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Reduction in the Free Androgen Index in Overweight Women After Sixty Days of a Low Glycemic Diet

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ABSTRACT

Background Hyperandrogenism is among the most common endocrine disorders in women. Clinically, it manifests as hirsutism, acne, and alopecia. A healthy lifestyle, including nutritious dietary patterns and physical activity, may influence the clinical manifestation of the disease. This study determined the effect of a low-glycemic index anti-inflammatory diet on testosterone levels and sex hormone-binding globulin (SHBG) and clinical symptoms in hyperandrogenic women at their reproductive age.

Methods The study included 44 overweight and obese women diagnosed with hyperandrogenism. The anthropometrics (weight, height, body mass index, waist circumference, hip circumference), physical activity, and dietary habits were assessed using valid questionnaires, scales, stadiometer, and tape meter. The significant p-value was <0.001. Serum testosterone and SHBG levels were measured using automated immunoassay instruments.

Results The intervention based on a low-glycemic index diet with anti-inflammatory elements and slight energy deficit decreased total testosterone levels ($p<0.003$), increased SHBG levels ($p<0.001$), and decreased the free androgen index (FAI; $p<0.001$). Post-intervention, overall well-being was much higher than in the pre-intervention period ($p<0.001$), and stress was diminished ($p<0.001$). Western nutritional patterns positively correlate with clinical hyperandrogenism progression, whereas several factors of the low-glycemic index diet with anti-inflammatory elements and slight energy deficit positively associate with reduced clinical hyperandrogenism symptoms.

Conclusions In overweight and obese women, proper selection of diet, introduction of moderate physical activity, and reduction in weight, stress factors, and alcohol consumption translate into several positive effects, including reduced FAI and symptoms such as acne, hirsutism, menstrual disorders, and infertility.

Introduction

Hyperandrogenism (androgen excess) is a common, heterogeneous, and endocrinal condition affecting 5–10 % of women in their reproductive age [1, 2]. Hyperandrogenism has several possible causes, including tumors of the adrenal or ovary, congenital or acquired adrenal hyperplasia, Cushing's disease, acromegaly, hyperprolactinemia, and various medications [1, 2]. However, there are also known clinical cases in which distinguishing specific causes related to androgen excess can be challenging. In women with hyperandrogenism, polycystic ovary syndrome (PCOS) is diagnosed in 80–85 % of cases [1, 3], making it the most common cause of androgen excess.

High heterogeneity in clinical manifestations is observed among women with androgen excess. For this reason, abnormalities of the hypothalamic-pituitary unit, the ovary, and the adrenal are usually described as the most probable, and primary pathogenesis involves the androgen excess [4–6]. Nowadays, it is well known that both environmental factors and insulin resistance have the most significant role in the pathogenesis of hyperandrogenism. Hyperinsulinemia induced by insulin resistance stimulates thecal androgen production and a decrease in hepatic sex hormone-binding globulin (SHBG). It is the strongest hypothetical pathology of hyperandrogenism, proved in many previous and recent reports [7–10]. Women with hyperandrogenism are at higher risk of many health problems, including hypertension, coronary heart disease, obesity, type 2 diabetes, gestational diabetes, anovulatory infertility, spontaneous abortion, and endometrial or breast cancer [10–13].

Moreover, the clinical phenotype of an individual patient may change over time [1]. Thus, hyperandrogenism diagnosis depends on clinical manifestation determination and biochemical androgen excess measurements. Obesity is a critical factor that worsens the clinical consequences of androgen excess, such as reduced frequency of ovulation, irregular menstrual cycles, reduced infertility, and polycystic ovaries. Obesity is also strongly related to high levels of male hormones such as testosterone. An increase in testosterone level causes hirsutism, defined as excessive male-pattern terminal hair growth [14, 15]. This unwanted facial or body hair growth is 'the most common clinical manifestation of hyperandrogenism. Hirsutism is diagnosed in about 80 % of women who suffer from androgen excess and is strongly related to psychological morbidity that negatively influences the quality of life of hyperandrogenic women [16]. The diagnosis of hyperandrogenism is based on hirsutism and includes other clinical criteria such as acne, androgenic alopecia, and virilization. Androgenic alopecia also worsens the quality of life, influencing psychological well-being and self-esteem [17]. Elevated circulating androgen levels cause virilization, a relatively uncommon clinical finding of hyperandrogenism [18]. However, virilization is characterized by many clinical features, such as deepening of the voice, increasing muscle mass, and decreasing breast size, which also influences psychological morbidity and can worsen anxiety and depression [18].

The primary management of hyperandrogenism is based on a healthy lifestyle, which consists of a nutritious diet, regular exercise, and achieving and maintaining a healthy weight. However, limited reports have explained the influence of diet and lifestyle modifications on the clinical manifestations of hyperandrogenism. Studies have mainly focused on managing the most common related causes or clinical symptoms and have shown the benefits of weight loss in women who are obese or overweight and with PCOS [19–22]. According to International Evidence-Based Guidelines, lifestyle interventions are considered to be the primary early management strategy for women with hyperandrogenism and PCOS. Lifestyle interventions are traditionally defined as those designed to improve dietary intake or physical activity through appropriate behavioral support.

This study aimed to assess the associations between lifestyle habits and dietary patterns in women with diagnosed hyperandrogenism. Then, the effectiveness of lifestyle modifications was determined, especially the influence of a reduced glycemic load diet and anti-inflammatory food intervention on the clinical manifestations of hyperandrogenism and anthropometry and biochemical results.

Material and Methods

Forty-four women of reproductive age (18–49 years) were enrolled in the study group. Fourteen women were control subjects. Informed consent to participate in this study was obtained from patients and healthy controls. All participants had the right to receive information and ask questions before, during, and even after the study. Four women resigned after 7 days of dietary intervention and 10 more women did not start the program when given the dietary advice. However, these 14 women gave their written consent to stay involved in the study as the control group. The 30 patients and 14 controls were under the care of a consultant gynecologist and endocrinologist from the Jagiellonian University Hospital in Krakow. The certified dietitian adapted and managed a dietetic and sports activity intervention. The inclusion criteria for the study were: age 18–49 years, no use of hormonal contraception for at least 6 months (all women involved in this study declared no use of contraception for one year before the study participation), and other health problems such as excessive body weight (body mass index [BMI] > 25 kg/m^2), excessive body hair, acne especially in the jaw area, irregular or lack of menstrual cycles for the last 6 months, hair loss with characteristic male pattern curves (Ferriman-Gallway score ≥ 8). Free androgen index (FAI) was considered one of the inclusion criteria. The FAI cut-off value was > 5 based on the recommendations for the Polish population constituted by the Polish Society of Endocrinology, the Polish Society of Gynecologists and Obstetricians, and the Polish Society of Gynecologic Endocrinology [23]. Menstrual problems were assessed according to the observations made and described by women from the study group. The menstrual problems or the lack of menstruation were assigned when periods occurred less than 25 days or more than 35 days apart, missing three or more periods in a row, much heavier or lighter than usual menstrual flow, periods lasting longer than seven days or were accompanied by pain, cramping, nausea, or vomiting, or when bleeding or spotting happened between menstrual periods. Exclusion criteria were age below 18 or more than 49 years, use of hormonal contraception within 6 months of study entry, pregnancy, congenital adrenal hyperplasia, Cushing's syndrome, hyperprolactinemia, and lack or withdrawal of consent to participate in the study.

▶ **Table 1** Characteristics of dietetic intervention.

Nutritional component	Nutrients	Potential effect
Carbohydrate products	Oatmeal, buckwheat groats, buckwheat flour, pearl groats, couscous groats, brown rice, quinoa, durum wheat, and pasta cooked al dente.	Avoiding carbohydrates with a high glycemic index can reduce the risk of endocrine disruption associated with hyperandrogenism.
Protein/ plant protein	Natural yogurt, cottage cheese, camembert cheese, cream cheese, cottage cheese, mozzarella cheese, goat cheese, feta cheese, 2 % milk, buttermilk, and kefir, chickpeas, lentils, beans, and animal protein sources, such as poultry meat (chicken, turkey), fish (cod, salmon, tuna), eggs, and shrimp.	Including more plant protein can lower androgen levels in women with PCOS and hyperandrogenism.
Fat	Avocados, pumpkin seeds, flax seeds, sunflower seeds, chia seeds, walnuts, cashews, hazelnuts, Brazil nuts, almonds, and vegetable fats such as canola oil, olive oil, and flaxseed oil	The fat intake should be in the proportions between 20 % and 35 % of total calories. High-fat diets, especially when coupled with nutrient excess, can trigger lipid accumulation in both fat and non-fat tissues.
Omega-3 fatty acids	Avocados and fatty fish such as salmon, seeds, and vegetable oils (canola oil, flaxseed oil, and olive oil).	Supplementation with these acids can lower testosterone levels in overweight and obese women and regulate menstruation
Vegetables, fruits, vitamins, minerals and fibers	Green and red vegetables such as red bell pepper, tomato, cherry tomato, broccoli, bean sprouts, lamb's lettuce, spinach, arugula, and lettuce accounted for the most significant proportion; berries with high anti-inflammatory potential, such as strawberries, raspberries, blueberries, and blackberries.	Increasing fiber intake can lower androgen levels and decrease free testosterone. Magnesium supplementation can lower testosterone and dehydroepiandrosterone-sulfate levels in women with hyperandrogenemia. Zinc has anti-androgenic effects and inhibits androgen production, and its deficiency can lead to endocrine disruption. Low vitamin D levels can predispose to insulin resistance and metabolic disorders

Dietetic intervention

A low glycemic index diet with anti-inflammatory elements and a slight energy deficit was applied in this study. Based on the literature, this type of diet can effectively affect the treatment of hyperandrogenism. The consumption of foods with a low glycemic index, such as a diet, helps keep blood glucose levels stable, which reduces insulin secretion. Reducing insulin levels is key to the treatment of hyperandrogenism, as it helps reduce the production of androgens by the ovaries, which can ultimately alleviate the symptoms of this condition. In addition, an anti-inflammatory diet reduces inflammation in the body that may be associated with hyperandrogenism, which aids in the comprehensive treatment of this disease [24–26]. The two-month, low glycemic index diet with anti-inflammatory elements and slight energy deficit was prepared and advised to all participants. The detailed characterization of diet components with potential influence is described in ▶ **Table 1**. The diets were in the calorie range of 1,600 to 1,900 kcal and were matched to the needs of patients in the study and control groups. The calories of the diets were adjusted, considering the total energy requirements and physical activity, general lifestyle, and eating habits. The product was considered to be of low glycemic index (GI) when its GI was less than 55 compared to products with an average GI, with values between 56 and 69, and those with a high GI ≥ 70. The assessment of the GI of the food products was based on the GI values of more than 2,480 individual food products (available in the online-only appendix), characterized by Fiona et al. [27]. The diet included a reduced intake of carbohydrates at approximately 45–50 % of the caloric requirements (200 g of carbohydrates in the 1600 kcal diet, 213 g in the 1700 kcal diet, and 238 g in the 1900 kcal diet). The intake of saturated fat was reduced to approximately 10 % (53 g of fat in the 1600 kcal diet, 57 g in the 1700 kcal diet, and 95 g in the 1900 kcal diet). For a higher protein intake, at approximately 20–30 % energy throughout the day, translated to 80 g protein in the 1600 kcal diet, 85 g in the 1700 kcal diet, and 95 g in the 1900 kcal diet. Dietary fiber intake in all diets (at 1600, 1700, and 1900 calories) was 40 g. The daily menus included four meals for the 1600 and 1700 kcal diets and five meals for the 1900 kcal diet; in the first two diets, the percentage distribution of energy was breakfast: 30 %, second breakfast: 15 %, lunch: 35 %, and dinner: 20 %. In the highest caloric diet, the energy distribution was breakfast: 25 %, second breakfast: 15 %, lunch: 30 %, afternoon tea: 10 % energy, and dinner: 20 % of the total energy. Breakfast and lunch were the most important meals of the day. Thus, they included the essential portions of food. Women ate cocoa pancakes with blackberries and almonds, avocado and soft-boiled egg sandwiches, wrapped omelets with kale and sprouts, oatmeal with berries and chia seeds, buckwheat with green pear, quinoa with berries, and tuna and vegetable sandwiches. The second breakfast included light snacks, such as sandwiches with homemade hummus and vegetables, pear and almond smoothie, country cheese with nuts and fruit, or chia pudding. For lunch, the participating women ate puff pasta with salmon and mushrooms, casserole with chicken and cauliflower, cod with vegetables, and buckwheat groats. Salads included red bean and tuna salad, pasta salad with cranberries and chicken, mini zucchini pizzas, buckwheat yogurt pancakes, and poultry strips in sesame with vegetables and yogurt sauce were often eaten for dinner.

Data collection

Data for dietary intake, health habits, and medical records were collected retrospectively (before dietetic intervention) and at the end of the study (post-dietetic intervention). The questionnaires were prepared based on the Food Frequency Questionnaires (FFQs), the most common and validated tool used in dietary surveys. The FFQs are a type of dietary assessment tool that attempts to capture the usual food consumption of an individual by querying the frequency at which the respondent consumed food items based on a predefined food list [28]. The FFQ was used in the context of specific food lists selected for this study. A questionnaire and medical interview were advised to collect the data mentioned above. Pre- and post-dietetic intervention data were compared to assess the influence of recommended diets and applied sports activities on anthropometrics, biochemistry, and changes in clinical symptoms. Physical and anthropometric parameters (weight, height, BMI, hirsutism) of all participants were measured. Body weight was taken using a high-precision digital scale, Charder MA601 (Charder Electronic, Taiwan). Height was determined using a high-precision digital stadiometer (Seca 242, Hamburg, Germany). BMI was calculated from the measured body weight and height by dividing weight [kg] by height [m^2] and calculated as kg/m^2. The individuals with a BMI >25 kg/m^2 were considered overweight, those with obesity had a BMI > 30 kg/m^2, while normal individuals had a BMI in the range of 18.5 to 24.9 kg/m^2 [29]. The measurements were taken in accordance with the criteria of the World Health Organization [30]. A physician specializing in gynecology and endocrinology graded hirsutism using the common modified Ferriman-Gallwey score (mFG) [31]. According to the mFG scale, hirsutism was diagnosed for scores > 5. To assess hirsutism, terminal hairs were scored in nine body areas, namely the upper lip, chin, chest, upper abdomen, lower abdomen, upper back, lower back, thighs, and upper arms. The clinical symptoms of hyperandrogenism were recorded at the beginning of the study and the end of the follow-up period. Blood samples were collected from all study participants after they fasted overnight between 7 and 9 AM during the first 5 days of the spontaneous menstrual cycles. Serum was collected and assayed to determine total testosterone, prolactin, cortisol, 17 hydroxy-progesterone, and serum hormone-binding globulin (SHBG) levels. The total testosterone, prolactin, cortisol, and 17 hydroxy-progesterone were measured based on electrochemiluminescence (ECL) technology on a biochemical autoanalyzer Cobas e 422 (Roche Diagnostics GmbH, Mannheim, Germany). SHBG was measured based on electrochemiluminescence in Elecsys 2010 (Roche Diagnostics GmbH, Mannheim, Germany). The free androgen index (FAI) was calculated based on total testosterone and SHGB concentration using the following formula: FAI = total testosterone [nmol/L]/SHBG [nmol/L] * 100. The intra-assay and interassay coefficients of variation of the aforementioned assays were all <10 %.

Statistical analysis

The SPSS software (version 16) was used to perform statistical analysis. The t-test method was applied for quantitative variables, presented as the mean (± standard deviation; SD). The qualitative variables were presented as the number (%) between the two groups. The chi-square method was used for the qualitative variables. The multivariate logistic regression model was used to examine the significant variables. The independent variables were determined using the backward method after adjusting for confounders. For classifying food products, the factor analysis model of main dietary components was used to determine the most significant food-related factors. The most significant food-related factors were entered into the univariate logistic regression model separately. Finally, the univariate analysis models were applied to the multivariate logistic regression model using the forward method to identify the independent risk factors. $P<0.05$ was considered statistically significant.

▶ **Table 2** Characteristics of patients and the differences between anthropometric, hormonal, and clinical variables pre- and post-intervention.

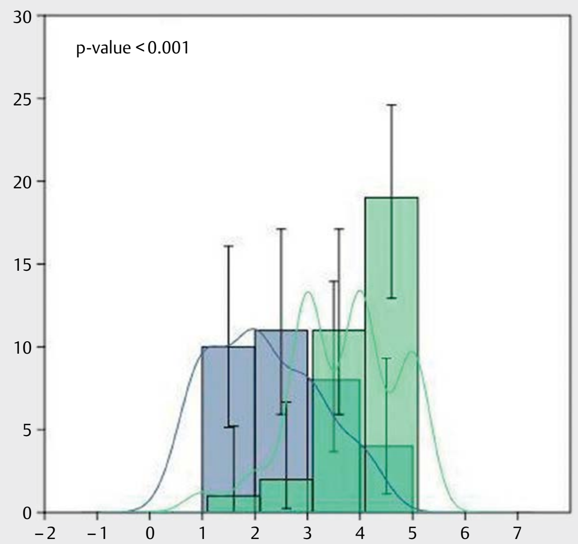
Variables	Pre-intervention	Post-intervention	P-value
	(N = 30)	**(N = 30)**	
	Mean	**Mean**	
Weight (kg)	82.65	79.03	0.350
BMI	29.61	27.85	0.070
Physical activity level	3.70	3.17	0.120
Overall well-being	2.23	3.52	**0.001**
Total testosterone (ng/dL)	75.73	64.67	**0.001**
SHBG (nmol/L)	26.78	40.92	**0.001**
FAI	10.21	5.97	**0.001**
Abnormal menstruations	0.70	0.37	**0.009**
Acne	0.58	0.34	0.050
The lack of symptoms	0.47	0.10	**0.001**
Hair loss	0.35	0.17	0.100
Hirsutism	0.50	0.41	0.500
Sleep disturbance	2.97	2.62	0.100
Stress	2.41	3.10	**0.001**

BMI: body mass index; FAI: free androgen index; SHBG: sex hormone-binding globulin.

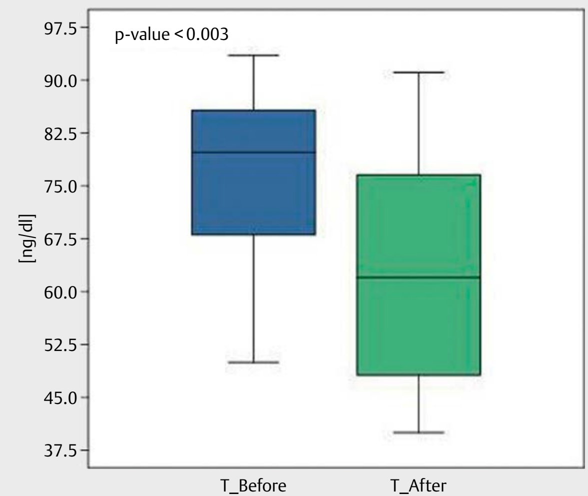
▶ **Table 3** The basic characteristics of the control group.

Variables	Pre-intervention	Post-intervention	P-value
	(N = 14)	**(N = 14)**	
	Mean	**Mean**	
Weight (kg)	82.65	83.03	0.520
BMI	29.61	29.69	0.710
Physical activity level	3.70	3.62	0.120
Overall well-being	2.23	2.25	**0.100**
Total testosterone (ng/dL)	75.73	76.1	**0.100**
SHBG (nmol/L)	26.78	27.01	**0.100**
Abnormal menstruations	0.70	0.67	**0.100**
Acne	0.58	0.54	0.100
The lack of symptoms	0.47	0.48	**0.100**
Hair loss	0.35	0.37	0.100
Hirsutism	0.50	0.51	0.100
Sleep disturbance	2.97	2.92	0.100
Stress	2.41	2.51	**0.100**
Overall well-being	2.23	2.25	**0.100**

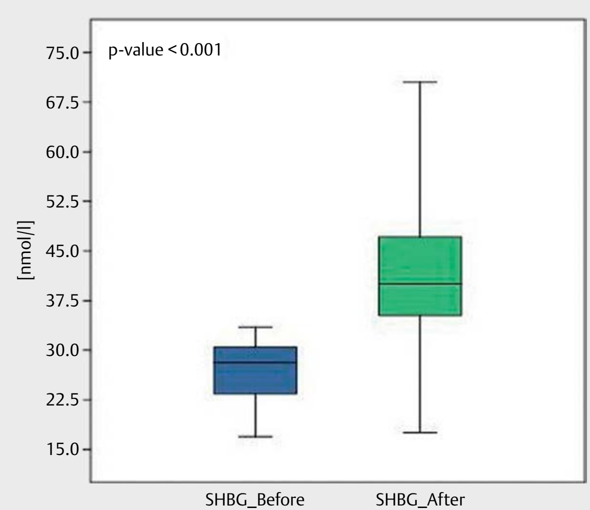
BMI: body mass index; FAI: free androgen index; SHBG: sex hormone-binding globulin.



► **Fig. 1** The level of reported general satisfaction was collected before and after the dietetic intervention. Data were collected using questionnaires based on a 1 to 5 points scale, where 1 means the lowest and 5 was the highest level of life satisfaction. The p-value was p<0,001.



► **Fig. 2** Total testosterone levels before (blue box) and after (green box) the dietetic intervention. Data are presented as ng/dl. The p-value<0.003.



► **Fig. 3** SHBG levels before (blue box) and after (green box) the intervention. Data are presented as nmol/l. The p-value<0.001.

► **Table 4** Pre- and post-dietetic intervention differences in dietary patterns. A lower value pre-intervention versus post-intervention means a greater tendency to consume a given product.

Product	**Pre-intervention**	**Post-intervention**	**P-value**
	(N=30)	**(N=30)**	
	Mean	**Mean**	
Pasta	2.94	1.89	**0.001**
Bread	2.11	1.31	**0.001**
Cereals	2.32	1.41	**0.001**
Supplements	3.23	2.38	**0.005**
Meat	2.00	2.55	0.059
Fish	3.58	3.17	0.053
Sweets	4.58	5.24	**0.006**
Legumes	4.03	2.55	**0.001**
Diary	1.85	2.07	0.249
Fatty products	2.70	2.34	0.170
Vegetables	2.00	1.17	**0.001**
Salad	2.91	2.38	**0.014**
Fruits	1.97	2.00	0.870
Nuts	3.62	2.03	**0.001**
Confection	2.76	3.10	**0.048**
Fast food	2.79	3.45	**0.003**
Chips	2.73	3.76	**0.001**
Sugar	2.17	3.89	**0.001**
Alcohol	2.88	3.27	**0.012**
Soft drinks	4.20	4.34	0.598
Coffee (black)	0.23	0.03	**0.017**
Milk	0.14	0.58	**0.001**

Results

Most women who participated in the study were aged between 18 and 23 years, whereas the minority was between 41 and 49 years old. The mean age of the participants was 31 years. The examined characteristics of the study participants are summarized in ► **Table 2** and **3**, respectively, for patients and healthy controls. The general satisfaction was assessed by asking the study group to rate their overall health-related well-being on a scale from 1 to 5, with 1 indicating poor well-being and 5 indicating excellent well-being (► **Fig. 1**.) The overall satisfaction presented as an increase in the mean value from 2.23 to 3.52 throughout the study ($p < 0.001$).

▶ **Table 5** A list of factors of significant correlation with observed changes in total testosterone and SHBG plasma levels.

Total Testosterone		SHBG	
Factor	**P-value**	**Factor**	**P-value**
Sleep disturbances	**0.006**	Sleep disturbances	**0.002**
Stress	**0.013**	Stress	**0.001**
Abnormal menstruation	**0.025**	Smoking	**0.023**
Increased androgens level	**0.014**	Increased androgens level	**0.001**
Physical activity	**0.006**	Abnormal menstruation	**0.047**
Overall well-being	**0.003**	Overall well-being	**0.001**
Fish consumption	**0.001**	Bread consumption	**0.001**
Vegetable consumption	**0.003**	Meat	**0.001**
Salad consumption	**0.009**	Fish	**0.001**
Nuts consumption	**0.019**	Salad consumption	**0.049**
Confection consumption	**0.003**	Fruits consumption	**0.023**
Sugar consumption	**0.001**	Alcohol consumption	**0.004**
		Soft drinks consumption	**0.001**

SHBG: sex hormone-binding globulin.

Pre- and post-dietetic intervention differences in food preferences are shown in ▶ **Table 4**. The observed changes were consistent with the applied dietary intervention and indirectly indicated a good level of compliance with the changes in the diet. As a result, a decrease in total testosterone levels and an increase in levels of SHBG, respectively, were observed (▶ **Fig. 2** and **3**). The differences between total testosterone and SHBG, measured before and after dietetic intervention, were statistically significant (▶ **Fig. 2** and **3**). Those changes correlated with the introduction of a low glycemic index diet ($p < 0.003$ and $p < 0.001$, respectively). The mean FAI values calculated before and after dietetic intervention in all hyperandrogenic women were 292 % and 172 %, respectively. The difference between FAI results before and after the dietetic intervention was statistically significant, and the p-value was 0.001. Additionally, the correlations between nutritional components, supplements, hyperandrogenic clinical symptoms, and testosterone, SHBG before and after the dietetic intervention were statistically analyzed. None of the consumed dietary supplements were associated with a decrease in total testosterone, with omega 6 acids supplementation correlating with higher concentrations of SHBG ($p < 0.001$). A decrease in total testosterone positively correlated with decreased symptoms of hirsutism ($p < 0.041$) and acne ($p < 0.012$). An increase in SHBG concentration correlated negatively with the prevalence of abnormal menstruation ($p < 0.010$) and infertility ($p < 0.012$). ▶ **Table 5** shows factors correlating significantly with decreased total testosterone levels and increased concentration of SHBG. These factors include probable causes (for example, dietary changes) and probable effects (for example, lower prevalence of hyperandrogenism symptoms) of observed results. Particularly, the selected factors differed among measured hormonal indicators.

Discussion

This study demonstrates a significant association between food-preferred status and dietary patterns with hyperandrogenism phenotype involving testosterone and SHBG levels. The results also showed an improvement in women’s well-being status after dietary intervention. A significant finding was the positive correlation between Western dietary patterns and the lack of physical activity with the progression of clinical hyperandrogenism in women before dietary intervention. Before starting the study, the food products used in the daily diet and individual meals differed significantly from the standards advised in the nutritional treatment of hyperandrogenism. After the dietary intervention, most women lost weight by following a reduced diet with a low glycemic index of anti-inflammatory nature. Similar observations were drawn in a study conducted by other researchers who showed that a low-calorie diet with a low glycemic index significantly affected weight loss and insulin resistance, and clinical and biochemical features of hyperandrogenism significantly improved after 6 months of using the diet [32]. In the current study, even a two-month dietary intervention and physical activity were enough to initiate positive effects in some of the clinical manifestations of hyperandrogenism and a decrease in testosterone and SHBG levels. Our study described similar, favorable effects over 2 months. Obtained results suggested that the long-term use of a low-IG diet could significantly reduce the symptoms of clinical hyperandrogenism and the problems related to menstruation and fertility. It is possible that hormonal regulation was achieved with the negative energy balance and the individual nutrients found in the advised diet. The introduction of omega-3 fatty acids decreased animal protein consumption in favor of plant-sourced protein, little sugar, and sweeteners. Including antioxidants and moderate physical activity may improve the overall health of women with PCOS and other endocrinopathies [33]. Our results are very similar to those of earlier published studies. Kazemi et al. [34] investigated the effect of the DASH diet (Dietary Approaches to Stop Hypertension, anti-inflammatory diet with low GI) on female hormonal parameters and the relationship with obesity. They showed that this way of nutrition translated into a decrease in insulin resistance, a decrease in hyperandrogenism symptoms and obesity phenotype, and an improvement in ovarian morphology [34]. Hormonal changes induced by dietary changes can be observed shortly after intervention onset. In one of the studies conducted among patients with endocrinopathy, there was a decrease in free testosterone in 5 out of 6 women by an average of 62 % after 90 min after eating a meal rich in complex carbohydrates and high in fiber [35]. Berrino et al. [36] investigated the relationship between the Mediterranean diet and hormonal changes. They observed a decrease in SHBG by an average of 25.2 % and a decrease in testosterone levels by an average of 19.5 % by switching from a typical Italian diet to a diet with a reduced glycemic index, a negative energy balance, and including anti-inflammatory elements. The women who followed this diet for 18 weeks noticed reduced body weight and improved lipid and hormonal parameters [36]. Women with hormonal problems often believe that accompanying diseases prevent them from achieving and maintaining proper body weight. Researchers studying the effect of diet on body weight in women with PCOS, particularly the hyperandrogenic type, often notice a relationship between the occurrence of the disease and the belief that it is difficult to lose body fat despite many attempts. Our study shows that introducing advised eating habits reduces body weight by an average of 1.3 kg per month. Physiologically, it is not clear why women with hyperandrogenism exhibit increased body weight. Women with hormonal problems may be predisposed to accumulate body fat, but this effect is usually caused by unhealthy eating habits and decreased physical activity. Before the dietetic intervention, most women in our study group were overweight or obese. Excessive body weight significantly affects SHBG and total testosterone [37]. The very change in eating habits often results in weight reduction, thus improving insulin sensitivity, removing excess testosterone, and alleviating symptoms caused by an increase in the level of this hormone. Our observations are consistent with those reported by Campbell et al. [38], who investigated the effects of a reduced diet on sex hormone levels. They observed that in women who reduced their body weight by at least 5 %, testosterone levels decreased and SHBG levels increased, followed by a decrease in hirsutism symptoms [38]. Hyperandrogenism, insulin resistance, and obesity are closely related and contribute to lowering SHBG and increasing free testosterone levels. These relationships are expected because SHBG binds to testosterone with high affinity, thus reducing free testosterone concentration [37]. Another dietary intervention carried out in a study on women of childbearing age aligns with our results and showed that using a reduced-calorie diet with a low GI and an anti-inflammatory diet helps in weight loss and contributes to better glucose tolerance and lower testosterone levels [39]. Our study showed an improvement in reproductive parameters and regulation of menstruation in many women using a low GI diet and an anti-inflammatory diet compared to the standard diet consumed before the study. Before the study, only 23.5 % of women had normal, regular cycles, while after finishing the diet, 42.9 % of women reported an improvement in the regularity of menstrual cycles [40]. Other researchers, such as Onieva-Zafra et al. [41], observed that after 12 weeks of dietary intervention, 63 % of the examined women began to have regular periods. They noted a correlation between the consumption of fish and nuts containing anti-inflammatory omega-3 fatty acids and their effects on the regulation of menstruation [41]. Stress plays a vital role by disrupting the proper secretion of testosterone and SHBG. The vast majority of women before the study were exposed to chronic stress. At the end of the study, the participants reported a reduction in stress factors, which correlated with decreased testosterone and higher SHBG levels. These results align with those of another study, which included 206 women with PCOS and hirsutism, and observed a significant impact of lifestyle changes, including a reduction in stress factors that translated into an increase in SHBG and a decrease in total testosterone levels [42]. Shafrir et al. [43] assessed the effects of stress and alcohol consumption on androgens and SHBG. In their study, women with hyperandrogenism resigned from shift work for full-time work, eliminated the most stressful factors from their lives, and reduced their alcohol consumption to two glasses of wine per month. These three changes improved the laboratory measurements of the above-mentioned parameters. The main limitation of our study was the relatively shorter duration of 2 months, which may be the possible cause of the lack of change in the incidence of hyperandrogenism-related illnesses. Nonetheless, this short period was sufficient to observe the decreased incidence of symptoms such as hirsutism, acne, or infertility and a significant increase in overall satisfaction. These observed changes could be attributed to weight loss. While there was an overall correlation between selected factors and measured hormones, it does not allow us to draw clear conclusions regarding their causality and effectiveness. Some limitations of our study warrant further discussion, such as the low participant number, the lack of detailed biochemical parameters examination or the absence of detailed endocrine profiles. However, referring to the work of other authors, we can base the results of our study and conclude that lifestyle modifications should be recommended in women with PCOS before conception [44, 45]. Lifestyle factors, especially diet, are significant determinants of many phenotypes. Importantly, these factors are modifiable and thus should be the focus in efforts to lower the risk or should be considered as the primary early management strategy. The results from this study indicate that interventions that modify diet quality (e. g., low-calorie and low-fat diet) and enhanced levels of physical activity can delay or prevent the onset of hyperandrogenism.

Conclusions

To sum up, in overweight and obese women, a proper selection of diet, introduction of moderate physical activity, and reduction of weight, stress factors, and alcohol consumption translates into several positive effects, in the form of reducing symptoms of acne, hirsutism, menstrual disorders, and infertility. Healthy dietary patterns, such as a diet with a low glycemic index, diet interventions including low-calorie and low-fat diets, combined diet, and physical activity interventions, should be promoted at both individual and population levels to prevent and reduce the burden of hyperandrogenism in the future. None of the currently performed studies have been conducted for a period longer than 1-year; therefore, subsequent studies should focus on the long-term assessment of the impact of the low-IG diet on the parameters we observed.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

All samples and archived data were obtained with full and informed patient consent, and all experiments followed the ethical principles outlined by the 1964 Helsinki Declaration and ethical standards. This study was approved by the Jagiellonian University Medical College Bioethics Committee (number 1072.6120.382.2020).

Conflict of Interest

The authors declare that they have no conflict of interest.

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