

PHENOTYPES OF POLYCYSTIC OVARY SYNDROME AND ACCOMPANYING HORMONAL DISTURBANCES

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Abstract: Objective: PCOS, which is known as a symptom complex including menstrual dysfunction (OD) and or hirsutism/androgen excess (HA), and/or polycystic ovaries (PCOM), induces women's health damage beyond this classical criteria. Subphenotypes of PCOS have different clinical properties and criteria, and the metabolic differences between these phenotypes have not been elucidated properly. Therefore, we aimed to investigate the metabolic and endocrinological differences between these sub-phenotypes.

Materials and Methods: 63 patients with PCOS followed by Istanbul Research and Education Hospital Endocrinology and Metabolism Department were included in the study. Patients were classified into subgroups according to phenotypes. The phenotype groups were compared according to blood glucose, lipid parameters, and serum hormone levels. MetS ratios between groups were also compared.

Results: Androgen excess/hirsutism was the most prominent character with a 95.2% (n = 60) rate in this study group, and ovulatory dysfunction was the least prominent one. (n = 43, 68.2%) PCOM has been detected in 50 patients (80.8%). Patients were grouped according to PCOS phenotypes. Phenotype C was the most common type, and about 65% of the patients were in this group. Triglyceride levels were statistically significantly higher in the Phenotype A group than in the Phenotype B group (p = 0.03). MetS was the highest in the Phenotype A group (45.4%) and the lowest in the Phenotype C group (34.7%).

Conclusions: Phenotype C has the highest prevalence in Turkish patients with PCOS, MetS was the highest in Phenotype A, and TG and LDL cholesterol

levels were higher in Phenotype A. More studies are needed to explain these differences and their lifetime consequences.

Keywords: Polycystic ovary syndrome, metabolic syndrome, hyperlipidemia, hirsutism, androgens.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) increasingly attracts more interest as a disease of women of reproductive age. Classically PCOS has been known as a symptoms complex, including menstrual dysfunction (OD) and or hirsutism/androgen excess (HA) and or polycystic ovaries (PCOM). Two of the three latter criteria are sufficient to define diagnosis according to Androgen Excess Society (Rotterdam) criteria (1). Besides these clinical properties, obesity, insulin resistance, and some psychiatric diseases have been attributed to PCOS. According to a meta-analysis of 910 patients, depression and anxiety disorders were more common than in a control group of 1347 subjects (2). According to a Swedish study, 22.4% of the 22385 women with PCOS had previously been diagnosed with at least one psychiatric disorder (2). There are different criteria to define this disorder. According to these criteria, it had been found better to clearly define the PCOS sub-phenotype. These PCOS phenotypes generally include four types: a) phenotype A, clinical or biochemical evidence of HA, OD (menstrual dysfunction), and PCOM; b) phenotype B: HA and OD, but not PCOM; c) phenotype C: HA and PCOM, but not OD; and d) phenotype D, with OD and PCOM, but not HA (3).

Additionally, metabolic syndrome, hyperprolactinemia, and insulin resistance could be other accom-

panying endocrine disorders in PCOS. One study has found a younger beginning and greater incidence of acne in PCOS patients with hyperprolactinemia (4). However, no study researched PCOS phenotypes and endocrine disturbances, so we aimed to document these endocrine disorders and their relationship with PCOS phenotype.

MATERIAL AND METHODS

63 patients who were routinely followed by Istanbul Research and Education Hospital Endocrinology and Metabolism Department were included in the study. The patients were diagnosed with PCOS according to Androgen Excess Society Criteria (1) and divided into subgroups according to phenotype (3). Height and weight were measured by accustomed methods, and BMI was calculated using the formula weight (in kg) divided by the square of height (in m). Serum lipid parameters, fasting glucose, and insulin were studied after 12 hours of night fasting. Serum estradiol, FSH, LH, testosterone, free testosterone, 17 (OH) Progesterone, and DHEA-S were studied at the follicular phase. Basal cortisol levels were measured at 08 00- 09 00. Overnight 1 mg dexamethasone was administered at 23 00 hrs, and serum cortisol level was measured at 08-09 00 hrs the next morning. The cut-off value for serum cortisol, which was less than 1.8 mcg/dl, was used to exclude hypercortisolism. The phenotype groups were compared according to blood glucose, lipid parameters, and serum hormone levels.

Institutional Ethical approval was taken from Istanbul Research and Education Hospital (27.04.2022/141)/ Helsinki guidelines were applied.

Statistical Analysis

Statistical analysis was performed using SPSS 22.0 (SPSS Inc., Chicago, IL, USA). The Chi-square

test or Fischer's test was used to measure the categorical parameters. Student's t-test was used for normal distributed two-group comparisons. A one-way ANOVA test was applied to compare more than two groups. descriptive statistical methods were used to define group characteristics.

RESULTS

63 PCOS patients with a mean age of 24.69 ± 4.76 have been included. Androgen excess/hirsutism was the most prominent characteristic with a 95.2% (n = 60) rate in this study group, and ovulatory dysfunction was the least prominent one (n = 43, 68.2%). PCOM has been detected in 50 patients (80.8%).

The patients were grouped according to PCOS phenotypes. Phenotype C was the most common type, and about 65% of the patients were in this group. The study population characteristics are shown in Table 1.

There were only two patients with phenotype group D (3.2%). It is not enough to make a statistical comparison with other groups, so phenotype groups A, B, and C were analyzed to compare physical and biochemical properties shown in Table 2. In two group comparisons, triglyceride levels were found to be statistically significantly higher in the phenotype A group than in the phenotype B group (p = 0.03). This rela-

Table 1. Study population characteristics

Age	24.69 ± 4.76
Ovulatory Dysfunction	43/63 (68.2 %)
Androgen Excess/Hirsutism	60/63 (95.2%)
PCO morphology	50/63 (80.8%)
Phenotype A	11/63 (17.4%)
Phenotype B	9/63 (14.3 %)
Phenotype C	41/63 (65.1%)
Phenotype D	2/63 (3.2%)

Table 2. Physical and biochemical properties of the groups

	A	B	P-value Between A and B	C	P-value Between A and C	P-value Between B and C	p Value
Weight	77.27 ± 20.08	79.00 ± 19.30	0.84	73.32 ± 15.47	0.48	0.35	0.58
BMI	29.55 ± 6.97	31.38 ± 7.47	0.63	28.57 ± 6.99	0.72	0.35	0.72
Waist	80.80 ± 34.01	90.77 ± 22.29	0.46	82.28 ± 25.32	0.88	0.36	0.33
Glucose	86.63 ± 5.98	91.75 ± 6.40	0.09	92.62 ± 13.11	0.14	0.85	0.32
PPG	105.75 ± 21.83	79.83 ± 21.70	0.07	97.13 ± 22.63	0.36	0.09	0.12
Triglyceride	154.50 ± 84.95	78.50 ± 29.71	0.03	100.89 ± 54.10	0.06	0.27	0.04
HDL	60.00 ± 22.44	56.80 ± 9.90	0.75	58.82 ± 18.64	0.88	0.80	0.95
LDL	125.42 ± 27.31	111.75 ± 20.45	0.32	96.03 ± 23.01	0.01	0.07	0.01
Insulin	12.53 ± 9.90	14.66 ± 5.20	0.69	10.67 ± 7.82	0.72	0.30	0.59

Table 3. Hormonal properties of the groups

	A	B	P-value Between A and B	C	P-value Between A and C	P-value Between B and C	P Value
Testosterone	0.64 ± 0.31	0.73 ± 0.24	0.63	0.56 ± 0.33	0.58	0.30	0.53
Free Testosterone	1.53 ± 0.73	1.96 ± 0.72	0.57	1.97 ± 0.75	0.44	0.98	0.73
Estradiol	55.16 ± 11.30	35.32 ± 30.02	0.17	50.28 ± 29.46	0.69	0.24	0.30
LH	7.55 ± 3.94	6.52 ± 5.16	0.70	7.57 ± 3.09	0.98	0.50	0.79
Prolactine	23.44 ± 12.05	21.05 ± 9.26	0.64	24.94 ± 13.97	0.76	0.41	0.70
Cortisole	16.90 ± 5.41	17.70 ± 5.20	0.33	14.08 ± 3.33	0.38	0.09	0.18
DHEAS	345.16 ± 89.22	238.57 ± 59.51	0.03	311.73 ± 101.43	0.46	0.08	0.11
Metabolic Syndrome	45.4% (5/11)	12.5% (1/8)	0.03	34.7% (8/33)	0.11	0.03	0.04

relationship was found not significant between groups A and C, and between groups, B and C. LDL levels were also significantly higher in group A compared to group C ($p = 0.01$). When the three groups were compared through an ANOVA test, triglyceride and LDL levels in group A were significantly higher ($p = 0.04$ and $p = 0.01$, respectively).

Table 3 shows the comparison of the hormonal properties of the groups. Although DHEAS levels were statistically higher in group A compared to group B ($p = 0.03$), the three groups' hormonal property comparisons have shown no significant difference between phenotype groups A, B, and C.

DISCUSSION

This study has demonstrated that PCOS is predominantly found in Phenotype C, and the most common PCOS component is hirsutism and/or androgen excess. On the other side, we couldn't discover any weight or BMI difference between PCOS phenotypes. Phenotype A, which had included all PCOS criteria, had the highest TG and LDL level and, as expected, had the highest DHEAS level.

Phenotype C (HA+PCOM) was the most common phenotype. This finding was different from previous studies. Panidis et al. found Phenotype A prevalence as 48.2% (5). Another study found A in 58% prevalence (6). Metabolic syndrome was highest in the Phenotype A group (45.4%). There have been ethnical differences according to different places and countries. For example, in contrast to the global prevalence of PCOS phenotypes, Phenotype D was found prevalent among Sudanese women (7). Diversity in frequencies of PCOS phenotypes could be clarified by whether the women were investigated in medical care or during an ordinary health control (8).

Serum triglyceride levels as a metabolic syndrome component was significantly the highest in Phenotype

A, but also serum LDL cholesterol was highest in Phenotype A. Phenotype A (complete phenotype) had the highest MetS ratio (45.4%) in the groups, Phenotype C had a similar ratio with Phenotype A (35.7%). Previous studies have found the MetS ratio in PCOS in similar proportions (6,9,10). The most common MetS Criterion was increased waist circumference by 60.3%. However, a recent study from China found low HDL was the most common MetS criterion in patients with PCOS (11). High TG was the most common in the complete phenotype (A). A study from India has found that Phenotype A had the most cardiovascular risk factors, highest waist, and BMI, but also in that study, this phenotype had the highest Clomiphene resistance (12). The difference in our study is there was no difference in weight, body mass index, and insulin levels between the groups, so the effect in blood lipids should not be affected by these parameters. Hyperlipidemia (elevated LDL Cholesterol) was more prominent in Phenotype A. A study from Poland of 93 patients also found higher LDL-cholesterol levels in patients with Phenotype A, while they didn't find a difference in TG levels (12). Total testosterone; FSH and LH and estradiol levels remained similar in phenotype groups. According to a cohort study, the PCOS phenotype didn't affect oocyte morphology and quality (13).

The importance of PCOS phenotyping lies in the fact that treatment response and cardiovascular prognosis. Adverse pregnancy outcomes were detected as more common in Phenotype A and D after in-vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) (14). Increased risk of abortion after frozen-thawed embryo transfer was found more common in phenotypes A and D (15). According to a cross-sectional study Phenotypes, A and B had weight-related problems in the quality of health, and phenotype D presented more emotional disturbance and relate health quality deterioration (16).

Limitations of this study are its cross-sectional design, small size, and of course, further studies with

more molecular investigating and treatment effects could be carried out.

CONCLUSION

Phenotype C has the highest prevalence in Turkish patients with PCOS, MetS was the highest in Phenotype A, and TG and LDL cholesterol levels were higher in phenotype A. More studies are needed to explain these differences and their lifetime consequences.

Abbreviations:

HA — Hyperandrogenism

MetS — Metabolic Syndrome

PCOS — Polycystic Ovary Syndrome

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Sažetak

FENOTIPOVI SINDROMA POLICISTIČNIH JAJNIKA I PRATEĆIH HORMONSKIH POREMEĆAJA

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Cilj: PCOS, koji je poznat kao kompleks simptoma koji uključuje menstrualnu disfunkciju (OD) i/ili hirzutizam/višk androgena (HA) i/ili policistične jajnike (PCOM), izaziva oštećenje zdravlja žena izvan ovog klasičnog kriterijuma. Subfenotipovi PCOS-a imaju različita klinička svojstva i kriterijume, a metaboličke razlike između ovih fenotipova nisu pravilno razjašnjene. Stoga smo imali za cilj da istražimo metaboličke i endokrinološke razlike između ovih subfenotipova.

Materijali i metode: U studiju su uključena 63 pacijentkinje sa PCOS-om, praćene na Odeljenju za endokrinologiju i metabolizam Istanbulske istraživačke i obrazovne bolnice. Pacijentkinje su klasifikovane u podgrupe prema fenotipovima. Fenotipske grupe su upoređivane prema glikemiji, lipidnim parametrima i nivou hormona u serumu. MetS odnosi između grupa su takođe upoređivani.

Rezultati: Višak androgena/hirzutizam je bio najistaknutiji karakter sa stopom od 95,2% (n = 60) u ovoj studijskoj grupi, a ovulatorna disfunkcija je bila najmanje izražena. (n = 43, 68,2%) PCOM je otkriven kod 50 pacijentkinja (80,8%). Pacijentkinje su grupisane prema fenotipovima PCOS. Fenotip C je bio najčešći tip, a oko 65% pacijentkinja je bilo u ovoj grupi. Nivo triglicerida je bio statistički značajno viši u grupi fenotipa A nego u grupi fenotipa B (p = 0,03). MetS je bio najveći u grupi fenotipa A (45,4%), a najmanji u grupi fenotipa C (34,7%).

Zaključak: Fenotip C ima najveću prevalenciju kod turskih pacijentkinja sa PCOS, MetS je bio najviši kod fenotipa A, a nivoi TG i LDL holesterola su bili viši kod fenotipa A. Potrebno je više studija da bi se objasnile ove razlike i njihove posledice tokom života.

KLjučne reči: sindrom policističnih jajnika, metabolički sindrom, hiperlipidemija, hirzutizam, androgeni.

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