CLINICAL AND BIOCHEMICAL CHARACTERISTICS IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME IN THE REGION OF POLLOG, REPUBLIC OF MACEDONIA

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Abstract

Polycystic ovary syndrome (PCOS) is a common endocrine disorder and is a major cause of an ovulatory infertility. The main objective is to estimate the prevalence of PCOS in the region of Pollog, Republic of Macedonia and to assess some clinical and biochemical parameters in patients with PCOS in comparison with normal women as control. Rotterdam criteria is used to evaluate 70 women diagnosed with PCOS, compared to 30 age matched controls to assess the clinical and biochemical abnormalities that occur in PCOS patients. All statistical analysis is done using SPSS (version 19.0). A P-value < 0.05 is considered statistically significant. Mean age in PCOS group is 25.11 ± 3.32, and 25.10 ± 3.91 in the control group. BMI of the women with PCOS is significantly higher than in the control group. Menstrual cycle abnormalities are observed in 71.4% of PCOS patients, and ultrasonographic appearance of polycystic ovaries is reported for all PCOS cases. Hirsutism (FG 8-9) is present in 42.9 %, hirsutism (FG 10-14) in 50% and 7.1% showed hirsutism (FG>15). We recorded significantly higher serum levels of luteinizing hormone (LH), total testosterone (TT), and insulin, while the serum levels of sex hormone binding globuline (SHBG) and follicular stimulating hormone (FSH) are significantly lower than in the control group. By analyzing the clinical and biochemical characteristics of our studied population of patients with PCOS, we can conclude that the majority of our patients expressed all three diagnostic features of PCOS (hyperandrogenism, menstrual abnormalities, and ultrasound findings of polycystic ovaries).

Keywords: Polycystic ovary syndrome, hirsutism, hyperandrogenism

Introduction

POLYCYSTIC OVARY SYNDROME (PCOS) is a heterogeneous disorder, characterized by chronic an ovulation and hyperandrogenism. It affects between 5 to10% of women of reproductive age, and it is considered one of the most common endocrine disorders in premenopausal women (Knochenhauser ES. et al, 1998).

PCOS manifests itself with an array of clinical features and symptoms, the three most common being: disorders of ovulation, excessive production of androgens, and polycystic ovaries on ultrasound. PCOS is often associated with obesity and insulin resistance. For a number of years PCOS has been associated with skin and reproductive manifestations. However, this syndrome became very interesting to the medical community in the 1980's, when it is found that women with PCOS have a higher risk of obesity, insulin resistance, glucose intolerance, type 2 diabetes mellitus, dyslipidemia, hypertension, and metabolic syndrome (Eggers S, et al, 2001).

The heterogeneity in the clinical signs of PCOS and the lack of uniformity in its defining symptoms hamper diagnosis. In recent years, specialists have attempted to reach a consensus regarding the definition of diagnostic criteria. In 1990, the National Institutes of Health (NIH) established that a diagnosis of PCOS required the simultaneous presence of two clinical criteria: oligoovulation or an ovulation and clinical and/or biochemical hyperandrogenism, after all other possible etiologies had been excluded. In 2003, the Rotterdam Consensus (RC), sponsored by the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine, stipulated that at least two of the following three criteria should be present: oligoovulation or an ovulation, clinical and/or biochemical hyperandrogenism and ultrasonographically detected polycystic ovaries, after the exclusion of all other possible etiologies (Group PCW 2003). Ovulation disorders usually become apparent in the form of oligomenorrhea, although about 20–30% of women with PCOS with oligomenorrhea have eumenorrhea (subclinical oligomenorrhea). Excessive production of androgens or hyperandrogenism (HA) is confirmed via laboratory analysis, characterized by elevated values of circulating androgens, or on the basis of clinical signs, primarily in the form of hirsutism. In the past, polycystic ovaries are determined on the basis of histopathological analysis, however, today evidence of polycystic ovaries on an ultrasound examination is sufficient. The ethnicity of patients influences the extent of this signs and symptoms, especially with regard to hirsutism

and obesity (Richardson MR, 2003). Therefore, the frequency of symptoms varies between different countries and ethnic groups.

In the light of this background the current study is conducted to estimate the prevalence of PCOS in the region of Pollog, Republic of Macedonia and to shed light on some biochemical parameters in patients with PCOS to reach some aspects of its pathogenesis through a comparison with normal women as control.

Materials and Methods:

Study population

Women attending the specialized gynecology ambulance Gyneco-Medica – Tetovo and gynecology hospital-Tetovo, diagnosed of PCOS according to the Rotterdam ESHRE/ASRM criteria (N=70), are included in the study. Age, and anthropometric measurements like height (in cm) and weight (in kg) and waist and hip circumference (in cm) is measured. BMI is calculated using the formula BMI= waist (in kg) x height (in m^2), and in the same time waist to hip ratio WHI is calculated as well. Diagnosis of PCOS is based on the presence of hirsutism by the presence of excessive body hair distributed in an androgen-depend pattern, using Ferriman-Gallwey index score (FG) and/or hyperandrogenemia and menstrual dysfunction. Women with other endocrine pathologies which may give similar signs as PCOS are exluded from the study according to the results from appropriated tests made for 17-hydroxyprogesterone, prolactin, thyroid stimulating hormone (TSH) and cortisol. None of the patients had other diseases or are taking any medication for at least 6 months prior to the study. In the control group, we included 30 patients, who had no disorders of the menstrual cycle without clinical biochemical signs of hyperandrogenism and without ultrasound findings of polycystic ovaries.

Biochemical analysis

Blood samples are collected from all subjects in the early follicular phase of a spontaneous or progesterone induced menstrual cycle (day 3-5). The levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone, sex homone binding globuline (SHBG), glucose and insulin are measured in the peripheral blood. Insulin sensitivity HOMA-IR is calculated according to the formula (insulin(mU/L x glucose (mmol/L)) / 22.5) (Ascaso JF et al, 2003). We defined insulin resistance as HOMA-IR $\geq$ 2.5 (Azziz R. et al, 2006).

Statistical analysis

The categorical variables are described by percentages, and the continuous as mean ± standard deviation. We used the independent Student's

t-test to compare the values of the means between cases and controls. Differences in categorical characteristics between cases and controls are assessed using x^2-test. All statistical analysis are done using SPSS (version 19.0). A p-value < 0.05 is considered statistically significant.

Results:

Anthropometric characteristics of PCOS cases and controls

The women diagnosed with PCOS are between 18 and 33 years old. Mean age in PCOS group is 25.11 ± 3.32, and 25.10 ± 3.91 in the control group. BMI of the women with PCOS is found to be 23.44 ± 2.81, significantly higher BMI than the control group ($p < 0.05$). As it is expected, the waist-to-hip ratio is significantly higher in the case group (Table 1).

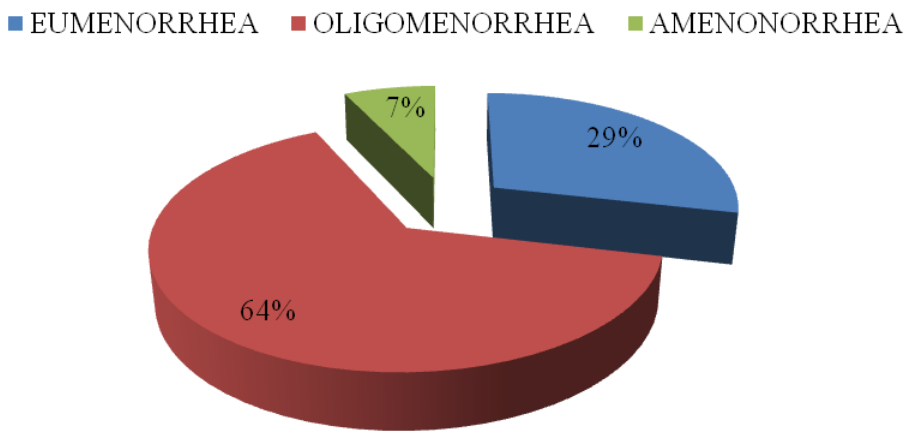
Table 1. Anthropometric characteristics of PCOS cases and controls

	PCOS (mean±SD)	Control (mean±SD)	p value
Age	25.11 ± 3.32	25.10 ± 3.91	p=0.985 NS
Weight	64.73 ± 8.45	55.00 ± 3.90	**$p=2.632^{E-7}$ S**
BMI	23.44 ± 2.81	20.22 ± 1.42	**$p=8.358^{E-7}$ S**
Waist	78.10 ± 2.40	70.87 ± 2.64	**$p=7.003^{E-24}$ S**
Hips	98.29 ± 2.14	92.17 ± 2.64	**$p=3.926^{E-22}$ S**
Waist/Hips	0.79 ± 0.03	0.77 ± 0.03	**$p=1.154^{E-4}$ S**

Prevalence of the diagnosis

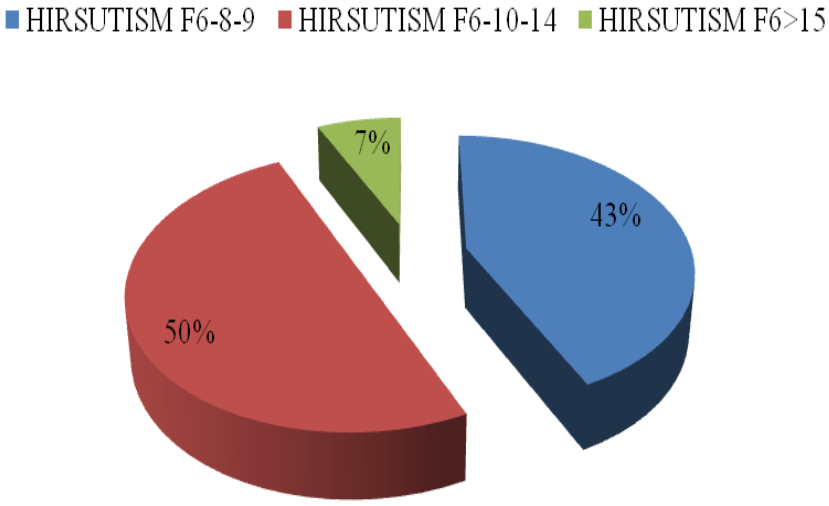
This study also found that from a total number of 70 women included, the higher percentage of PCOS patients are with oligomenorrhea 45(64.3 %), with amenorrhea 5(7.1 %) and cases with regular menstrual cycle are 20 (28.6 %). (Figure 1)

Figure 1.Distribution of women diagnosed with PCOS according to menstrual cycle



We defined hirsutism based on Ferriman-Gallwey index score (FG) of greater than 8 (Ferriman D et al, 1961), which is further divided into three categories : mild (FG 8-9) which in our study group is present in 30(42.9 %), moderate hirsutism (FG 10-14) present in 50% and 5 (7.1%) women diagnosed with PCOS showed hirsutism (FG>15). (Figure 2).

Figure 2. Distribution of women diagnosed with PCOS according to hirsutism



Biochemical analysis

As expected, we recorded significantly higher serum levels of LH, total testosterone (TT), and insulin, while the serum levels of SHBG and FSH are significantly lower than in the control group. The levels of LH/FSH ratio are significantly higher in the PCOS group when compared with the control group. The results are shown in Table 2. Values of glucose are within in normal limits in both groups of women, however values are significantly lower in the PCOS patient group.

Table 2. Diffrences between biochemical and hormonal concentrations in PCOS and control group

	Values in PCOS (mean±SD)	**Values in controls (mean±SD)**	**Significance**
Glucose mmol/l	4.58 ± 0.52	5.08 ± 0.53	p=3.377E-5 S
Insulin mIU/ml	11.59 ± 2.92	8.36 ±1.08	**p=2.095E-12 S**
Total Testosterone (nmol/L)	2.15 ± 0.34	1.29 ±0.30	**p=5.090^{E-21} S**
FSH mIU/ml	4.37 ± 0.53	5.13 ±0.34	**p=3.264^{E-13} S**
LH mIU/ml	7.25 ± 0.68	4.37 ±0.63	**p=4.192^{E-36} S**
LH/FSH	1.68 ± 0.26	0.85 ±0.14	**p=2.682^{E-15} S**
SHBG nmol/l	48.76 ± 6.62	73.53 ±6.16	**p=6.502^{E-32} S**

Conclusion

In the present study, we evaluated the clinical and biochemical characteristics of women with polycystic ovary syndrome in the region of Pollog, Republic of Macedonia. The advantage of our research is the fact that all ultrasound examinations are performed at one institution, with the same transvaginal ultrasound device, and by a physician who strictly kept to the Rotterdam criteria for the diagnosis of PCOS. In our study, among 70 patients included, 42.9% had hirsutisms (FG 8-9), 50 % hirsutism (FG 10-14) 7.1% of women diagnosed with PCOS showed hirsutism (FG>15). This is explained by the increased level of androgen which lead to increased secretion of testosterone, the causative agent of the appearance of male pattern (hirsutism). Effect od disease on menstrual cycle prevalence showed that the overall prevalence are 64.3 % out of women diagnosed with PCOS with oligomenorrhea, 7.1 % with amenorrhea and cases with regular menstrual cycle are 20 (28.6 %).

In PCOS women, normal gonadotropin-ovarian axis is disturbed. This is reflected by the higher levels of LH, lower FSH levels and reversal of LH: FSH ratio. In our study, FSH level showed a significant difference ($P<0.05$) between PCOS patients and control, which is in agreement with previous studies (Eden J. et al, 1989), and it fits with the criteria for diagnosis of PCOS, where the levels of FSH hormone in PCOS patients and control group are within normal range. The level of LH is approximately more than two times of FSH level. These results agreed with previous studies (Atiomo W. et al, 2009), and with the criteria for diagnosis of PCOS. Finally serum testosterone showed highly significant difference between PCOS patients and the control group.

By analyzing the clinical and biochemical characteristics of our studied population of patients with PCOS, we can conclude that the majority of our patients expressed all three diagnostic features of PCOS (hyperandrogenism, menstrual abnormalities, and ultrasound findings of polycystic ovaries).

The available literature on PCOS emphasizes clinical and physiopathological aspects. Further studies encompassing sociocultural aspects of this syndrome must be carried out, focusing on questions related both to its causality and to its consequences on social trajectories, elements that may enrich the understanding of the phenomenon and its effect on the life of women affected by the syndrome.

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