BMC Research Notes

RESEARCH NOTE Open Access

Distribution of polycystic ovary syndrome (PCOS) phenotypes in Iranian women: a cross-sectional study

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Abstract

Objective Polycystic ovary syndrome (PCOS) is a heterogeneous disorder characterized by diverse clinical and metabolic manifestations. This study aimed to investigate the prevalence of PCOS phenotypes and their association with hematological, biochemical, and hormonal parameters in PCOS, with a particular focus on infertile women and those with recurrent pregnancy loss (RPL).

Results Phenotype A was the most prevalent phenotype overall and within both infertile and RPL subgroups. However, no significant differences in hematological, biochemical, or hormonal parameters were observed among the PCOS phenotypes, except for lower RBC and hematocrit levels in phenotype F. PCOS women with RPL demonstrate significantly lower levels of RBC, hemoglobin, and hematocrit in phenotype F.

Keywords Polycystic ovary syndrome, PCOS phenotypes, Infertility, Recurrent pregnancy loss

Introduction

Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder affecting approximately 5–7% of women of reproductive age [1]. It is characterized by a constellation of symptoms including irregular menstrual cycles, hyperandrogenism, and polycystic ovarian morphology, and is associated with a range of metabolic disturbances such as insulin resistance, obesity, and inflammation [2, 3]. The revised consensus Rotterdam criteria, which incorporate clinical, biochemical, and ultrasound findings or elevated anti-mullerian hormone (AMH) levels [4], provide a standardized diagnostic framework for PCOS [5]. While the precise etiology remains elusive, genetic, epigenetic, and environmental factors are implicated in the pathogenesis of PCOS [6, 7].

Recognizing the heterogeneity of PCOS, researchers have increasingly focused on identifying distinct phenotypic subpopulations within the syndrome. These PCOS phenotypes, characterized by specific combinations of clinical and biochemical features, offer a more nuanced understanding of the disorder [8]. Early attempts at phenotype classification primarily relied on clinical criteria, but advancements in diagnostic technology and molecular biology have enabled a more comprehensive approach that includes metabolic and ovarian characteristics [9]. This phenotypic heterogeneity underscores the complex pathophysiology of PCOS [8]. Given this complexity, researchers emphasize the need for tailored treatment strategies. Phenotype-specific approaches can optimize treatment outcomes and facilitate risk stratification for associated comorbidities, such as metabolic syndrome, cardiovascular disease, infertility [10].

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Women with phenotype A often face the greatest challenges in achieving and maintaining pregnancy due to irregular ovulation and hormonal imbalances. In contrast, women with phenotype B, who may have regular ovulation but still exhibit metabolic disturbances, can also experience infertility and recurrent pregnancy loss (RPL), albeit potentially to a lesser extent. The underlying pathophysiological mechanisms, such as hormonal imbalances, insulin resistance, chronic inflammation, ovarian follicle development and endometrial dysfunction, contribute to the increased risk of infertility and miscarriage across all PCOS phenotypes [10–13]. In addition, obesity, age, family history, and metabolic syndrome can increase the likelihood of developing PCOS, infertility and miscarriage. Understanding these differences is essential for altering management strategies to improve reproductive outcomes for women with PCOS, as each phenotype may require specific interventions to address their unique challenges related to fertility and pregnancy loss [10, 13, 14].

It is notable that the clinical presentation of PCOS exhibits significant heterogeneity across geographical and ethnic populations [15]. The current study aims to investigate the clinical manifestations of PCOS phenotypes and the prevalence of PCOS phenotypes in Iranian women. Furthermore, we investigated the relationship between PCOS phenotypes and a range of hematological, biochemical, and hormonal markers, with particular attention to infertile and RPL subgroups.

Materials and methods

Study population

In this study, the inclusion criteria were women aged 22 to 40 years who were diagnosed with PCOS according to the Rotterdam criteria, which requires the presence of at least two of the following three features: oligo- or anovulation, clinical or biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound [5]. Additionally, infertile women, defined as those unable to achieve pregnancy despite engaging in regular unprotected sexual intercourse for 12 months or longer, and women with a history of recurrent pregnancy loss, defined as two or more consecutive pregnancy losses before the 20th week, were included.

Exclusion criteria included individuals with Cushing's syndrome, thyroid dysfunction, androgen-secreting tumors, or those who had undergone hormonal treatment or used drugs such as steroids that could induce insulin resistance for at least 6 months prior to the evaluation. Participants with parathyroid disorders, chronic kidney disease, or other chronic illnesses were also excluded.

The study involved 242 women with PCOS (aged 22 to 40 years), including 143 infertile patients and 99 individuals with a history of recurrent pregnancy loss. Participants were selected from the Obstetrics and Gynecology Department of the Ibn Sina Infertility Center in Tehran, Iran. We utilized the Rotterdam criteria for patient selection, while also acknowledging the various phenotypes of PCOS as defined by the AES criteria, which allows for the identification of patients with a single feature as having a mild phenotype of PCOS [16]. Therefore, patients were categorized into seven distinct phenotypes based on the presence or absence of hyperandrogenemia/hirsutism, oligo/anovulation, and polycystic ovaries [17]. As shown in Table 1, participants with PCOS were categorized into seven phenotypic subtypes: phenotype A (hyperandrogenism/hirsutism, oligo/anovulation and polycystic ovaries); phenotype B (hyperandrogenism/hirsutism and oligo/anovulation); phenotype C (hyperandrogenism/hirsutism and polycystic ovaries); phenotype D (oligo/anovulation and polycystic ovaries); phenotype E (hyperandrogenism/hirsutism); phenotype F (polycystic ovaries), and phenotype G (oligo/anovulation).

All study procedures involving human participants were conducted in accordance with ethical guidelines established by institutional and national review boards and the 1975 Helsinki Declaration (as revised in 2008). This study was approved by the Ethics Committee of the Ibn Sina Infertility Center (IR.ACER.Avicenna.Res.1395.6).

Laboratory analysis

Blood samples were collected from fasting participants (12 h) under strict aseptic conditions at the follicular phase (days 7–14) of menstrual cycle. Samples were processed and stored at -80 °C for subsequent analysis. Hematological, biochemical and hormonal parameters, including FBS, insulin, lipid profile, urea, creatinine, HomoCys, RBC, WBC, PLT, Hb, Hct, MCV, MCH, MCHC, FSH and LH, were quantified as detailed in our previous publications [18–20].

Table 1 Clinical manifestations of PCOS phenotypes [17]

Characteristics	PCOS Phenotypes						
	A	B	C	D	E	F	G
Hyperandrogenemia/Hirsutism	Present	Present	Present	Absent	Present	Absent	Absent
Oligo/Anovulation	Present	Present	Absent	Present	Absent	Absent	Present
Polycystic Ovaries	Present	Absent	Present	Present	Absent	Present	Absent

Table 2 Distribution of various PCOS phenotypes

	PCOS Phenotypes *n* (%)				
	A	**B**	**C**	**E**	**F**
PCOS	166 (68.6%)	11 (4.5%)	53 (21.9%)	10 (4.1%)	2 (0.8%)
PCOS-infertile	116 (81.1%)	2 (1.4%)	24 (16.8%)	1 (0.7%)	0 (0%)
PCOS-RPL	50 (50.5%)	9 (9.1%)	29 (29.3%)	9 (9.1%)	2 (2%)

Table 3 Hematological, biochemical, and hormonal characteristics among the PCOS phenotypes in Iranian women with PCOS

Parameters	**PCOS Phenotypes**					***p*-value**
	A	**B**	**C**	**E**	**F**	
Age (year)	29.9 ± 4.79	28.9 ± 5.5	29.8 ± 3.5	29.3 ± 3.5	30.0 ± 7.07	NS
BMI (kg/m^2)	27.3 ± 4.1	27.3 ± 6.1	25.7 ± 4.58	26.1 ± 2.4	26.1 ± 2.4	NS
FBS (mg/dL)	90.05 ± 9.2	88.8 ± 8.02	86.2 ± 7.7	88.5 ± 7.4	89.5 ± 3.5	NS
Insulin (µU/mL)	5.8 ± 3.9	7.7 ± 6.5	5.7 ± 3.6	5.6 ± 2.7	2.4 ± 0.8	NS
HOMA-IR	1.32 ± 0.9	1.72 ± 1.5	1.2 ± 0.8	1.2 ± 0.6	0.5 ± 0.2	NS
TG (mg/dL)	130.7 ± 60.3	143.09 ± 67.4	115.7 ± 47.1	141.04 ± 61.8	78.0 ± 36.7	NS
TC (mg/dL)	173.6 ± 35.8	190.09 ± 47.55	167.1 ± 35.8	166.6 ± 31.3	116 ± 41.01	NS
LDL (mg/dL)	98.9 ± 30.4	115.2 ± 36.3	90.8 ± 27.4	98.9 ± 26.8	57.5 ± 21.9	NS
HDL (mg/dL)	44.7 ± 12.2	45.2 ± 13.4	46.1 ± 11.7	42.4 ± 7.4	46.0 ± 8.4	NS
Urea (mg/dL)	23.1 ± 6.8	21.9 ± 4.9	22.6 ± 7.02	22.2 ± 8.5	24.5 ± 2.1	NS
Cr (mg/dL)	0.8 ± 0.3	0.7 ± 0.08	0.8 ± 0.07	0.8 ± 0.07	0.8 ± 0.2	NS
HomoCys (µU/mL)	12.8 ± 5.7	9.62 ± 3.43	12.2 ± 7.1	10.06 ± 1.9	12.7 ± 2.1	NS
WBC (10^3/µL)	5.9 ± 6.51	8.8 ± 2.8	-	5.7 ± 1.7	7.7 ± 1.9	NS
RBC (10^6/µL)	4.7 ± 0.39^a	4.7 ± 0.2^b	4.6 ± 0.3^c	4.6 ± 0.2^e	3.8 ± 0.3$^{a, b,c, e}$	0.006
Hb (g/dl)	13.1 ± 1.07	13.2 ± 0.4	12.9 ± 1.1	13.4 ± 0.7	11.3 ± 0.5	NS
Hct (%)	39.9 ± 2.9 ^{a}	40.4 ± 1.6 ^{b}	39.2 ± 3.2 ^{c}	40.7 ± 1.9 ^{e}	33.6 ± 2.3 $^{a, b,c, e}$	0.014
MCV (fL)	84.07 ± 6.4	80.8 ± 15.4	84.7 ± 4.2	87.8 ± 3.6	87.8 ± 2.8	NS
MCH (pg)	27.8 ± 2.2	27.9 ± 1.3	27.8 ± 2.08	28.9 ± 1.2	29.5 ± 1.4	NS
MCHC (%)	32.9 ± 1.15	32.7 ± 0.8	32.8 ± 1.2	32.9 ± 0.6	33.5 ± 0.6	NS
Platelet (10^6/µL)	214.3 ± 23.7	255 ± 63.4	392 ± 26.3	252 ± 62.2	285 ± 0.0	NS
LH (IU/L)	8.1 ± 5.6	5.04 ± 2.4	6.8 ± 3.9	7.02 ± 3.5	5.3 ± 1.9	NS
FSH (IU/L)	6.6 ± 3.3	6.2 ± 5.2	6.7 ± 3.7	6.8 ± 5.1	4.3 ± 1.4	NS
LH/FSH ratio	1.38 ± 1.01	1.03 ± 0.65	1.1 ± 0.56	1.4 ± 0.98	1.38 ± 0.91	NS

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used to evaluate data normality. For normally distributed data, the ANOVA test was applied. Post hoc comparisons utilized the Bonferroni method. A two-tailed p-value of less than 0.05 was considered statistically significant.

Results

A total of 242 women with PCOS were classified into seven phenotypic subgroups (A-G) for this study. The frequencies of phenotypes D and G were zero; therefore, these phenotypes were excluded from the analysis. As outlined in Table 2, phenotype A was the most prevalent among PCOS women overall and maintained this predominance within both infertile and RPL subpopulations. The distribution of phenotypes A, B, C, E, and F within the total PCOS population was 68.6%, 4.5%, 21.9%, 4.1%, and 0.8%, respectively. The phenotypic distribution was similar across infertile and RPL subgroups. However, a higher proportion of women with phenotype A (81%) was identified in the infertile compared to the RPL (50.5%) subgroup. Conversely, the RPL subgroup exhibited a higher prevalence of phenotypes C, B, and F relative to the infertile group.

Table 3 presents the clinical characteristics of each PCOS phenotype. No significant differences were observed among the phenotypes regarding hematologic, biochemical, or hormonal parameters. However, phenotype F exhibited significantly lower levels of red blood cell (RBC) and hematocrit compared to the other phenotypes (3.8 ± 0.3, $p = 0.006$).

Within the infertile PCOS subgroup, phenotypes showed a significant difference in mean corpuscular volume (MCV) (Table 4) (Phenotypes A, B, and

Table 4 Hematological, biochemical, and hormonal characteristics among the PCOS phenotypes in PCOS women with infertility

Parameters	PCOS Phenotypes				*p*-value
	A	B	C	E*	
Age (year)	30 ± 4.9	29 ± 5.6	29.7 ± 3.7	27	NS
BMI (kg/m2)	27.1 ± 4.3	29.5 ± 5.5	24.9 ± 3.6	26.7	NS
FBS (mg/dL)	89.4 ± 9.1	80 ± 4.2	86.1 ± 6.6	82	NS
Insulin (µU/mL)	5.9 ± 3.8	5.3 ± 5.3	5.6 ± 3.5	6	NS
HOMA-IR	1.3 ± 0.9	1.02 ± 0.9	1.2 ± 0.7	1.2	NS
TG (mg/dL)	124.5 ± 61.5	152 ± 67.8	100 ± 34.6	63	NS
TC (mg/dL)	170.3 ± 33.8	184 ± 72.1	160.3 ± 30.3	170	NS
LDL (mg/dL)	96.7 ± 28.3	106.1 ± 45.1	89.5 ± 23.9	118.4	NS
HDL (mg/dL)	44.9 ± 13.2	40 ± 2.8	45.7 ± 9.7	39	NS
Urea (mg/dL)	22.9 ± 6.4	25.5 ± 2.1	21.09 ± 7.09	15	NS
Cr (mg/dL)	0.8 ± 0.3	0.7 ± 0.01	0.8 ± 0.08	0.7	NS
HomoCys (µU/mL)	12.4 ± 4	-	12.5 ± 3.2	-	NS
WBC (103/µL)	8 ± 7.7	8.3 ± 2.2	4.2 ± 1.4	7.3	NS
RBC (106/µL)	4.7 ± 0.3	4.7 ± 0.1	4.6 ± 0.4	4.4	NS
Hb (g/dl)	13.07 ± 1.07	13.4 ± 0.7	12.8 ± 1.1	13.4	NS
Hct (%)	39.6 ± 2.9	41.8 ± 3.1	39.2 ± 3.3	41.1	NS
MCV (fL)	84.1 ± 7.07	63.6 ± 39.7	84.5 ± 3.9	93	0.001
MCH (pg)	27.8 ± 2.3	28.5 ± 0.8	27.6 ± 2.05	30.3	NS
MCHC (%)	32.8 ± 1.2	32.1 ± 0.6	32.6 ± 1.3	32.6	NS
Platelet (106/µL)	290.3 ± 28.2	189.5 ± 74.2	81.6 ± 38.7	338	NS
LH (IU/L)	9.06 ± 6.2	5.7 ± 1.06	7.5 ± 5.3	8	NS
FSH (IU/L)	6.2 ± 2.3	6.6 ± 0.9	6.3 ± 2.4	5.9	NS
LH/FSH ratio	1.54 ± 1.11	0.86 ± 0.4	1.18 ± 0.65	1.35	NS

* Only one woman categorized in this phenotype. So, it was not compared with others

C; 84.1 ± 7.07, 63.6 ± 39.7,and 84.5 ± 3.9, respectively, $p = 0.001$).

Among PCOS women with a history of RPL, Table 5 demonstrates significantly lower levels of RBC, hemoglobin, and hematocrit in phenotype F compared to the remaining phenotypes.

Discussion

PCOS is a multifactorial endocrine disorder among women of reproductive age [7]. To account for the heterogeneity of PCOS, patients have been classified into distinct phenotypes based on clinical and biochemical characteristics [21]. These phenotypic variations consider factors including hyperandrogenism, ovulatory dysfunction, and polycystic ovary morphology [22]. To date, some studies have reported the prevalence of PCOS phenotypes across different populations and ethnicities [8, 23–25]. This study aimed to determine the prevalence of these phenotypes in an Iranian cohort of women with PCOS. Additionally, the study assessed the prevalence of PCOS phenotypes among Iranian women with PCOS who have infertility and RPL.

Some studies focused on biochemical parameters in different PCOS phenotypes [26–29]. However, the infertility and abortion approach in various PCOS phenotypes was ignored, so far. This study represents a novel investigation into the association between hematological, biochemical, and hormonal parameters and distinct PCOS phenotypes among infertile and RPL patients.

Consistent with findings from Sachdeva et al. and Głuszak et al., phenotype A was the most prevalent among women with PCOS in the present study [8, 23]. Phenotype A is the most commonly reported PCOS manifestation in the majority of published clinical studies [30]. However, in contrast to these findings, a study conducted in Sudan by Elasam et al. reported phenotype D as the most prevalent among Sudanese women with PCOS [24]. The study findings revealed that the prevalence of phenotype A (characterized by hyperandrogenism/hirsutism, oligo/anovulation and polycystic ovaries) was 68.7%. Phenotypes B (hyperandrogenism/hirsutism and oligo/anovulation), C (hyperandrogenism/hirsutism and polycystic ovaries), E (hyperandrogenism/hirsutism), and F (polycystic ovaries) had prevalence rates of 4.5%, 21.9%, 4.1%, and 0.8%, respectively. In this context, Farhadi-Azar identified classical phenotypes A and B as the most prevalent among Iranian women with PCOS [25]. Our findings suggest that most Iranian women diagnosed with PCOS according to the Rotterdam criteria present with all three primary features: hyperandrogenism, polycystic ovaries, and ovulatory dysfunction. Approximately 22% of patients exhibited hyperandrogenism and polycystic ovaries. To date, no studies have reported the prevalence of PCOS phenotypes in PCOS women with

Table 5 Hematological, biochemical, and hormonal characteristics among the PCOS phenotypes in PCOS women with a history of recurrent pregnancy loss

Parameters	PCOS Phenotypes					*p*-value
	A	B	C	E	F	
Age (year)	29.9 ± 4.4	28.8 ± 5.8	30 ± 3.5	29.5 ± 4.03	30 ± 7.07	NS
BMI (kg/m2)	27.6 ± 3.7	26.8 ± 6.4	26.4 ± 5.2	26.07 ± 2.5	26.6 ± 2.9	NS
FBS (mg/dL)	91.3 ± 9.3	90.7 ± 7.3	86.2 ± 8.6	89.2 ± 7.4	89.5 ± 3.5	NS
Insulin (µU/mL)	5.8 ± 4.04	8.3 ± 6.9	5.7 ± 3.8	5.6 ± 2.9	2.4 ± 0.8	NS
HOMA-IR	1.3 ± 0.9	1.8 ± 1.6	1.2 ± 0.8	1.2 ± 0.7	0.5 ± 0.2	NS
TG (mg/dL)	144.9 ± 55.5	141.1 ± 71.3	128.6 ± 52.5	149.7 ± 58.8	78 ± 36.7	NS
TC (mg/dL)	181.3 ± 39.3	191.4 ± 46.5	172.8 ± 39.4	166.3 ± 33.2	116 ± 41	NS
LDL (mg/dL)	104 ± 34.6	117.5 ± 37.1	92 ± 30.5	96.7 ± 27.5	57.5 ± 21.9	NS
HDL (mg/dL)	44.3 ± 9.4	46.5 ± 14.8	46.4 ± 13.3	42.7 ± 7.7	46 ± 8.4	NS
Urea (mg/dL)	23.6 ± 7.8	21 ± 5	23.9 ± 6.8	23.2 ± 8.6	24.5 ± 2.1	NS
Cr (mg/dL)	0.8 ± 0.1	0.7 ± 0.09	0.8 ± 0.06	0.8 ± 0.06	0.8 ± 0.2	NS
HomoCys (µU/mL)	13.1 ± 6.9	9.6 ± 3.4	12 ± 8.2	10 ± 1.9	12.7 ± 2.1	NS
WBC (103/µL)	7.7 ± 2	10.8 ± 3.1	7.5 ± 1.7	6.4 ± 1.8	7.7 ± 1.9	NS
RBC (106/µL)	4.8 ± 0.4[a]	4.7 ± 0.2[b]	4.6 ± 0.3[c]	4.6 ± 0.2[e]	3.8 ± 0.3[a, b,c, e]	0.001
Hb (g/dl)	13.4 ± 1 [a]	13.1 ± 0.4	13 ± 1.1	13.4 ± 0.7 [e]	11.3 ± 0.5 [a, e]	0.007
Hct (%)	40.6 ± 2.9 [a]	40 ± 1.2 [b]	39.1 ± 3.2 [c]	40.7 ± 2 [e]	33.6 ± 2.3 [a, b,c, e]	0.041
MCV (fL)	83.9 ± 4.8	84.6 ± 3.1	84.9 ± 4.5	87.3 ± 3.3	87.9 ± 2.8	NS
MCH (pg)	27.8 ± 1.8	27.7 ± 1.4	28.1 ± 2.1	28.8 ± 2.1	29.5 ± 1.4	NS
MCHC (%)	33.1 ± 0.8	32.8 ± 0.8	33 ± 1.2	32.9 ± 0.6	33.5 ± 0.6	NS
Platelet (106/µL)	285.4 ± 68.1	270.5 ± 54.6	279.9 ± 71.3	243 ± 57.8	285 ± 0.0	NS
LH (IU/L)	6.1 ± 3	4.8 ± 2.7	6.3 ± 2.1	6.9 ± 3.7	5.3 ± 1.9	NS
FSH (IU/L)	7.5 ± 4.8	6.1 ± 5.8	7 ± 4.5	6.9 ± 5.4	4.3 ± 1.4	NS
LH/FSH ratio	1.01 ± 0.6	1.07 ± 0.72	1.04 ± 0.48	1.4 ± 1.04	1.38 ± 0.91	NS

infertility and RPL. Our findings indicate that phenotype A remains the most prevalent phenotype among infertile and RPL subgroups. Phenotype A of PCOS, which recognized as full Rotterdam criteria, probably is associated with an increased risk of infertility and miscarriage. The anovulation characteristic can lead to irregular menstrual cycles and difficulty in conceiving. Additionally, women with this phenotype may experience hormonal imbalances that can affect pregnancy outcomes, increasing the likelihood of abortion. It seems that proper management and treatment are essential for women with this phenotype who are trying to conceive or are pregnant.

Chang et al. reported that biochemical profiles exhibit significant differences across these phenotypes [31]. This study investigated the relationship between PCOS phenotypes and hematological, biochemical, and hormonal parameters. Compared to phenotype C and D, patients with phenotype A and B (classical phenotype) are more often obese, with hirsutism, more likely to have insulin resistance, dyslipidemia, and metabolic syndrome in later life.

PCOS is a complex syndrome associated with metabolic disturbances such as insulin resistance, dyslipidemia, and obesity. Although previous studies have suggested that classical phenotypes (A and B) are more strongly linked to these abnormalities [32, 33], our study did not find significant differences in metabolic parameters such as BMI, fasting insulin, and lipid profile among the phenotypes. These findings align with some studies on Iranian women with PCOS [28]. The limited sample size or ethnic, epigenetic and environmental and developmental differences may have influenced these results [34]. However, the metabolic aspect of PCOS remains crucial. Future studies with larger sample sizes and more detailed metabolic assessments, including HOMA-IR and inflammatory markers, could further clarify the relationship between PCOS phenotypes, infertility, and recurrent pregnancy loss.

In the current study, phenotype A have shown the most level of insulin resistance and LH/FSH ratio in PCOS with infertility, which did not receive to significant level. Our findings did not reveal significant differences in BMI, fasting blood sugar (FBS), insulin, lipid profile, urea, creatinine, LH, FSH, homocysteine, WBC, Hb, MCV, MCHC, MCH and platelet counts among the different PCOS subgroups. These results align with the observations of Elasam et al. regarding BMI and LH/FSH levels [24]. Similarly, our lipid profile findings concur with those of Gluszak et al. [23]. However, these results contrast with those of several other studies, including Sachdeva et al., Jamil et al., and Abashova et al., which reported significant variations in lipid and glucose profiles across PCOS phenotypes [8, 35, 36]. Nevertheless, Hosseinpanah et al. in line with our findings showed there was no

difference regarding metabolic characteristics between different PCOS phenotypes in Iranian women [28]. These discrepancies may be attributed to differences in study populations, diagnostic criteria, sample sizes, or other methodological factors. Further research is warranted to elucidate the complex interplay between PCOS phenotypes and metabolic disturbances.

Previous research has linked increased oxidative stress in PCOS to shortened RBC lifespan due to membrane alterations [37]. While studies have reported varying RBC parameters among PCOS women [38, 39], others have found no significant differences in blood-related factors between women with and without PCOS [40]. We investigate that phenotype F in PCOS women with RPL, probably suffer from anemia like megaloblastic anemia, because of higher level of RBC and MCV, as well as lower level of Hct and Hb. Interestingly, this pattern was not found in PCOS women with infertility. A decrease in red blood cell count, hematocrit, and hemoglobin can be associated with folic acid deficiency. Folic acid, a member of the B vitamin group, plays a vital role in the production and proliferation of blood cells [41]. This vitamin is especially essential for DNA and RNA synthesis and is necessary for the production of healthy red blood cells. Folic acid has crucial role in the one-carbon metabolism cycle. This cycle contributes to the production of methionine and other essential compounds that are critical for fetal growth and development. Disruptions in this cycle can increase the risk of abortion [42, 43]. PCOS women with phenotype F known as" non-hyperandrogenic" PCOS which is characterized only by PCO on ultrasound. This phenotype has unknown and unclear pathophysiology. The observed hematological changes within phenotype F is intriguing and warrants further exploration with a larger sample size about the role of one-carbon metabolism cycle to validate these preliminary findings.

Conclusion

Our study investigate the possible impact of PCOS phenotypes in an Iranian population in relation to reproductive outcomes. The findings indicate that women with PCOS, especially those exhibiting phenotype A, face increased challenges regarding infertility and a higher risk of repeated pregnancy loss. These results indicate that comprehensive metabolic screening may not be necessary for different phenotypes of PCOS. To gain a deeper understanding of hematological parameters effect in women with various PCOS phenotypes who experience pregnancy loss, further research through larger population-based studies is essential.

Limitations

Despite the novel nature of this investigation, certain limitations warrant consideration. The relatively small sample size limits the generalizability of our findings. Additionally, the study's focus on Iranian women restricts definitive conclusions about racial and environmental factors. Future research involving larger and more diverse populations is necessary to validate and expand upon these results. Another limitation of this study was the inability to assess additional factors such as QUICKI, G/I ratio, and biomarkers like free and bound testosterone, SHBG, estradiol, and DHEA-sulphate and AMH due to financial constraints. Future research incorporating these parameters may offer a more comprehensive understanding of the pathophysiology of PCOS.

Abbreviations

BMI	Body Mass Index
FBG	Fasting Blood Glucose
FSH	Follicle-Stimulating Hormone
HDL-C	High-Density Lipoprotein Cholesterol
HOMA-IR	Homeostasis Model Assessment of IR
LDL-C	Low-Density Lipoprotein Cholesterol
LH	Luteinizing Hormone
PCOS	Polycystic Ovary Syndrome
TC	Total Cholesterol
RPL	Recurrent Pregnancy Loss

Acknowledgements

The authors are grateful to the University of Tehran for the support of this project.

Author contributions

AK: Conceptualization and Supervision; HH: Writing original draft, Investigation; AV: Conceptualization and Statistical Analysis. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Funding

This study was supported by the University of Tehran.

Data availability

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1975 Helsinki declaration as revised in 2008. The present research was approved by the Ethics Committee of Ibn Sina Infertility Center. Informed consent was obtained through a written consent form before starting the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 24 August 2024 / Accepted: 25 March 2025
Published online: 13 May 2025

References

1. Carmina E, Lobo RA. Polycystic ovary syndrome (PCOS): arguably the most common endocrinopathy is associated with significant morbidity in women. J Clin Endocrinol Metabolism. 1999;84(6):1897–9.

2. Hull MGR. Epidemiology of infertility and polycystic ovarian disease: endocrinological and demographic studies. Gynecol Endocrinol 1987 1987/01/01;1(3):235–45.
3. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. Diabetes. 1989;38(9):1165–74.
4. Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, et al. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Eur J Endocrinol. 2023;189(2):G43–64.
5. Revised. 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19(1):41–7.
6. Ehrmann DA. Polycystic ovary syndrome. N Engl J Med. 2005;352(12):1223–36.
7. Franks S. Polycystic ovary syndrome. N Engl J Med. 1995;333(13):853–61.
8. Sachdeva G, Gainder S, Suri V, Sachdeva N, Chopra S. Comparison of the different PCOS phenotypes based on clinical metabolic, and hormonal profile, and their response to clomiphene. Indian J Endocrinol Metab 2019 May-Jun;23(3):326–31.
9. Rosenfield RL, Ehrmann DA. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocr Rev. 2016;37(5):467–520.
10. Wartena R, Matjila M. Polycystic ovary syndrome and recurrent pregnancy loss, a review of literature. Front Endocrinol. 2023;14:1183060.
11. Palomba S, Falbo A, Chiossi G, Tolino A, Tucci L, La Sala GB, et al. Early trophoblast invasion and placentation in women with different PCOS phenotypes. Reprod Biomed Online. 2014;29(3):370–81.
12. Kollmann M, Klaritsch P, Martins WP, Guenther F, Schneider V, Herzog SA, et al. Maternal and neonatal outcomes in pregnant women with PCOS: comparison of different diagnostic definitions. Hum Reprod. 2015;30(10):2396–403.
13. Palomba S, De Wilde MA, Falbo A, Koster MPH, La Sala GB, Fauser BCJM. Pregnancy complications in women with polycystic ovary syndrome. Hum Reprod Update. 2015;21(5):575–92.
14. Hoeger KM. Role of lifestyle modification in the management of polycystic ovary syndrome. Best Pract Res Clin Endocrinol Metab. 2006;20(2):293–310.
15. Zhao H, Song X, Zhang L, Xu Y, Wang X. Comparison of androgen levels, endocrine and metabolic indices, and clinical findings in women with polycystic ovary syndrome in Uygur and Han ethnic groups from Xinjiang Province in China. Med Sci Monitor: Int Med J Experimental Clin Res. 2018;24:6774.
16. Moran L, Teede H. Metabolic features of the reproductive phenotypes of polycystic ovary syndrome. Hum Reprod Update. 2009;15(4):477–88.
17. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The androgen excess and PCOS society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril. 2009;91(2):456–88.
18. Kheirollahi A, Teimouri M, Karimi M, Vatannejad A, Moradi N, Borumandnia N, et al. Evaluation of lipid ratios and triglyceride-glucose index as risk markers of insulin resistance in Iranian polycystic ovary syndrome women. Lipids Health Dis. 2020;19:1–9.
19. Sadeghi A, Fadaei R, Moradi N, Fouani FZ, Roozbehkia M, Zandieh Z, et al. Circulating levels of C1q/TNF-α-related protein 6 (CTRP6) in polycystic ovary syndrome. IUBMB Life. 2020;72(7):1449–59.
20. Shanaki M, Moradi N, Fadaei R, Zandieh Z, Shabani P, Vatannejad A. Lower Circulating levels of CTRP12 and CTRP13 in polycystic ovarian syndrome: irrespective of obesity. PLoS ONE. 2018;13(12):e0208059.
21. Elsayed AM, Al-Kaabi LS, Al-Abdulla NM, Al-Kuwari MS, Al-Mulla AA, Al-Shamari RS, et al. Clinical phenotypes of PCOS: A cross-sectional study. Reproductive Sci. 2023;30(11):3261–72.
22. Lee HJ, Jo HN, Noh HK, Kim SH, Joo JK. Is there association between thyroid stimulating hormone levels and the four phenotypes in polycystic ovary syndrome? Ginekologia Polska. 2023;94(3):203–10.
23. Głuszak O, Stopińska-Głuszak U, Glinicki P, Kapuścińska R, Snochowska H, Zgliczyński W, et al. Phenotype and metabolic disorders in polycystic ovary syndrome. Int Sch Res Notices. 2012;2012(1):569862.
24. Elasam AN, Ahmed MA, Ahmed AB, Sharif ME, Abusham A, Hassan B, et al. The prevalence and phenotypic manifestations of polycystic ovary syndrome (PCOS) among infertile Sudanese women: a cross-sectional study. BMC Womens Health. 2022;22(1):165.
25. Farhadi-Azar M, Behboudi-Gandevani S, Rahmati M, Mahboobifard F, Khalili Pouya E, Ramezani Tehrani F, et al. The prevalence of polycystic ovary syndrome, its phenotypes and cardio-metabolic features in a community sample of Iranian population: Tehran lipid and glucose study. Front Endocrinol. 2022;13:825528.
26. Mehra T, Sharma S, Zahra T, Jangir S, Gupta B. Correlation of body mass index with anthropometric and biochemical parameters among polycystic ovary syndrome phenotypes. Indian J Clin Biochem. 2023;38(2):231–41.
27. Amiri M, Bidhendi Yarandi R, Nahidi F, Tohidi M, Ramezani Tehrani F. The relationship between clinical and biochemical characteristics and quality of life in patients with polycystic ovary syndrome. Clin Endocrinol. 2019;90(1):129–37.
28. Hosseinpanah F, Barzin M, Keihani S, Ramezani Tehrani F, Azizi F. Metabolic aspects of different phenotypes of polycystic ovary syndrome: Iranian PCOS prevalence study. Clin Endocrinol. 2014;81(1):93–9.
29. Bil E, Dilbaz B, Cirik DA, Ozelci R, Ozkaya E, Dilbaz S. Metabolic syndrome and metabolic risk profile according to polycystic ovary syndrome phenotype. J Obstet Gynecol Res. 2016;42(7):837–43.
30. Wild RA, Carmina E, Diamanti-Kandarakis E, Dokras A, Escobar-Morreale HF, Futterweit W, et al. Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the androgen excess and polycystic ovary syndrome (AE-PCOS) society. J Clin Endocrinol Metabolism. 2010;95(5):2038–49.
31. Chang WY, Knochenhauer ES, Bartolucci AA, Azziz R. Phenotypic spectrum of polycystic ovary syndrome: clinical and biochemical characterization of the three major clinical subgroups. Fertil Steril. 2005;83(6):1717–23.
32. Borzan V, Lerchbaum E, Missbrenner C, Heijboer AC, Goschnik M, Trummer C, et al. Risk of insulin resistance and metabolic syndrome in women with hyperandrogenemia: a comparison between PCOS phenotypes and beyond. J Clin Med. 2021;10(4):829.
33. Piché M-E, Tchernof A, Després J-P. Obesity phenotypes, diabetes, and cardiovascular diseases. Circul Res. 2020;126(11):1477–500.
34. Helvaci N, Yildiz BO. Polycystic ovary syndrome as a metabolic disease. Nat Reviews Endocrinol. 2024:1–15.
35. Jamil AS, Alalaf SK, Al-Tawil NG, Al-Shawaf T. Comparison of clinical and hormonal characteristics among four phenotypes of polycystic ovary syndrome based on the Rotterdam criteria. Arch Gynecol Obstet. 2016;293:447–56.
36. Abashova EI, Yarmolinskaya MI, Bulgakova OL, Misharina EV. Lipid profile in women of reproductive age with various polycystic ovary syndrome phenotypes. J Obstet Women's Dis. 2020;69(6):7–16.
37. Andrisani A, Donİ G, Sabbadin C, Tibaldi E, Dessole F, Bosello Travain V, et al. Ameliorative effect of myo-inositol on red blood cell alterations in polycystic ovary syndrome: in vitro study. Gynecol Endocrinol. 2018;34(3):233–7.
38. Ali IN, Alhiti MAJ, Jawad HG. The correlation between the blood and hormonal disorders with syndrome of polycystic ovaries in women of the Baghdad City. Eur J Biomedical. 2016;3(9):65–9.
39. Ha L-X, Du Y-D, Qu X-X, Wang J-J. Correlation between hemoglobin levels and polycystic ovary syndrome metabolic disorder. Diabetes, Metabolic Syndrome and Obesity. 2023:3019-27.
40. Alhabardi NA, Al-Wutayd O, Eltayieb KM, Shiha YS, Al-Shafei AI, Adam I. Peripheral hematological parameters in women with polycystic ovary syndrome. J Int Med Res. 2020;48(9):0300060520952282.
41. Shulpekova Y, Nechaev V, Kardasheva S, Sedova A, Kurbatova A, Bueverova E, et al. The concept of folic acid in health and disease. Molecules. 2021;26(12):3731.
42. Diao J, Luo L, Li J, Zhang S, Li Y, Qin J. Maternal homocysteine and folate levels and risk of recurrent spontaneous abortion: A metaâ€کanalysis of observational studies. J Obstet Gynecol Res. 2020;46(12):2461–73.
43. Lei F, Zhang L, Wang L, Wu W, Wang F. Association between early spontaneous abortion and homocysteine metabolism. Front Med. 2024;11:1310112.

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