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REVIEW

Polycystic ovary syndrome: Criteria, phenotypes, race and ethnicity

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a complex endocrinopathy, which leads to ovulation dysfunction and infertility, as well as metabolic and mental disorders. Women with PCOS exhibit several characteristic symptoms, with marked heterogeneity across different races and ethnicities.

Methods: In this review, the author outlines the phenotypic disparities of PCOS among various racial and ethnic populations. First, the prevalence of major symptoms in different racial and ethnic groups with PCOS is summarized. Next, the effects of four phenotypes, derived from the Rotterdam criteria for PCOS, on metabolic and reproductive features are recapitulated.

Main Findings: A growing body of evidence suggests that East Asian populations exhibit less hirsutism and adiposity compared with other groups. However, hirsutism is more prevalent in South Asian, Middle Eastern, and Hispanic populations. Hispanic and African American populations have more frequent obesity and insulin resistance. With regard to the association between mental disorders and racial and ethnic differences, limited studies exist; therefore, no conclusions can be drawn.

Conclusion: Race and ethnicity-specific factors related to PCOS must be considered in clinical practice. The diagnostic criteria of PCOS should be specific to race and ethnicity to avoid missing treatment opportunities.

KEYWORDS
diagnosis, ethnicity, phenotype, polycystic ovary syndrome, race

1 | INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrinopathy, which is characterized by ovulation disorder, hyperandrogenism, and polycystic ovarian morphology (PCOM). The pathogenesis of PCOS is yet to be elucidated, although it was recognized in 1935 by Stein and Leventhal.[1] Women with PCOS have certain endocrinological and metabolic characteristics, such as hyperandrogenism, elevated luteinizing hormone (LH) and LH/follicle-stimulating hormone (FSH) ratio, obesity, and insulin resistance (Figure 1).[2–4] Among these features, androgen excess is regarded as a chief cause of PCOS and is a prerequisite for PCOS in most diagnostic criteria.[5–7]

The clinical manifestations in women with PCOS are diverse and complicated. Diagnosing PCOS and detecting its various manifestations are valuable for lifelong health care in affected women. Ovulation dysfunction raises the risk of infertility,

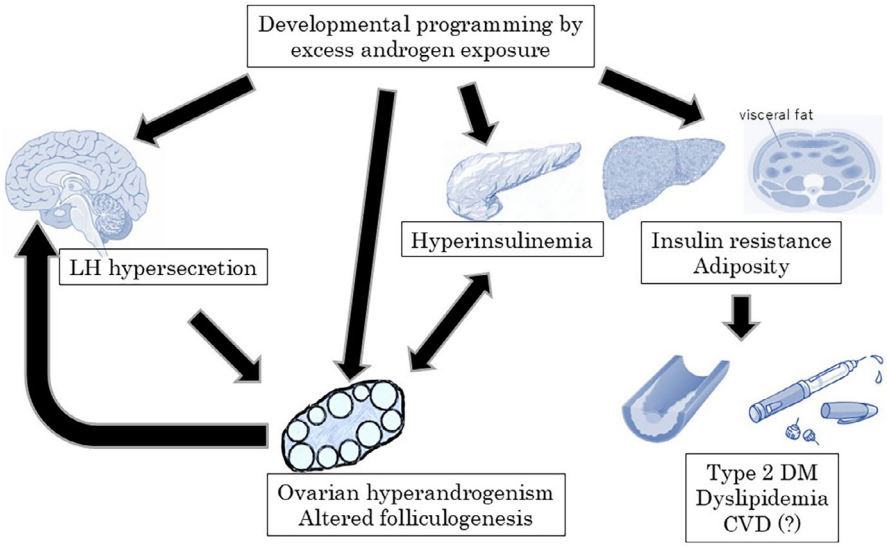

FIGURE 1 Putative pathogeneses of PCOS. Hypothetical etiology of excessive prenatal androgen exposure owing to genetic or prenatal environmental factors affecting various organs, which leads to programming of PCOS, such as hypothalamic dysregulation, functional ovarian hyperandrogenism, and metabolic disorders. CVD, cardiovascular disease; DM, diabetes mellitus; LH, luteinizing hormone; PCOS, polycystic ovary syndrome.

menstrual irregularity, and abnormal uterine bleeding. Women with PCOS possess unique follicular development, which is an upstream factor of ovulation. A previous study proposed that follicular development in PCOS is characterized by both increased initial recruitment of primordial follicle growth and mature arrest in the antral stage, which subsequently accumulates small antral follicles in the ovaries and causes PCOM.[8] Accumulated antral follicles are merely stalled in their growth; the follicles can restart growth once iatrogenic FSH increment is initiated for ovulation induction and ovarian stimulation. PCOM is a serious problem in infertility treatment because it is directly associated with multiple pregnancies and ovarian hyperstimulation syndrome. Hirsutism, acne, seborrhea, and female pattern hair loss are considered to be consequences of hyperandrogenism. Such skin manifestations can lead to psychosocial problems.[9] Obesity is associated with various manifestations of PCOS, such as insulin resistance and hyperandrogenism.[10] Racial and ethnic differences in dietary habits and physical activity greatly influence the occurrence of obesity. Insulin resistance promotes PCOS development and has serious health consequences. Insulin resistance subsequently triggers type 2 diabetes mellitus (T2DM), dyslipidemia, and cardiovascular events (endothelial dysfunction).[11–13] Additionally, psychiatric problems (anxiety, depression, sleeping, and eating disorders), uterine endometrial neoplasm, and pregnancy complications are prevalent in women with PCOS.[14]

Polycystic ovary syndrome is considered a multifactorial disorder with marked heterogeneity. In particular, genetic predisposition, environmental conditions, cultural differences, and dietary habits determine the body composition and modify the various symptoms of PCOS. Understanding racial and ethnic differences in PCOS can influence screening and management of this condition. In this review, the author summarizes and discusses how race and ethnicity as well as diagnostic criteria affect phenotypic differences. The aim is to enhance the recognition of racial and ethnic variations in routine clinical practice and guide future research.

2 | DIAGNOSTIC CRITERIA AND CLINICAL MANIFESTATIONS

Statistical investigations of PCOS are challenging. There is no international standard for diagnosing PCOS; several diagnostic criteria are advocated because the etiology of PCOS is not fully understood and racial and ethnic differences exist in the clinical manifestations of PCOS. Phenotypic diversity among women with PCOS might be somewhat dependent on the diagnostic criteria applied. The National Institutes of Health (NIH) first suggested diagnostic criteria for PCOS in 1990, which comprised the presence of both clinical/biochemical hyperandrogenism and chronic anovulation.[5] PCOM was not emphasized in the NIH 1990 criteria. In 2003, the European Society of Human Reproduction and Embryology and the American Society for Reproductive Medicine defined the Rotterdam 2003 PCOS criteria. These criteria involve the presence of at least two of the following: (1) oligo-anovulation (O-ANOV), (2) clinical/biochemical hyperandrogenism, and (3) PCOM.[15] Notably, PCOS may be diagnosed even in cases without androgen excess using the Rotterdam 2003 criteria. Women with hyperandrogenic PCOS are at increased risk of metabolic abnormality,[16] and PCOS diagnosed using the Rotterdam criteria includes mild metabolic phenotype. That is, the Rotterdam 2003 criteria, which are currently accepted worldwide, include a wide variety of phenotypes compared with the NIH 1990 criteria. Thus, the prevalence of PCOS according to the Rotterdam 2003 criteria differs from that according to the NIH 1990 criteria (5%–8% vs. 8%–13%).[17] The Japanese Society of Obstetrics and Gynecology (JSOG) revised the diagnostic criteria in 2024; the JSOG 2007 criteria were used prior to 2024.[7,18] The previous criteria defined PCOS as the presence of the following: (1) ovulation disorder, (2) PCOM, and (3) biochemical hyperandrogenism and/or LH hypersecretion. LH hypersecretion indicates ovarian hyperandrogenism.[19] In this regard, the JSOG 2007 criteria are stricter than the Rotterdam 2003 criteria, and women with PCOS according to the JSOG 2007 criteria fulfill both the NIH 1990 and the Rotterdam 2003 criteria.

As will be discussed later, significant variations exist regarding the reported prevalence of manifestations in women with PCOS. This might be owing to the diagnostic criteria applied (whether milder phenotypes are included), racial and ethnic differences, and bias in the study population (many studies are based on the selected population).

3 | CLINICAL MANIFESTATIONS OF PCOS

In this review article, the author discusses clinical manifestations of PCOS in the following three parts: (A) reproductive and endocrinological features, (B) metabolic features, and (C) mental problems (Table 1).

TABLE 1 Clinical manifestations in PCOS.

Characteristic features	Manifestations
Reproductive features	
Ovulation dysfunction	Infertility, AUB
Polycystic ovarian morphology	Risk of iatrogenic OHSS
Endocrinological features	
Hyperandrogenism	Hirsutism, acne
	Obstructive sleep apnea?
Metabolic features	
Insulin resistance	Obesity
Adiposity	Type 2 DM
	Dyslipidemia
	CVD?
Mental problems	
Impaired body image?	Anxiety
	Depression
	Low self-esteem

Abbreviations: AUB, abnormal uterine bleeding; CVD, cardiovascular disease; DM, diabetes mellitus; OHSS, ovarian hyperstimulation syndrome; PCOS, polycystic ovary syndrome.

3.1 | Reproductive and endocrinological features

Polycystic ovary syndrome is a disease of reproduction and endocrinology. Hyperandrogenism, PCOM, and ovulation disorder are crucial features of PCOS. These symptoms are related to many health concerns including infertility, abnormal uterine bleeding, metabolic disturbance, and iatrogenic ovarian hyperstimulation syndrome.

3.1.1 | Biochemical and clinical hyperandrogenism

Both biochemical and clinical hyperandrogenism are key manifestations in PCOS. Biochemical hyperandrogenism refers to hyperandrogenemia, which is the state of excess androgen(s) in the circulating blood. This is a simple but an abstruse definition. First, there is no consensus regarding androgens for diagnostic use, although there are many types and forms of androgens including total testosterone, free testosterone, androstenedione, and dehydroepiandrosterone sulfate. Second, no universal cutoff value for androgen level exists, with cutoffs being defined in different laboratories. Third, data regarding circulating androgen concentrations in women are scarce, and commercially available immunoassays have limited sensitivity for precise measurement. These facts might contribute to the risk of bias in diagnosing hyperandrogenemia.

Animal studies indicate that excess androgen causes increased food intake, reduced energy expenditure, skeletal muscle insulin resistance, and beta-cell dysfunction.[20] Accordingly, hyperandrogenemia is closely related to the metabolic characteristics of PCOS, such as insulin resistance and obesity (Figure 2).[21–24] In this respect, the prevalence of hyperandrogenemia theoretically mirrors heterogeneity across geographic regions, as in the prevalence of insulin resistance and obesity. However, a cross-sectional study showed that White women with PCOS were more likely to have elevated serum androgens than their Asian counterparts, although this was not statistically significant (63.5% vs. 48.0%, $p=0.15$).[25] In a study at a single tertiary hospital in Japan, 60.2% of women with PCOS had hyperandrogenemia, according to the Rotterdam 2003 criteria.[26] According to a survey involving 643 hospitals in Japan, the

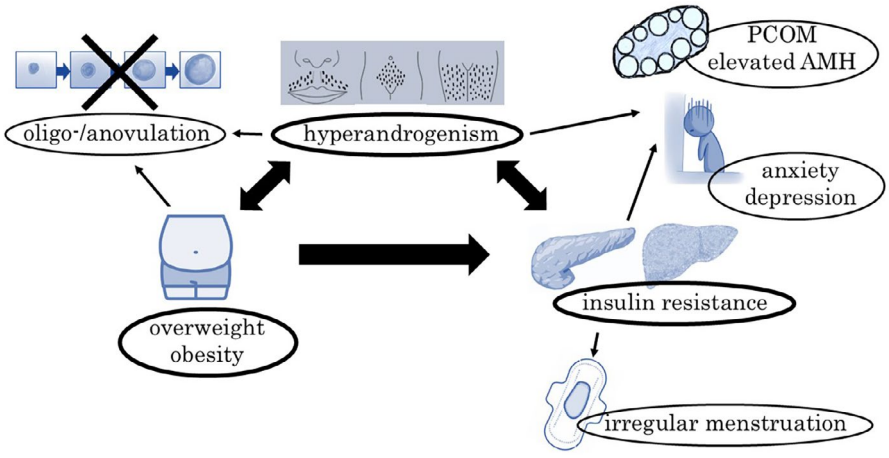

FIGURE 2 Relationships among various symptoms of PCOS. Hyperandrogenism, overweight/obesity, and insulin resistance are cardinal components of PCOS and are closely related to each other. The line thickness denotes the strength of the effect. AMH, anti-Müllerian hormone; PCOM, polycystic ovarian morphology; PCOS, polycystic ovary syndrome.

prevalence of hyperandrogenemia is 37.6% among women with PCOS per the JSOG 2003 criteria.[27] Even within the same racial and ethnic population, selection bias and different diagnostic criteria yield somewhat diverse results, which complicates the evaluation of racial and ethnic differences. A recent meta-analysis concluded that androgen concentrations in women with PCOS appeared similar among diverse racial and ethnic populations.[28] Sophisticated comparative analyses of biochemical hyperandrogenism in multi-racial and ethnic cohorts are needed.

Hirsutism is one of the symptoms of clinical hyperandrogenism. Several factors, which are modified by race and ethnicity, regulate the development of hirsutism. Increased 5α-reductase (5AR) activity, which converts testosterone into dihydrotestosterone—a more potent androgen—is important for hirsutism development. Whites have more 5AR activity than Asians.[29] Intriguingly, obesity is positively correlated with 5AR activity[30] and racial and ethnic differences might affect 5AR activity. Also related to hirsutism, 17β-hydroxysteroid dehydrogenase (HSD) and 3β-HSD are involved in testosterone metabolism, and steroid hormone-binding globulin and albumin affect testosterone clearance. The binding capacity of androgens to androgen receptors might also affect hair growth. These factors might be genetically modified, giving rise to racial and ethnic disparities.[31] In this context, hirsutism does not always accompany hypersecretion of ovarian androgen, which is considered to be the pathogenesis of PCOS.[32] In support of the aforementioned fact, the serum testosterone concentration is not correlated with the Ferriman–Gallwey (FG) score, an evaluation method for hirsutism.[33]

Geographic differences in hirsutism are reported among women with PCOS. East Asian women with PCOS exhibit lower modified FG (mFG) scores and South Asian, Middle Eastern, and Hispanic women with PCOS have higher mFG scores (Table 2).[28] At present, it is considered that the prevalence of hyperandrogenemia is similar among different races and ethnicities, although geographic disparities exist regarding hirsutism.

TABLE 2 Summary of phenotypic variations among distinct ethnic groups (compared with European population).

Asian	
East Asian	Lean but central adiposity
	Less hirsute
South Asian	More hirsute
	More insulin resistant
	Lean but central adiposity
Hispanic	More obese
	More insulin resistant
	Worse lipid profile
	More hirsute?
Middle Eastern	More insulin resistant
	More hirsute?
African American	More obese?
	More insulin resistant
	Favorable lipid profile
European (White)	Reference

3.1.2 | Polycystic ovarian morphology (PCOM)

Polycystic ovary syndrome refers to the ultrasonographic finding of follicle excess. PCOM is correlated to hyperandrogenism and these are thought to have a causal relationship (Figure 2).[34,35] Additionally, women with PCOS and PCOM have a higher body mass index (BMI) than those without PCOM.[36] The definition of PCOM varies among several diagnostic criteria because the cutoff value for the antral follicle count (AFC) and the application of ovarian volume are different. The frequency of ultrasound transducer affects strictness in the determination of follicle count. That is, several factors might have an impact on the estimation of PCOM prevalence. Nevertheless, there is no difference among racial and ethnic populations in most published studies,[28] and more than 90% of women with PCOS exhibit PCOM in all races and ethnicities.[37]

To assess the effects of PCOM on metabolism, some studies have compared metabolic profiles in normoandrogenic anovulatory women with PCOS and those without PCOS. These studies suggest that the presence of PCOM does not affect the lipid profile, insulin resistance, the prevalence of T2DM, or metabolic syndrome when BMI and waist circumference are matched.[38–40]

3.1.3 | Elevated serum anti-Müllerian hormone (AMH)

Anti-Müllerian hormone is mainly secreted by the granulosa cells of secondary, preantral, and small antral follicles.[41,42] AMH appears to inhibit the follicle growth response to FSH and contributes to the development of PCOM.[43] There is a clear correlation between serum AMH levels and AFC; therefore, women with PCOS have elevated levels of serum AMH.[44] Evaluation of AFC lacks objectivity to a certain degree, in comparison with serum AMH measurement, because AFC is affected by the resolution of the ultrasound device and interobserver bias. In fact, AFC exhibits significantly greater variability than AMH in women with PCOS.[45] That is, serum AMH might be a more precise marker of PCOM than AFC.

Intriguingly, granulosa cells from women with PCOS produce AMH that is more potent than AMH in controls.[46,47] Genetic predisposition is considered one of the determining factors of AMH levels.[48] Racial and ethnic differences are suspected to exist with regard to AMH levels. In general population studies, it is suggested that AMH levels are highly variable among races and ethnicities.[49] AMH levels tend to be higher in White and Asian women compared with Black and Hispanic women when age is matched. Although there are no studies evaluating the racial and ethnic differences in AMH levels among women with PCOS, differences in the general population might be applicable to PCOS populations.

3.1.4 | Irregular menstrual cycles and ovulatory dysfunction

For reproductive-aged women, irregular menstrual cycles are defined as <21 or >35 days or <8 cycles per year.[50] An irregular menstrual cycle is a surrogate marker of ovulation dysfunction, although some women with regular menstrual cycles have chronic anovulation.[51] According to the NIH 1990 criteria, most women with PCOS have menstrual irregularity owing to the presence of chronic anovulation, which is a key component of the NIH 1990 criteria. Women with so-called ovulatory PCOS, a subset of women diagnosed using the Rotterdam 2003 criteria, tend to have regular menstruation. In a few studies among women who met the Rotterdam 2003 criteria, the prevalence of O-ANOV ranged from 84% to 94%, and this rate was similar among different races and ethnicities.[26,52,53]

Several studies have investigated the relationship between menstrual irregularity and insulin resistance, with conflicting results. One report suggested that menstrual irregularity is not associated with insulin resistance.[54] However, several studies have demonstrated that the severity of menstrual disturbance is associated with insulin resistance.[55,56] Interestingly, some studies indicate that women with PCOS who exhibit eumenorrhea have a lower prevalence of insulin resistance than those with oligomenorrhea or amenorrhea, irrespective of ovulatory status.[57,58] In this regard, ovulatory status might be an independent feature of PCOS, with ovulation dysfunction rarely affecting the metabolic phenotypes of PCOS.

3.1.5 | Hypersecretion of luteinizing hormone

Although several diagnostic criteria for PCOS do not include LH hypersecretion, elevated serum LH levels and normal FSH levels are another characteristic of PCOS.[59] Increased gonadotropin-releasing hormone (GnRH) pulse frequency and amplitude in PCOS cause excess LH, which stimulates theca cells to produce androgens. However, obesity decreases the GnRH pulse amplitude and basal LH level.[60] Limited studies have investigated the proportion of patients with PCOS who have an elevated LH and LH/FSH ratio. In a survey of a Japanese population, elevated basal LH levels were seen in 77.8% of women with PCOS without overweight/obesity and in 69.1% of those who were overweight or obese ($p < 0.05$).[26] In East Asian women with PCOS, which have a lower BMI and lower frequency of hirsute, measuring the basal LH level and/or LH/FSH ratio is useful for assessing hyperandrogenism.[26,61] In women with PCOS and obesity, high LH can be evaluated using elevation of the LH/FSH ratio.

3.2 | Metabolic features

Although the diagnostic criteria for PCOS do not include metabolic factors, PCOS is closely related to metabolic disorders. Metabolic characteristics are affected by genetic, cultural, and dietary factors; therefore, racial and ethnic differences are suspected to modify metabolic features.

3.2.1 | Overweight and obesity

The World Health Organization defines overweight and obesity as BMI 25.0–29.9 and ≥30 kg/m^2, respectively.[62] Strictly, these cutoffs have White, Hispanic, and African origins; the definition underestimates the adiposity levels in Asian people. For Asian populations, overweight and obesity are defined as BMI 23.0–24.9 and ≥25 kg/m^2, respectively. In this article, the definition for other races and ethnicities was tentatively applied to Asian populations for the sake of simplicity.

Overweight and obesity are increasing in the general population, leading to serious problems worldwide. The estimated prevalence of obesity in European women increased from 12.8% in 1975 to 24.5% in 2016.[63] In contrast, the estimated prevalence of obesity among Japanese women has not changed dramatically over time. The estimated prevalence of obesity among adult Japanese women in 1975 and in 2016 was 1.3% and 3.7%, respectively.[63] Accordingly, the number of overweight/obese women with PCOS is small in Japan compared with the number in Western countries, although obesity is considered to be a pathognomonic characteristic of PCOS. A previous meta-analysis showed that the prevalence of overweight/obesity among women with PCOS in East Asia, West Asia, Europe, and the United States was roughly 40%, 40%–70%, 40%–85%, and 80%–90%, respectively (Table 2).[64] In Japan, the prevalence of overweight/obese women with PCOS is 26.0%.[27]

Overweight and obesity contribute to the severity of PCOS phenotypes, although they are not included in the diagnostic criteria. Excess weight adversely affects reproductive, metabolic, and mental health (Figure 2).[65–69] Lifestyle intervention (exercise, dietary management, behavioral approaches, and stress management) for obese women with PCOS is the first choice of treatment, with a 5%–10% weight reduction yielding metabolic, reproductive, and psychological benefits.[65,68,70–73] However, obesity itself is likely not a cause of PCOS as demonstrated by the high prevalence of PCOS among individuals with relatively normal weight.[64] This is supported by the fact that the prevalence of PCOS is similar in different regions and among races and ethnicities worldwide.[74] Additionally, women with infertility and obesity respond similarly to lifestyle intervention, irrespective of PCOS.[75] That is, women with obesity might have similar characteristics, even if they have PCOS.

3.2.2 | Insulin resistance

Insulin resistance is thought to be a pathognomonic feature of PCOS, although it is not considered a diagnostic criterion. It is important to evaluate and manage insulin resistance in women with PCOS, which can lead to T2DM, dyslipidemia, and cardiovascular disease (CVD). Insulin resistance is also affected by adiposity, dietary habits, and

genetic predisposition. In this regard, race and ethnicity-based differences in insulin resistance are likely.

The gold standard method for the determination of insulin resistance is the hyperinsulinemic–euglycemic clamp or glucose clamp.[76] However, owing to its complexity, several surrogate indices, such as the homeostasis model assessment of insulin resistance (HOMA-IR), have been proposed and validated.[77] HOMA-IR is calculated based on blood glucose and insulin at fasting. It is a simple but controversial method. In a retrospective study of Chinese women with PCOS, the prevalence of insulin resistance estimated using HOMA-IR was lower than that determined using the clamp method.[78] Also, several cutoff values of HOMA-IR have been suggested; thus, the lack of consensus in diagnosing insulin resistance complicates its estimated prevalence among women with PCOS.

A limited number of studies support racial and ethnic variations in insulin resistance. A previous case–control study with a small sample size suggested that South Asian women with PCOS are more insulin resistant than Whites, despite having a similar BMI.[79] Also, Hispanic and Black women with PCOS are more insulin resistant than Whites.[80,81] Apparently, race and ethnicity modifies the prevalence of insulin resistance in women with PCOS, irrespective of body adiposity (Table 2).

3.2.3 | Impaired glucose tolerance and type 2 diabetes

Women with PCOS are at increased risk of developing impaired glucose tolerance (IGT) and T2DM because insulin resistance and obesity are common features of PCOS. Accordingly, women with PCOS show an increased prevalence of IGT, regardless of race and ethnicity. When BMI is matched, Asian populations have a greater risk of IGT (odds ratio [OR]: 3.16, 95% confidence interval [CI]: 1.27–7.87, $p=0.014$) than European (OR: 1.83, 95% CI: 1.09–3.05, $p=0.022$) and American (OR: 5.26, 95% CI: 0.63–44.00, $p=0.126$) populations.[82] Typically, the general population with IGT at baseline develops T2DM at a yearly rate of 5.7%.[83] T2DM is also more prevalent among women with PCOS. However, there are no statistically significant differences in the risk of T2DM among women of different races and ethnicities in BMI-matched studies.[82]

It should be noted that ovarian hyperandrogenism and ovulation dysfunction in PCOS improve with age.[84,85] Hyperandrogenism is closely related to several metabolic phenotypes, including T2DM. In this context, women with PCOS might have less severe metabolic phenotypes when they reach the perimenopausal stage. However, T2DM commonly occurs with increased age. The risk of T2DM is likely increased in perimenopause and beyond among women with PCOS.[14]

3.2.4 | Dyslipidemia

Dyslipidemia is another common metabolic complication in PCOS. Several features of PCOS exacerbate dyslipidemia, such as hyperandrogenism, obesity, and insulin resistance.[12,65,86] In particular, obesity has a substantial impact on lipid metabolism. A meta-analysis suggested that women with PCOS show higher low-density lipoprotein cholesterol (LDL-C) and triglyceride levels, and lower high-density lipoprotein cholesterol (HDL-C) levels, than women in a control group.[87] Intriguingly, LDL-C levels in women with PCOS remained significantly higher than those among controls in a BMI-matched population. This suggests that PCOS itself is involved.

Genetic and environmental factors, especially dietary habits, also modify lipid metabolism; therefore, the lipid profile is suspected to differ by race and ethnicity. In fact, various studies suggest that African American women with PCOS have more favorable lipid profiles and that Hispanic populations have worse lipid metabolism (Table 2), although some studies suggest that the lipid profiles are similar among these groups after adjustment for BMI and age.[28]

3.2.5 | Metabolic syndrome

Metabolic syndrome is defined as increased blood pressure, hyperglycemia, central obesity, hypertriglyceridemia, and decreased HDL-C level. Metabolic syndrome is correlated to CVD, T2DM, and chronic kidney disease. This is also known as insulin-resistant syndrome and is a condition similar to insulin resistance, which also worsens the metabolic profile; most people with metabolic syndrome have insulin resistance. In fact, metabolic syndrome is more likely among women with PCOS than healthy women. Hyperandrogenism and obesity are characteristic features of PCOS and increase the prevalence of metabolic syndrome.[87,88]

The prevalence of metabolic syndrome in women with PCOS differs among racial and ethnic populations. East Asian populations have the lowest prevalence of metabolic syndrome. Previous studies indicate that the prevalence of metabolic syndrome is 40%–45% among African Americans, 20%–30% among White Americans, 35% among Hispanics, 30%–40% among South Asians, and 15%–25% in the East Asian population.[52,89–94]

3.3 | Mental disorders

A growing body of evidence suggests that mental disorders are also important issues for women with PCOS. The characteristic features of PCOS include insulin resistance, chronic inflammation, hyperandrogenism, obesity, and body image distress, which might affect mental disorders. Additionally, geographic background as well as race and ethnicity determine one's psychological environment, and racial and ethnic disparities in psychological outcomes might exist.

3.3.1 | Anxiety, depression, and other disorders

Many confounding factors exist with regard to psychiatric disorders in women, such as hormonal (premenstrual syndrome, infertility) and

psychosocial (education, occupation, stress, income) factors, which complicate the ascertainment of a causal relationship between PCOS itself and psychiatric disorders. Women with PCOS have an increased prevalence of anxiety, depression, and other psychiatric problems, although their etiology remains obscure.[95] The likely cause might be impaired body image owing to obesity and clinical hyperandrogenism, infertility, and long-term health concerns. Also, insulin resistance and biochemical hyperandrogenism are associated with anxiety and depression (Figure 2).[96,97] However, obesity is not a stigma but a symbol of prosperity in some cultures. Genetic and cultural diversity partially influence psychological distress among women with PCOS. In the general population, the Black–White mental health paradox refers to Black Americans having fewer psychiatric disorders than White Americans.[98] In this regard, sociodemographic differences must be taken into account to understand mental problems in PCOS.

Several studies have evaluated the prevalence of anxiety and depression in women with PCOS. In the Pakistani population, the prevalence of anxiety and depression is 20.3% and 17.6%, respectively.[99] In India, these prevalence rates are 59.5% and 17.7%, respectively.[100] According to former studies, the prevalence of mental disorders can vary widely, even within the same region. In East Asia, the prevalence of anxiety and depression is 13.3% and 27.5% among Chinese women with PCOS and 2.0% and 2.9% among Taiwanese women.[101,102] Regarding the population with PCOS in the United States, the prevalence of anxiety and depression is 61.3% and 29% among Black women and 75.9% and 24.4% among White women, respectively.[103] In the United Kingdom, the prevalence of anxiety and depression in the population with PCOS is 50.0% and 13.9%, respectively.[100] It should be noted that many confounding factors such as income, educational level, and BMI exist with regard to psychological problems,[99] which complicate surveys on racial and ethnic differences. Further studies are needed to better understand psychological problems among different racial and ethnic populations.

3.3.2 | Low self-esteem

Self-esteem is frequently defined as an individual's negative or positive perception of their self-worth, sense of pride, positive self-evaluation, or self-respect. A previous study suggested that there are significant interactions of race and ethnicity with income and education in predicting self-esteem.[104] Health care providers should bear in mind that PCOS is also a risk factor for low self-esteem, which is partially owing to obesity, hirsutism, and infertility.[105] In an Australian study, the prevalence of low self-esteem among women with PCOS was 31.7%, which is 1.3 times higher than the rate among those without PCOS.[105] In an Indian cohort study, 21.9% of women with PCOS had low self-esteem.[106] Another study suggested that as many as 33.7% of Turkish women with PCOS have low self-esteem.[107] Among women with PCOS, the prevalence of low self-esteem might not be related to racial and ethnic or geographic differences, although relevant studies are limited.

3.3.3 | Eating disorders

The etiology of eating disorders in PCOS is estimated to include genetic, psychological, endocrinological, and metabolic factors. A previous study indicated that women with PCOS are three to six times more likely to have eating disorders compared with women in a control group.[108] Among several types of eating disorder, bulimia nervosa and binge eating disorder are significantly associated with PCOS.[109] However, the method for diagnosing eating disorders varies among studies and the prevalence of eating disorders cannot simply be compared among different racial and ethnic populations. Further studies are needed to reveal how racial and ethnic as well as phenotypic differences in PCOS affect eating disorders.

3.3.4 | Sleep disorders

Women with PCOS are at increased risk of sleep disorders.[109,110] Sleep disorders disrupt energy expenditure, leading to obesity and insulin resistance.[111] Obesity, characteristic of PCOS, contributes to the risk of developing obstructive sleep apnea.[109] In this context, sleep disorders and PCOS each contribute to development of the other. Moreover, testosterone administration is associated with obstructive sleep apnea[112]; this in turn is associated with depressive disorder, which is prevalent among women with PCOS.[113]

Obesity is not a globally equivalent phenomenon among women with PCOS, and race and ethnicity can influence the prevalence of sleep disorders in PCOS. However, there are limited studies on the association of sleep disorders with race and ethnicity in PCOS.

4 | PHENOTYPIC DISPARITIES AND RELATED CHARACTERISTICS

In this section, the author discusses the association between racial and ethnic differences and the proportion of different PCOS phenotypes and how phenotypic disparities affect metabolic and reproductive outcomes.

4.1 | Prevalence of different PCOS phenotypes by race and ethnicity

The Rotterdam 2003 criteria define four phenotypes in PCOS: (A) hyperandrogenism, O-ANOV, and PCOM; (B) hyperandrogenism and O-ANOV; (C) hyperandrogenism and PCOM (ovulatory PCOS); and (D) O-ANOV and PCOM (normoandrogenic PCOS). Phenotypes A and B are referred to as classical PCOS because they fulfill the historical NIH 1990 criteria. Although the same diagnostic criteria are used, different races and ethnicities modify the prevalence of the PCOS phenotypes. Additionally, the study population is important when comparing the prevalence of each phenotype. Referral populations tend to be more obese and have a more severe manifestation of

the disease than unselected populations.[114,115] Our Japanese study population fulfilled the Rotterdam 2003 criteria; the prevalence of phenotypes A, B, C, and D was 45.8%, 3.4%, 11.0%, and 39.8%, respectively.[26] In a study among Korean women, the prevalence of these phenotypes was 52.4%, 13.9%, 2.4%, and 31.3%, respectively.[116] Among South Asian women, the prevalence of phenotypes A–D was 54.6%, 17.5%, 7.7%, and 20.3%, respectively.[90] Focusing on regions outside of Asia, the proportion is quite different. A study among participants from Chile (Ch) and Argentina (Ar) showed that the proportion of phenotype A was 72% (Ch) and 50.4% (Ar), that of B was 10.5% (Ch) and 19.4% (Ar), C was 16.5% (Ch) and 20% (Ar), and the proportion of D was 1% (Ch) and 10% (Ar).[117] In the United States, the proportion of phenotypes A, B, C, and D is 65.1%, 5.1%, 24.6%, and 5.2%, respectively.[118] A study among Iranian women indicated that the prevalence of phenotypes A to D was 54%, 28%, 5%, and 13%, respectively.[119] These studies indicate that hyperandrogenism is less prevalent among East Asian women with PCOS, which is partially explained by the fact women in this group have less hirsute (clinical hyperandrogenism) than those of other races and ethnicities. As mentioned earlier, the prevalence of hyperandrogenemia is similar among different races and ethnicities; therefore, hyperandrogenemia might not be a determinant of this difference.

4.2 | Association of PCOS phenotypes with metabolic features

Evidence suggests that women with classical PCOS (phenotypes A and B) have the most risky metabolic features, such as increased insulin resistance, elevated triglyceride levels, and lower HDL-C levels.[120] Furthermore, women with classical PCOS tend to have elevated BMI and waist circumference, which worsen the metabolic profile.[120] When BMI is matched, the metabolic profiles in classical PCOS and phenotype C (ovulatory PCOS) are similar. In the same way, all PCOS phenotypes are metabolically equivalent unless BMI is discordant.[120] This implies that central obesity appears to be the chief determinant of metabolic characteristics and hyperandrogenism contributes to adiposity in PCOS. This is in accordance with the fact that East Asian women with PCOS have low BMI and less frequent metabolic syndrome. In a previous study in a Japanese population, no statistically significant difference was found with regard to BMI and the index of insulin resistance among the four different phenotypes.[26]

4.3 | Association of PCOS phenotypes with reproductive characteristics

The prevalence of PCOS-associated infertility has been growing for decades, with Italy, Japan, and Malaysia showing the highest rates. Albania, Bosnia and Herzegovina, and Serbia have the lowest prevalence of PCOS-associated infertility.[121] Thus, no racial and ethnic or regional predisposition to PCOS-associated infertility exists. This is partially explained by the hypothesis that advanced health care infrastructure increases the diagnostic rate of PCOS and increases access to medical interventions. Additionally, a high cost, limited availability, and social stigma regarding assisted reproductive technology might interfere with treatment, resulting in persistent infertility.

The ovarian response to controlled ovarian stimulation and oocyte quality are important factors in successful infertility treatment. Several investigations have indicated that women with PCOS might have low oocyte quality and impaired endometrial receptivity.[122,123] Additionally, obesity decreases the rates of pregnancy and live birth.[124,125] Questions arise as to whether PCOS itself is a detrimental factor for pregnancy or a mere confounding factor. Several studies have been conducted on the association between PCOS phenotypes and the aforementioned factors, ovarian response, and oocyte quality. Phenotypic differences in PCOS do not seem to affect the total number of retrieved oocytes and their morphology.[126,127] Previous studies suggest that lean PCOS is superior to obese PCOS regarding the number of oocytes retrieved, live birth rate, miscarriage rate, and time to pregnancy.[128,129] At present, no phenotypic difference in PCOS, except underlying metabolic characteristics, affect fertility outcomes.

5 | CONCLUSIONS

Polycystic ovary syndrome is a reproductive disorder that can lead to problems in diverse areas of health care. Therefore, efforts to improve diagnostic methods are needed. The prevalence of PCOS is similar across various regions and among different races and ethnicities, but phenotypic disparities exist according to race and ethnicity. Thus, factors specific to race and ethnicity must be considered in clinical practice.

East Asian populations are less likely to develop hirsute, and reference levels of clinical hyperandrogenism in East Asia should be lower than those in other regions. In this regard, the diagnostic criteria of PCOS should be race and ethnicity-specific to avoid missing treatment opportunities. Additionally, East Asian women tend to exhibit central adiposity even with a normal BMI; therefore, metabolic profiles should be thoroughly evaluated irrespective of BMI. It should be kept in mind that hirsutism is more prevalent in South Asian, Middle Eastern, and Hispanic women with PCOS and insulin resistance is more frequent among South Asian, Middle Eastern, Hispanic, and African American women with PCOS. Moreover, obesity is common among Hispanic and African American women with PCOS. The risk of metabolic disorders varies among racial and ethnic populations.

Health concerns in women with PCOS are classified into the following three general categories: reproductive, metabolic, and mental health issues. Ovulation disorder and PCOM are common reproductive problems in women with PCOS, however, these do not seem to affect other characteristics of PCOS, such as insulin resistance. Metabolic problems seem to be related to race and ethnicity (genetic predisposition), as well as body composition and adiposity,

and not to the PCOS phenotype. Regarding mental disorders, there is little evidence to support racial and ethnic differences. Larger observational or randomized controlled trials are urgently needed to clarify the remaining questions surrounding PCOS as well as to determine the optimal strategy to address mental health concerns across different races and ethnicities.

Currently, the only available diagnostic criteria for PCOS do not reflect racial and ethnic differences. Recent genome-wide association studies indicate that genetic susceptibility influences PCOS development. The pathogenesis of PCOS and racial and ethnic differences will be better understood as more studies are conducted using innovative methods.

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CONFLICT OF INTEREST STATEMENT

The author declares no conflict of interest for this article.

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