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Hyperandrogenism in Adolescent Girls—May Serum Androgen Concentration Be Related to Macronutrient Intake? †

Małgorzata Mizgier [1,*], Grażyna Jarząbek-Bielecka [2], Elżbieta Jodłowska-Siewert [3], Natalia Wendland [4] and Justyna Opydo-Szymaczek [4]

[1] Dietetic Department, Poznan University of Physical Education, Faculty of Physical Culture in Gorzów Wlkp., Gorzów Wielkopolski 66-400, Poland
[2] Department of Perinatology and Gynecology, Division of Developmental Gynecology and Sexology, Poznan University of Medical Sciences, Poznan 60-535, Poland
[3] Department of Computer Science and Statistics, Poznan University of Medical Sciences, 60-806 Poznan, Poland; youleadmeastray@gmail.pl
[4] Department of Pediatric Dentistry, Chair of Pediatric Dentistry, Poznan University of Medical Sciences, Bukowska St., Poznan 60-812, Poland
* Correspondence: m.mizgier@awf-gorzow.edu.pl; Tel: +48-95-72-79100; Fax: +48-61835-50-99
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Abstract: The cause of hyperandrogenism in adolescent girls, which is typical for polycystic ovary syndrome (PCOS) is still not fully understood. The aim of the study was to check whether there is a correlation between macronutrient intake and testosterone, androstenedione, dehydroepiandrosterone-sulfate (DHEA) and the sex hormone binding globulin (SHBG) serum concentration in adolescent girls. The study included Caucasian girls aged 14–18 years: 61 girls with PCOS and 35 girls from the control group. A fasting blood sample was obtained for measurement of serum dehydroepiandrosterone (DHEA-S), sex hormone-binding globulin (SHBG), total testosterone (T) and androstenedione (A). Macronutrient intake was assessed using the three-day food record method. There was a significant positive correlation between total fat, monosaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA), and T and A, and between saturated fatty acids (SFA) and T. Fiber showed a negative correlation with the concentration of A. SHBH concentration showed a positive correlation only with total dietary protein. ClinicalTrial.gov Identifier: NCT04738409.

Keywords: adolescents; adolescent girls; hyperandrogenism; polycystic ovary syndrome; macronutrients; diet; nutrition

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1. Introduction

Polycystic ovary syndrome (PCOS) affects 5–10% of women of reproductive age and is the most common endocrinopathy diagnosed in this group. At the same time, it is one of the most frequently diagnosed endocrinopathy in obese women. About 50% of women with PCOS are overweight or obese. Mainly typical for PCOS abdominal obesity leads to carbohydrate and lipid metabolism disorders, inflammation, and increases the risk of developing hypertension. The metabolic profile observed in PCOS is very similar to that found in metabolic syndrome. In the group of women diagnosed with PCOS, obesity, type 2 diabetes, atherosclerosis cardiovascular failure and osteoporosis, as well as infertility are significantly more frequent [1–3].

Polycystic ovary syndrome (PCOS) is also one of the most common causes of hyperandrogenization in women. The consequences of the hormonal changes include hirsutism, acne and/or seborrhea, androgenic alopecia, which occurs in both adult and

adolescent women [4,5]. Despite several decades of research into the etiopathogenesis of PCOS, the exact causes of PCOS and the mechanism leading to the development of this syndrome have not been fully elucidated yet. In many cases, insulin resistance is found, which in turn leads to hyperinsulinemia, which in turn contributes to the stimulation of the ovaries and/or adrenal glands to increase the production of androgens [6,7].

The studies conducted so far have mostly included adult female patients [1–4]. This makes it difficult to assess the dynamics of PCOS development and to identify early risk factors accompanying the occurrence of this syndrome [8]. In recent decades, publications have been appeared the in the literature on the clinical picture of PCOS in adolescent girls [5,9,10]. That is why the current treatment profile for PCOS includes therapy associated with lifestyle changes, including weight loss and diet modification, to improve insulin sensitivity and prevent PCOS-related complications [11]. But since there is not known specific model of diet and macronutrient profile that could be directly related to androgen levels, lifestyle-related PCOS etiological factors, including diet, are still being sought [10,12–14]. Therefore, the aim of this study is to assess the relationship between the consumption of dietary macronutrients: saturated fatty acids (SFA) and monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA), cholesterol, protein, carbohydrates, including fiber, and the concentration of androstenedione (A), testosterone (T), DHEA-S, and also SHBG.

2. Methods

The study which was carried out from 2018 to 2020, included sixty-one Caucasian girls, patients of the Gynecology and Perinatology Medical Clinic at the Gynecology and Obstetrics Hospital of Poznan University of Medical Sciences, diagnosed with PCOS, according to the Rotterdam criteria [15], aged 15–17 years and thirty-five girls of the same age from the Department of Developmental Gynecology and Sexology of Poznan University of Medical Sciences, in whom PCOS was excluded.

The Bioethics Committee at the Poznan University of Medical Sciences approved this research (resolution no. 553/18, annex no. 161/20) conducted in accordance with the Helsinki Declaration. The girls and their parents gave their informed consent for inclusion before they participated in the study. This trial was registered at clinicaltrails.gov as NCT04738409.

The exclusion criteria were: medications of continuous use, the use of hormonal therapy, antibiotics, supplements in the past three months, smoking, presence of any chronic and endocrine diseases.

Biochemical parameters, including total testosterone, DHEA-S, SHBG were measured in the morning after overnight fasting, were performed in the central hospital laboratory.

Total testosterone, DHEA-S, SHBG were measured by the electrochemiluminescence (ECLIA) immunoassay method (Elecsys) (Roche Diagnostics GmbH, Mannheim, Germany). The details were described previously [16–18].

Serum concentrations of the androstenedione was measured with DRG Androstenedione ELISA kit (enzyme linked immunosorbent assay) in the Chair Department of Medical Chemistry and Laboratory Medicine of Poznan University of Medical Sciences.

All girls underwent general clinical assessment (hirsutism and puberty assessment, the presence of any symptoms of hormonal disturbances), gynecological examination with ultrasound, and anthropometric assessment (body weight and high). The test and examination were realized from 3–5 day of the follicular phase, apart from patients with secondary amenorrhea.

The patient's diet were evaluated using the current quotation method: 3-day food record, described previously [16,19].

PQStat v.1.8.0 software was used for statistical analysis. Descriptive statistics were presented as median and quartiles or mean and standard deviation (SD). The Shapiro-Wilk test was used to verify normal distribution of quantitative data. For the comparison

of two groups, the unpaired t-test was used, for normally distributed data and the Mann-Whitney test for data that was not normally distributed or ordinal data. *p* value and r were computed for each variable. For analyzing correlations, the Spearman's rank correlation coefficient was calculated. All analyses were considered as statistically significant when $p \leq 0.05$.

3. Results

The PCOS group differed significantly from the control group in the androstenedione (median: 3.4 vs. 1.85 ng/mL, $p = 0.000004$) and total testosterone serum concentration level (median: 1.7 vs. 1.01 nmol/L, $p = 0.00001$). There were no significant differences between the group in the serum concentration level of DHEA-S and SGBG.

A significant correlation was found between androstenedione serum concentration and total fat, monosaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA) intake ($p = 0.02$, r = 0.24; $p = 0.007$, r = 0.27; $p = 0.03$, r = 0.22, respectively). While fiber intake negatively correlated with androstenedione ($p = 0.02$, r= −0.24). There were also observed correlation between total testosterone and total fat, SFA, MUFA and PUFA intake ($p = 0.001$, r = 0.33; $p = 0.02$, r = 0.24; $p = 0.001$, r = 0.32; $p = 0.01$, r = 0.26, respectively). SGBG concentration showed a positive correlation only with total dietary protein intake ($p = 0.03$, r = 0.23). We did not find correlation between DHEA-S concetration and macronutrients intake Table 1.

Table 1. Correlations among serum androgen level and macronutrient intake in adolescent girls.

Variables	Total Protein [g]	Total Fat [g]	Total Carbohydrates [g]	Fiber [g]	Plant Protein [g]	SFA [g]	MUFA [g]	PUFA [g]	Cholesterol [mg]
Androstendion *p* value	0.380	***0.020***	0.865	***0.015***	0.303	0.166	***0.007***	***0.034***	0.718
r	−0.091	***0.238***	−0.018	***−0.248***	−0.106	0.142	***0.272***	***0.216***	−0.037
Total testosteron *p* value	0.801	***0.001***	0.092	0.310	0.793	***0.017***	***0.001***	***0.012***	0.980
r	−0.026	***0.327***	0.173	−0.105	0.027	***0.242***	***0.321***	***0.256***	0.003
DHEA-S *p* value	0.552	0.855	0.505	0.987	0.853	0.459	0.725	0.525	0.786
r	−0.062	0.019	0.069	0.002	−0.019	−0.076	0.036	0.066	−0.028
SHBG *p*-value	***0.026***	0.631	0.327	0.101	0.288	0.220	0.747	0.511	0.180
r	***0.227***	0.050	0.101	0.168	0.110	0.126	−0.033	−0.068	0.138

Abbreviations: DHEA-S—dehydroepiandrosterone; SHBG—sex hormone-binding globulin; SFA, saturated fatty acid; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; the r coefficients are Spearman's correlation coefficients. All the *p*-value marked in italics were statistically significant.

4. Discussion

In recent years, the results of research have been published showing the role of diet in PCOS mainly through the treatment of overweight, obesity and insulin resistance [10,12–14]. However, it is still difficult to assess which macronutrient profile in the diet is the most effective in the treatment of girls with PCOS and which of them directly affects the concentration of androgens and SHBS (influences on total androgen level). Therefore, the aim of our research was to check whether there is correlation between the concentrations of androstenedione, testosterone, DHEA-S and SHBG and certain macronutrients of the diet.

The results of previous studies show that there is a correlation between a specific diet and testosterone level. Research by Hu et al. confirmed presence of a correlation between the lower concentration of this hormone in men and the preference to eat the Western diet. The so-called Western model of nutrition concerned the consumption of, inter alia, low-

fiber products (including confectionery, cookies, pasta), and not including high-fiber products like vegetables, including dark green. [20]. In turn, Gower et al. proved that a low-carbohydrate diet contributes to a reduction in the testosterone level [21]. The studies by Douglas et al. [22] and Moran et al. [23] did not confirm this relationship. Nevertheless, in our study there was no correlation between this hormone and carbohydrate consumption, while an inverse correlation was observed between fiber intake and androstendione.

In our research, a significant correlation was also found between androstenedione and intake of total fat, MUFA and PUFA. Total testosterone, like androstenedione showed a significant correlation with total fat, MUFA and PUFA intake as well as with SFA. Azadi-Yazdi et al. proved that a low-fat and low-cholesterol DASH diet promotes the reduction of androstenedione levels and an increase in SHBG levels in adult PCOS patients [24].

On the other hand, a high-protein diet is associated, in particular, with an increase in SHGB concentration, as demonstrated by the study by Vermuelen et al. on adult men [25] In our study of adolescent girls, the SGBG concentration also showed a positive correlation with dietary protein.

Our research aimed to identify the relationship between the concentration of androgens and SHBG, and macronutrients intake. The results obtained indicate that there is a relationship between the levels of sex hormones, as well as SHBG, and the specific macronutrients composition of the girls' diet. Randomized control studies would be necessary to confirm these findings as hyperandrogenism-related dietary factors.

Further research should focus on identifying a nutrition model that can be used by family doctors, pediatricians, and pediatric gynecologists in the non-pharmacological treatment of girls with PCOS. It will also enable early preventive actions in girls with an increased risk of PCOS.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee at the Poznan University of Medical Sciences, protocol code no. 553/18, annex no. 161/20

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The datasets may be available by the corresponding author on reasonable request.

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