International Journal of Medical Science and Health Research

Vol.7, No. 04; 2023

ISSN: 2581-3366

Ovulatory Versus Anovulatory Polycystic Ovary Syndrome Phenotypes: is There Really Any Effect on Laboratory, Clinic and Metabolic Profiles for Turkish Women?

Emre Sinan GÜNGÖR[1]; Assoc Prof.
Ayça K. KÜÇÜKYURT[1]; M.D.
Melek KARA[2]; M.D.
[1]: Istanbul Education and Research Hospital; Department of Obstetrics and Gynecology; Istanbul, TURKEY
[2]Çanakkale Gelibolu Martyr Koray Onay State Hospital

Corresponding Author: Ayça K. KÜÇÜKYURT[1]; M.D. İstanbul Education and Research Hospital; Department of Obstetrics and Gynecology, İstanbul; TURKEY
Phone number: +90 5412428966

doi: 10.51505/ijmshr.2023.7404 URL: http://dx.doi.org/10.51505/ijmshr.2023.7404

Received: July 29, 2023 Accepted: Aug 08, 2023 Online Published: Aug 15, 2023

Abstract

Aim

Polycystic ovary syndrome (PCOS) is a common disorder and different diagnostic criterias are used for its diagnosis. The purpose of this study is to evaluate any change in insulin metabolism in anovulatory PCOS patients and compare laboratory and clinical parameters between ovulatory and anovulatory PCOS patients diagnosed using Rotterdam criteria

Methods

Hyperandrogenic women with ovulatory cycles and polycystic ovarian morphology (PCOM) and hyperandrogenic women with oligo anovulation and PCOM, respectively, were found in two groups of 132 people with PCOS between the ages of 20 and 40. Blood pressure, waist-to-hip ratio, and Body Mass Index (BMI) were mentioned as demographic factors. Blood samples were taken on days three through five of a menstrual cycle. Initial laboratory testing included measurements of fasting blood sugar and insulin levels, luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), total and free testosterone, prolactine, free T3, free T4, thyroid stimulating hormone (TSH), and lipid profile.

Results

Anovulatory patients were significantly younger than ovulatory patients. Bleeding day in mens were similar between the groups but menstrual cycle length was significantly longer among women with anovultory PCOS (p=0.0001).BMI values, waist/hip ratios and diastolic blood pressures were similar but systolic blood pressures were significantly higher for anovultory patients (p=0.003).LH, total testosteron levels,fT3 and fT4 levels were significantly higher for

Vol.7, No. 04; 2023

ISSN: 2581-3366

anovulatory patients. Lipid profiles were similar between the groups but total cholesterol levels were higher among anovulatory group (p=0.02).

Conclusions

The outcomes of various PCOS phenotypes from various nations and ethnic backgrounds may differ in the lab and in the clinic. To develop a successful therapeutic and preventive strategy for PCOS patients, we need to understand the local phenotypic characteristics of women with the condition rather than simply using data from published research from people of different ethnic origins.

Keywords: Anovulation, blood pressure, hyperandrogenism, insulin resistance, lipid profile, polycystic ovary syndrome.

1. Introduction

The prevalence of PCOS, a prevalent endocrine condition in women of reproductive age, is estimated to be 4-7%. (1). Clinical and/or biochemical hyperandrogenism, oligo/amenorrhea, and polycyctic ovary shape are frequent characteristics (PCOM).

There are numerous diagnostic standards for PCOS, but the Roterdam Consensus (2). explains that when at least two of the symptoms listed below are satisfied, PCOS can be diagnosed. Initially, ovarian dysfunction (oligo or amenorrhea) Hyperandrogenicity 2. (either biochemical or clinical being hirsutism) 3. The appearance of polycystic ovaries and ruling out endocrinopathies including hyperprolactinemia, tumors that secrete androgen, and thyroid disease. The Rotterdam criteria state that a polycystic ovary on ultrasound should either contain >12 follicles measuring 2-9 mm in diameter or both. Ovulatory dysfunction is one of these diagnostic criteria for PCOS, however it is not a "must" for PCOS diagnosis when these criteria are reviewed.

Some patients with this disease may not exhibit all of its symptoms (3,4). The pathophysiology, clinical presentation, and biochemical profile of PCOS individuals vary depending on the interplay of several hormones.

According to multiple studies, women with oligomenorrhoea were more likely than women with regular periods to develop diabetes or the metabolic syndrome (5,6). One of the main symptoms of PCOS, which is made up of irregular menstruation and ovulatory dysfunction, is increased testosterone levels. According to Hart et al., adolescent girls with PCOS who had increased testosterone but no menstrual irregularities also had insulin resistance (7).

PCOS patients have insülin resistance as a result of altered lipid and carbohydrate metabolism, which increases their risk of cardiovascular disease (8). Similar to how hypertension can be seen as one of insulin resistance's symptoms (9).

Vol.7, No. 04; 2023

ISSN: 2581-3366

This study compares laboratory and clinical data between Rotterdam criteria-diagnosed ovulatory and anovulatory PCOS patients in order to determine whether there is a disruption in insülin metabolism for anovulatory patients.

2. Materials and Methods

Patients between 20-40 years old diagnosed as PCOS from Suleymaniye Maternity Research and Training Hospital, which is the annex building of Istanbul Education and Research Hospital, according to Roterdam were prospectively included to study between July 2017 and July 2018. Patients were divided into two groups: group 1 included hyperandrogenic women who had ovulatory cycles and PCOM, whereas group 2 included those who had oligo anovulation and polycystic ovarian morphology on transvaginal/pelvic ultrasound. On day 21 of the menstrual cycle, blood progesterone levels of 3 ng/ml were considered to indicate anovulatory. Menstruation every 21 to 35 days, with no more than a 4 to 7 day difference between cycles, was considered to be a typical menstrual cycle. Ultrasound scans were done transvaginally if the patient is not virgin or transabdominally if the patient is virgin through a full bladder. All PCOS women had polycystic ovaries on ultrasound scanning. PCOM was determined via ultrasound by counting the number of intermediate follicles (defined as more than 10 peripheral follicular cysts with a single plane diameter of less than or equal to 8 mm). The ultrasound tests were all done by the same operator. They also had clinical features of hyperandrogenism (hirsutism, acne or androgenetic alopecia) or biochemical hyperandrogenism. The method used to visually quantify the degree of excessive terminal hair in hirsutism is called the Ferriman-Gallwey scale. A modified Ferriman-Gallwey (mFG) score cut-off point of >7 was used to diagnose it. The Ludwig scale was used to evaluate androgenic alopecia (10). Using the American Academy of Dermatology 1990 criteria, the severity of acne was assessed (11).

Anovulation and acne symptoms are much more seen in patients under 20, so we excluded these patints. We also excluded patients whose BMI is lower than 18.5, who have abnormal TSH results (<0.5 or >3 mIU/l), prolactin levels over 25 mcg/l, patients who use antihypertansive, hypoglisemic and antilipidemic drugs. The protocol was approved by the Institutional Review Board of Suleymaniye Maternity Research and Training Hospital, which is the annex building of Istanbul Education and Research Hospital, and every patient included in this study signed an informed consent.

Among the anthropometric measurements obtained were height, weight, body mass index (BMI), waist circumference measured halfway between the arcus costae and anterior superior iliac spine, and hip circumference measured at the level of the anterior superior iliac spine. After at least 15 minutes in a resting position, blood pressure (systolic and diastolic) was taken with a mercury sphygmomanometer. After a recommended 12-hour fast, blood samples for a hormone assay and a glucose test were taken in the early follicular phase between 7:00 and 09:30 a.m. On days 3–5 of a naturally occurring or progestin-induced menstrual cycle, blood samples were obtained. Fasting blood sugar and insulin levels, serum LH, FSH, E2, total and free testosterone, prolactine, free T3, free T4, TSH, and lipid profiles including LDL, HDL, triglycerides, and total cholesterol were all included in the initial laboratory tests.

Vol.7, No. 04; 2023

ISSN: 2581-3366

Chemiluminescent immunoassays were used to measure the levels of E2, FSH, LH, and testosterone on an Accessw 2 analyzer (Beckman Coulter, Inc., Brea, USA). The ADVIA Centaurw XP immunoassay system was used to measure the amount of insulin in the sample (Siemens Healthcare Diagnostics, Inc., Tarrytown, USA). Hexokinase was used to measure the amount of glucose in the blood (Beckman Coulter, Inc.). The following formula was used to construct the homeostasis model assessment for insulin resistance index (HOMA-IR): HOMA-IR 14 [fasting insulin (mIU/ml) fasting glucose (mmol/l)]. /22.5 (12). (12).

3. Statistical Analysis

The statistical analysis was performed using SPSS, Inc.'s (Chicago, Illinois) version 22.0 of the Statistical Package for the Social Sciences. The clinical and laboratory data were reported along with their means, standard deviations, minimum and maximum values. To examine group differences, the sample t-test and the Mann-Whitney U test were both applied. The chi-square test was used to compare percentages.

4. Results

Variation among the factors64/132 (48.48%) of PCOS patients were ovulatory and 68/132 (51.51%) patients were anovulatory. Anovulatory patients were significantly younger than ovulatory patients ($p < 0.05$). BMI levels, parity results and infertility rates were similar between the groups. Bleeding day in mens were similar between the groups but menstrual cycle length was significantly longer for anovultory patients (29.7±3.1 vs 79.0±63.3 day; p=0.0001) (Table 1). Waist/hip ratios and diastolic blood pressures were similar but systolic blood pressures were significantly higher for anovultory patients without reaching the hypertension cutoff value (113.4±10.8mmHg vs 118.7±12.5 mmHg; p=0.003)(Table 1).

LH levels (9.09.8 vs 11.26.4 mIU/ml, p=0.014) and total testosterone levels (0.670.28 vs 0.80.26 ng/ml, p=0.006) were considerably higher for anovulatory patients. FSH, E2, TSH, prolactin, and free testosterone levels were identical between the groups. The anovulatory group also had considerably greater fT3 and fT4 levels (Table 2).

When the patients were analysed according to metabolic serum parameters; there were not significant differences for LDL, HDL and triglyceride levels; fasting plasma glucose, insulin levels and HOMA-IR scores ($p > 0.05$) (Table 3). The only PCOS patient subgroup with significantly increased cholesterol levels was the anovulatory subgroup.

Vol.7, No. 04; 2023

ISSN: 2581-3366

Table 1. Demographic characteristics of patients

	Ovulatory PCOS patients		Anovulatory PCOS patients		p
	Mean±sd/n-%	Median	Mean±sd/n-%	Median	
Age (years)	27,4 ± 4,6	28,0	24,0 ± 4,2	23,0	***0,000***
BMI (kg/m2)	26,4 ± 5,5	25,7	25,7 ± 6,6	24,2	0,328
Married	46 67,6%		27 42,2%		***0,003***
Gravidy	0,7 ± 1,1	0,0	0,4 ± 0,8	0,0	***0,033***
Parity	0,6 ± 1,0	0,0	0,3 ± 0,7	0,0	0,061
Presence of infertility	14 20,6%		13 20,3%		0,969
Bleeding day in mens	6,0 ± 2,0	6,0	5,6 ± 1,8	6,0	0,465
Menstrual cycle(days)	29,7 ± 3,1	30,0	79,0 ± 63,3	60,0	***0,000***
FG score	9.02±0.67		9.17±0.86		0.356
SBP (mmHg)	113,4 ± 10,8	110,0	118,7 ± 12,5	120,0	***0,003***
DBP (mmHg)	69,9 ± 6,5	70,0	72,4 ± 9,3	72,5	0,050
Waist circ. (cm)	79,8 ± 15,3	75,0	80,4 ± 18,8	80,0	0,728
Waist/hip ratio	0,8 ± 0,1	0,9	0,9 ± 0,1	0,9	0,654

Waist circ: Waist circumference FG: Ferriman-Galwey
SBP: Systolic Blood Pressure DBP: Diastolic Blood Pressure

Table 2. Endocrine characteristics of patients

	Ovulatory PCOS patients		Anovulatory PCOS patients		p
	Mean±sd	Median	Mean±sd	Median	
FSH (mIU/ml)	6,3 ± 2,2	6,2	6,7 ± 1,6	6,6	0,268
LH (mIU/ml)	9,0 ± 9,8	7,7	11,2 ± 6,4	9,5	***0,014***
E2 (pg/ml)	86,3 ± 63,3	65,0	72,1 ± 48,2	56,0	0,235
fT3 (pg/ml)	3,6 ± 0,4	3,5	3,9 ± 0,5	3,8	***0,022***
fT4 (mIU/L)	0,8 ± 0,1	0,8	0,9 ± 0,2	0,9	***0,018***
TSH (mIU/L)	2,0 ± 0,6	2,1	1,9 ± 0,7	1,9	0,401
Prolactin (ng/ml)	18,2 ± 12,6	14,5	14,8 ± 8,6	10,9	0,133
TT (ng/ml)	0,67 ± 0,28	0,66	0,80 ± 0,26	0,85	***0,006***
FT (pg/ml)	0,71 ± 0,16	0,68	0,75 ± 0,16	0,74	0,218

FSH: Follicle stimulating hormone; LH: Luteinizing hormone; E2: Estradiol; fT3: Free T3
fT4: Free T4; TSH: Thyroid stimulating hormone; TT: Total Testosterone;
FT: Free Testosterone

Vol.7, No. 04; 2023

ISSN: 2581-3366

Table 3. Metabolic and lipid profiles of both groups

	Ovulatory PCOS patients		Anovulatory PCOS patients		p
	Mean±sd	Median	Mean±sd	Median	
TC (mg/dl)	174,0 ± 37,2	178,0	197,3 ± 43,0	169,0	***0,004***
LDL-c (mg/dl)	98,3 ± 21,3	95,0	102,1 ± 19,1	98,5	0,311
HDL-c (mg/dl)	53,0 ± 12,0	53,0	56,3 ± 13,6	54,0	0,330
Triglycerides (mg/dl)	109,3 ± 66,3	96,5	104,3 ± 59,3	93,0	0,764
FG (mg/dl)	88,1 ± 10,6	88,0	91,7 ± 10,4	92,0	0,078
FI (µlU/ml)	18,8 ± 21,2	10,8	17,7 ± 16,1	12,0	0,309
HOMA-IR	2,6 ± 1,4	2,4	3,0 ± 2,0	2,3	0,762

TC: Total Cholesterol LDL-c: Low-density lipoprotein cholesterol
HDL-c: High-density lipoprotein cholesterol FG: Fasting glucose FI: Fasting insulin

5. Discussion

We compared laboratory and clinical parameters between ovulatory and anovulatory PCOS patients with this study. Systolic blood pressures, fT3-fT4, LH, total testosteron and total cholesterol levels were significantly different for anovulatory patients when compared with ovulatory patients.

The stimulation of androgen release from the ovary by LH and insulin is said to increase the levels of androgens in the serum (13). Robinson et al showed that reduced insulin sensitivity is a feature of oligo and amenorrhoeic women with PCOS but we could not find such a relation between the groups (14). Similarly, LH levels were significantly higher for anovulatory PCOS patients; but there was not statistically significant difference for insülin and fasting plasma glucose levels between the groups.

Higher fT3-fT4 levels and higher systolic blood pressure levels for anovulatory PCOS patients may signify a systemic effect; so if a patient diagnosed PCOS have anovulatory cycles she might be especially informed about long-term health risks related with such a systemic interference.

Although acne may be a sign of hyperandrogenism, the majority of acne patients do not have an excess of androgens (15). Likewise, we were unable to discover a connection between acne symptoms and elevated testosterone levels.

Şahin et al. studied 40 BMI-matched Turkish controls and 50 lean Turkish women with PCOS, and they discovered no variations in the plasma levels of total cholesterol (TC), LDL, HDL, and triglycerides in either group (16). Despite the fact that both of our study groups had PCOS, we were unable to identify any variations in our patients' TC, LDL, HDL, or triglyceride values.

In people with a normal glucose tolerance, the HOMA-IR index is regarded as a good metric for assessing insulin resistance and insulin sensitivity (17). Our amenorrheic PCOS group showed

Vol.7, No. 04; 2023

ISSN: 2581-3366

lower HOMA-IR scores despite the fact that the difference did not achieve statistical significance. It is important to keep in mind that the absence of statistically significant connections does not imply that no associations exist.

Castillo-Martinez et al. discovered that obese women are more likely than non-obese women to experience monthly irregularities, but unlike them, the BMI ratings of our patients who experience anovulation and not (18). De Guavera et al. classified patients into four groups after analyzing PCOS patients from Chile and Argentina who had been diagnosed using Rotterdam criteria. Transvaginal ultrasound revealed that hyperandrogenic women with oligo anovulation and PCOM had a higher frequency of metabolic syndrome than those with ovulatory cycles and PCOM (19).

On the other hand, we could not find such a significant difference between our patient groups and this may be because of ethnic diffreneces between the study populations of both studies. De Guavera et al. emphasized the need of taking into account ethnic impacts on the health implications of PCOS by mentioning that the distribution of ethnic origin varied.

Higher TC levels were seen in lean PCOS patients with irregular menstrual periods than in patients with regular cycles among lean patients classified into four phenotypes (20). Similar to them, our anovulatory PCOS group's TC levels were likewise considerably higher.

We have some restrictions on our investigation. Our study's first drawback is the tiny sample size we used. It might have had a limited ability to identify slight variations between PCOS-diagnosed patients. It is recommended that bigger sample trials be conducted in the future to validate our findings.

On the other hand, we excluded adolescent PCOS group because diagnostic criterias for polycystic ovary syndrome in adolescents may be problematic, so we could evaluate a more homogynous group of patients

Our hypothesis before starting the study was to find differences between anovulatory and ovulatory PCOS patients according to their lipid profiles, metabolic parameters and maybe hormon profiles when we analysed previous reports related with different PCOS phenotypes. Nonetheless, our study's findings revealed a few small variations between the groups. If we are aware of the regional phenotypic traits of women with PCOS, we can create an effective therapeutic and preventive strategy for this patient population.

6. Conclusion and Recommendations

The outcomes of various PCOS phenotypes from various nations and ethnic backgrounds may differ in the lab and in the clinic. To develop a successful therapeutic and preventive strategy for PCOS patients, we need to understand the local phenotypic characteristics of women with the condition rather than simply using data from published research from people of different ethnic origins.

Vol.7, No. 04; 2023

ISSN: 2581-3366

7. Disclosure

No author has any potential conflict of interest.

References

Leerasiri P, Wongwananuruk T, Indhavivadhana S, Techatraisak K, Rattanachaiyanont M, Angsuwathana S. Correlation of clinical and biochemical hyperandrogenism in Thai women with polycystic ovary syndrome. J Obstet Gynaecol Res. 2016; 42: 678–683.

Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004;19:41-7.

Ramanand SJ, Ghongane BB, Ramanand JB, Patwardhan MH, Patwardhan VM, Ghanghas R, et al. Hormonal Profile of Polycystic Ovary Syndrome (PCOS) In Indian Women. Res J Pharm Biol Chem Sci. 2012; 3: 1159-1172.

Kumar AN, Naidu JN, Satyanarayana U, Ramalingam K, Anitha M. Metabolic and Endocrine Characteristics of Indian Women with Polycystic Ovary Syndrome. Int J Fertil Steril 2016; 10:22-28.

Solomon CG, Hu FB, Dunaif A, Rich-Edwards JE, Willet WC, Hunter DJ, et al. Long or highly irregular menstrual cycles as a marker for risk of type 2 diabetes mellitus. JAMA, 2001;286:2421–2426.

Solomon CG, Hu FB, Dunaif A, Rich-Edwards JE, Stampfer MJ, Willet WC, et al. Menstrual cycle irregularity and risk for future cardiovascular disease. Journal of Clinical Endocrin Met.,2002;87: 2013–2017.

Hart R, Doherty DA, Mori T, Huang RC, Norman RJ, Franks S, et al. Extent of metabolic risk in adolescent girls with features of polycystic ovary syndrome. Fertility and Sterility, 2011;95:2347–2353.

Siddiqui IA, Tamimi W, Tamim H, AlEisa N, Adham M. A study on clinical and sonographic features in obese and nonobese patients with polycystic ovary syndrome. Arch Gynecol Obstet 2010;281:467–471.

Lewy VD, Danadian K, Witchel SF, Arslanian S. Early metabolic abnormalities in adolescent girls with polycystic ovarian syndrome. J Pediatr 2001; 138:38–44.

Ludwig E. Classification of the types of androgenetic alopecia (common baldness) occurring in the female sex. Br J Dermatol 1977; 97: 247–254.

American Academy of Dermatology. Guidelines of care for acne vulgaris. J Am Acad Dermatol 1990; 22: 676–680.

Dewailly D, Alebic MS, Duhamel A, Stojanovic N. Using cluster analysis to identify a homogeneous subpopulation of women with polycystic ovarian morphology in a population of non-hyperandrogenic women with regular menstrual cycles. Hum Reprod 2014; 29, 2536-2543.

Ateş S, Aydın S, Özcan P, Soyman Z, Karasu AF, Şevket O. Clinical and metabolic characteristics of Turkish adolescents with polycystic ovary syndrome. J Obstet Gynaecol 2018; 38:236-40.

Vol.7, No. 04; 2023

ISSN: 2581-3366

Robinson S, Kiddy D, Gelding SV, Willis D, Niththyananthan R, Bush A, et al. The relationship of insulin insensitivity to menstrual pattern in women with hyperandrogenism and polycystic ovaries. Clin Endocrin 1993;39:351-55.

Leerasiri P, Wongwananuruk T, Indhavivadhana S, Techatraisak K, Rattanachaiyanont M, Angsuwathana S. Correlation of clinical and biochemical hyperandrogenism in Thai women with polycystic ovary syndrome. J Obstet Gynaecol Res. 2016;42:678-83.

Sahin S, Eroglu M, Selcuk S, Turkgeldi L, Kozalı S, Davutoğlu S, et al. Intrinsic factors rather than vitamin D deficiency are related to insulin resistance in lean women with polycystic ovary syndrome. Eur Rev Med Pharmacol Sci. 2014;18: 2851–2856

Fruzzetti F, Perini D, Lazzarini V, Parrini D, Genazzani AR. Adolescent girls with polycystic ovary syndrome showing different phenotypes have a different metabolic profile associated with increasing androgen levels. Fertil Steril 2009;92:626–34.

Castillo-Marrtinez L, Lopez-Alvarenga JC, Villa AR, Gonzalez-Barranco J. Menstrual cycle length disorders in 18- to 40-y-old obese women. Nutrition, 2003;19, 317–320.

de Guevara AL, Fux-Otta C, Crisosto N, de Mereshian PS, Echiburu B, Iraci G, et al. Metabolic profile of the different phenotypes of polycystic ovary syndrome in two Latin American populations. Fertil Steril 2014;101:1732-9.

Spalkowska M, Mroziska S, Galuszka-Bednarczyk A, Gosztyla K, Przywara A, Guzik J, et al. The PCOS Patients differ in Lipid Profile According to their Phenotypes. Exp Clin Endocrinol Diabetes. 2018; 126:437-444.