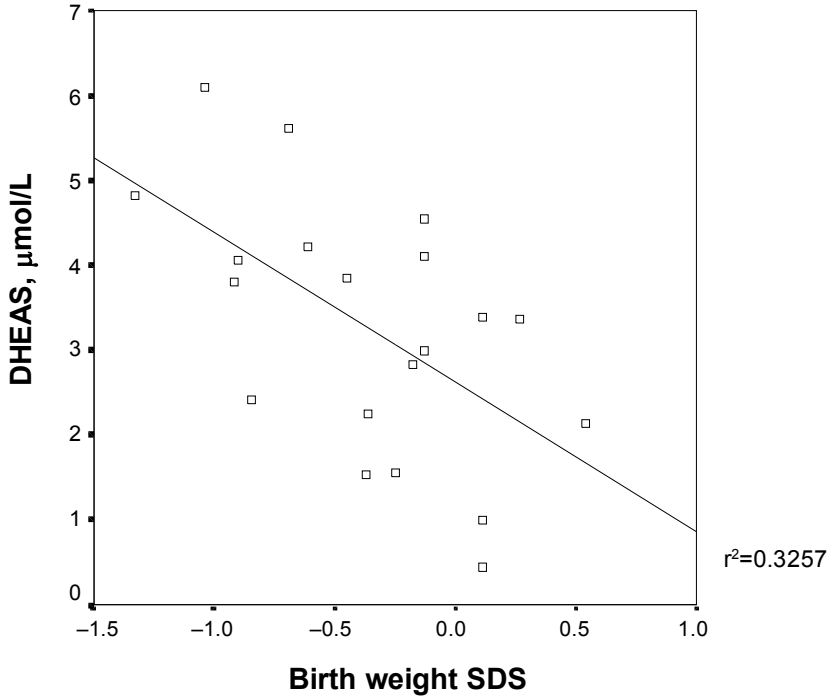

Fig. 3. **Basal serum dehydroepiandrosterone sulfate (DHEAS) values are plotted against birth weight standard deviation score (SDS) in girls with premature adrenarche** (r=–0.57, p<0.001)

levels (11). We found a positive association between fasting insulin and leptin levels, and negative association between insulin and SHBG, and between leptin and SHBG, especially in the group of adolescent girls with hyperandrogenism. Therefore, we can speculate that when these patients had significantly (almost two-folds) lower SHBG levels and higher leptin levels, their insulin levels during the day should be higher than in comparison girls. No significant differences between patients and controls in terms of frequency of presence of *acanthosis nigricans* were found, however, this might be attributable to a small study size. This group of girls also had significantly higher waist-to-hip ratio and subscapular (but not triceps) skinfold thickness than the comparison group, what implicates bigger amount of abdominal fat, therefore higher insulin resistance. Whether leptin can be "blamed" for insulin resistance and increased risk for developing PCOS, or the *vice versa*, needs further elucidations.

Hyperinsulinemia and insulin resistance has been consistently reported in obese and lean women with functional ovarian hyperandrogenism, PCOS patients, and hyperandrogenic adolescents, although some reports failed to find a linear relationship between hyperinsulinemia and hyperandrogenism in hirsute patients (6). We found significant linear correlations between fasting insulin levels and androgen levels (T and 17-OHP) in hirsute adolescent girls.

Leptin levels were significantly higher in hirsute patients than controls, but no difference in leptin levels was seen in PA girls *vs.* comparison group. As could be expected, subscapular skinfold thickness, insulin, DHEAS and SHBG were significant predictors of leptin levels in the studied girls. Leptin levels in girls increase with age (21), however, our data did not demonstrate that. Significant associations were found between leptin and insulin resistance in children by some recent studies (22). Leptin has a specific role in stimulating the activity of enzymes essential for the synthesis of adrenal androgens (23). A significant ratio of women with PCOS exhibits leptin levels that are higher than expected for their BMI, free testosterone, and insulin resistance. The higher levels of leptin are likely to be implicated in the pathogenesis of various PCOS cases (21).

Subscapular skinfold thickness and waist-to-hip ratio are good field indicators of intra-abdominal fat deposition (24). According to literature, low serum SHBG levels were associated not only with hyperinsulinemia but also with high BMI and waist-to-hip ratio as well as with high serum levels of leptin and low serum levels of HDL-cholesterol (25). Therefore, our adolescent girls with hyperandrogenism having higher waist-to-hip ratio, thicker subscapular skinfold, lower SHBG levels, higher leptin levels, and higher diastolic blood pressure than healthy adolescent girls, show higher risk for metabolic abnormalities and cardiovascular diseases.

Girls with premature adrenarche did not show any signs for higher insulin resistance than the comparison group. We also did not find significant differences in birth weight SDS between both groups of patients *vs.* controls. However, relationship between lower birth weight SD score and higher DHEAS levels in girls with premature adrenarche was demonstrated, when there was no confounding correlation between age and birth weight SDS. This is consistent with reported results about DHEAS levels in young children before adrenarche, which correlated inversely with weight at birth, indicating a relationship with fetal growth (26).

Girls with clinical hyperandrogenism had significantly earlier onset of menarche than controls and general population, as it is known that mean age of menarche of Lithuanian girls is 13–13.5 years in cities and 13.5–14 years in rural areas (27). Higher circulating leptin levels are associated with a younger age at menarche (28). Earlier onset of menarche could implicate early and, perhaps, exaggerated puberty in these girls. Conflicting and sparse results about the age of menarche and hyperandrogenism in adulthood are available from different populations. For instance, PCOS has been related to younger age of puberty and age of menarche (29), however, in one recent retrospective Dutch study, PCOS patients were significantly older at menarche (30).

Conclusions

Inverse correlation of DHEAS levels and weight SDS at birth indicates relationship between premature adrenarche in girls and fetal growth.

Higher leptin levels in adolescents with hyperandrogenism than in healthy girls show possible involvement of leptin in pathogenesis of hyperandrogenism.

Earlier onset of menarche in adolescents with hyperandrogenism than in general population indicates earlier or exaggerated puberty in this group.

Mergaičių, turinčių hiperandrogenizmo simptomų, hormonų kiekis kraujyje ir antropometriniai duomenys

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Raktažodžiai: hiperandrogenizmas, priešlaikinė adrenarchė, mergaitės.

Santrauka. Policistinių kiaušidžių sindromas moterims, manoma, prasideda brendimo metu. Darbo tikslas. Išanalizuoti mergaičių, turinčių priešlaikinę adrenarchę, ir paauglių, turinčių hiperandrogenizmo simptomų, serumo hormonų kiekį kartu su antropologiniais duomenimis, nes jos turi didesnę riziką susirgti policistinių kiaušidžių sindromu.

Medžiaga ir metodai. Tyrime dalyvavo 20 mergaičių, turinčių priešlaikinę adrenarchę (4,9–10,2 metų), 21 paauglė po menarchės, turinti hirsutizmą (13,3–17,8 metų); dvi kontrolinės grupės (n=13 kiekvienoje) panašaus amžiaus ir kūno masės indekso sveikų savanorių mergaičių ir merginų.

Rezultatai. Testosterono ir dehidroepiandrosterono sulfato kiekis kraujyje nustatytas didesnis visoms tiriamosioms palyginti su sveikomis mergaitėmis. Laisvų androgenų indeksas ir leptino kiekis kraujyje buvo reikšmingai didesnis, o lytinius hormonus surišantis globulinas mažesnis paauglėms, turinčioms hirsutizmą, palyginti su sveikomis merginomis. Gimimo svorio standartinio nuokrypio skaičius (SDS) buvo panašus visose keturiose grupėse. Dehidroepiandrosterono sulfatas neigiamai koreliavo su gimimo svorio standartiniu nuokrypiu mergaitėms, turinčioms priešlaikinę adrenarchę ($r=-0,57$; $p<0,001$), bet šio ryšio nenustatyta kitose grupėse. Visoms dalyvėms linijine regresija nustatyta, kad 76 proc. serumo leptino dispersiją galima paaiškinti subskapuliarinės odos klostės storio standartiniu nuokrypiu bei serumo lytinius hormonus surišančio globulino, insulino ir dehidroepiandrosterono sulfato kiekiu. Mergaičių, turinčių hirsutizmą, vidutinis menarchės amžius buvo jaunesnis negu sveikų paauglių (atitinkamai – 12,1±1,3 ir 13,5±1,3; $p=0,004$).

Išvados. Dehidroepiandrosterono sulfato kiekio serume ir gimimo svorio atvirkštinė koreliacija rodo ryšį tarp mergaičių priešlaikinės adrenarchės ir vaisiaus augimo. Didesni leptino kiekiai paauglėms su hiperandrogenizmu palyginti su sveikomis merginomis rodo galimą leptino dalyvavimą hiperandrogenizmo patogenezėje.

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