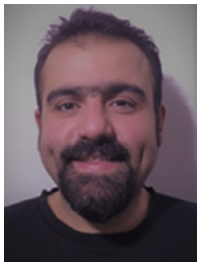
RBMO

REVIEW

Influence of ethnicity on different aspects of polycystic ovary syndrome: a systematic review



BIOGRAPHY

Suleyman Nahit Sendur completed his training in internal medicine and endocrinology at Hacettepe University, Turkey. He was appointed as an Assistant Professor at the same institution in 2020. His research and clinical interests are in pituitary, adrenal and gonadal disorders.

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KEY MESSAGE

Ethnicity affects the clinical presentation of PCOS and needs to be taken into consideration in evaluating and managing the syndrome.

ABSTRACT

This systematic review aimed to assess variations in the clinical presentation and treatment outcomes of patients with polycystic ovary syndrome (PCOS) belonging to different ethnicities. A search was performed for studies comparing various clinical aspects of PCOS in two or more different ethnic groups. After screening 2264 studies, 35 articles were included in the final analysis. In comparison with White women with PCOS (wPCOS), East Asian women with PCOS (eaPCOS) were less hirsute, whereas Hispanic women with PCOS (hPCOS), South Asian women with PCOS (saPCOS) and Middle Eastern women with PCOS (mePCOS) were more hirsute. saPCOS had higher androgen and lower sex hormone-binding globulin (SHBG) concentrations, mePCOS had higher DHEAS concentrations, and hPCOS and Black women with PCOS (bPCOS) had lower SHBG and DHEAS measures than wPCOS. Menstrual disturbances were more frequent in eaPCOS. Both saPCOS and eaPCOS had lower body mass index with increased central adiposity. hPCOS and bPCOS were more obese. saPCOS, mePCOS, hPCOS and bPCOS had a higher prevalence of insulin resistance than wPCOS. bPCOS had a better lipid profile but higher blood pressure and cardiovascular risk. Indigenous Australian women with PCOS were more obese and more insulin resistant with higher androgen concentrations. The clinical phenotype of PCOS therefore shows a wide variation depending on ethnicity.

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KEYWORDS

Ancestry
Ethnicity
Hirsutism
Insulin resistance
Obesity
Polycystic ovary syndrome (PCOS)

INTRODUCTION

Rationale

Polycystic ovary syndrome (PCOS) is a common endocrine disorder that is characterized by clinical and/or biochemical androgen excess, ovulatory dysfunction and polycystic ovarian morphology (PCOM). Women with PCOS have an increased risk of metabolic and cardiovascular comorbidities, infertility, pregnancy complications, psychological disorders and cancer (*Azziz et al., 2016*).

PCOS is a complex disorder in which the interaction between genetic, epigenetic and environmental factors initiates and perpetuates the syndrome (*Azziz et al., 2016*). Considering these pathophysiological factors, ethnicity might affect the pathogenesis of PCOS. Although many studies have shown that ethnicity has an impact on the prevalence and clinical manifestations of PCOS, information regarding the variability of PCOS in different ethnic groups is scant (*Huddleston et al., 2010*; *Qiao, 2013*; *Zhao and Qiao, 2013*; *Huang and Yong, 2016*). In 2018, by defining clinical consensus recommendations (CCR), the International PCOS Network recommended that health professionals should consider the individual's ethnicity when assessing a patient with PCOS (*Teede et al., 2018*). However, high-quality evidence regarding the variability of PCOS in individuals from different ethnic backgrounds is currently lacking.

Objectives

The main objective of this review was to summarize the available data on the impact of ethnicity on the different aspects of PCOS in patients presenting to clinics. The main research questions were as follows:

1. Is there any ethnic difference in women with PCOS in terms of clinical or biochemical hyperandrogenism, menstrual dysfunction and PCOM?
2. Is there any ethnic difference in women with PCOS in terms of metabolic and cardiovascular comorbidities?
3. Is there any ethnic difference in women with PCOS in terms of infertility and obstetric complications?
4. Is there any ethnic difference in women with PCOS in terms of mood disorders and quality of life (QoL)?
5. Is there any ethnic difference in women with PCOS in terms of treatment outcomes?

MATERIALS AND METHODS

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (*Moher et al., 2015*).

Search strategy

A literature search was performed in the PubMed database. Bibliographies of relevant studies were also searched to identify additional sources. Three different key word sets were used for the search:

1. (polycystic ovary syndrome OR pcos OR stein-leventhal syndrome OR hirsutism OR oligomenorrhea OR polycystic ovaries OR hyperandrogenism OR hyperandrogenemia) AND (ethnicity)
2. (polycystic ovary syndrome OR pcos OR stein-leventhal syndrome OR hirsutism OR oligomenorrhea OR polycystic ovaries OR hyperandrogenism OR hyperandrogenemia) AND (race)
3. (polycystic ovary syndrome OR pcos OR stein-leventhal syndrome OR hirsutism OR oligomenorrhea OR polycystic ovaries OR hyperandrogenism OR hyperandrogenemia) AND (ancestry OR hispanic OR american OR oceanic OR brazilian OR russian OR middle eastern OR turkish OR iranian OR european OR australia OR african OR asian OR black OR white OR thai OR caucasian OR mexican OR latin OR chinese OR arab OR japanese OR indian OR pakistani OR korean OR african american OR american indian OR alaska native OR asian indian OR filipino OR vietnamese OR native hawaiian OR chamorro OR samoan OR jews OR inuits OR other pacific islander OR amish OR other asian OR some other races OR migrant OR indigenous OR aboriginal).

Inclusion and exclusion criteria

Articles that were designed to compare two or more different ethnic groups in the same study and were published between April 1990 and February 2020 were included. Only studies that assessed the clinical characteristics of patients with PCOS who were referred (i.e. patients presenting to the clinic but not those in unselected populations) were included. Studies with non-human subjects, those published before 1990 and in languages other than English, and those that were meta-analyses, case reports, case series, editorials or reviews were excluded.

Data extraction

Data were extracted on the following: the author of the publication; publication year; number, age and ethnicity of the participants; mean modified Ferriman–Gallwey (mFG) scores or prevalence of subjects with hirsutism; serum androgen concentrations; prevalence of acne; prevalence and type of menstrual disturbances; ovarian morphology; fertility status; mean body mass index (BMI), waist–hip ratio (WHR) or prevalence of obesity; surrogate markers of glucose metabolism such as fasting insulin concentrations and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) index; prevalence of acanthosis nigricans; and lipid profile and systolic and diastolic blood pressure (SBP and DBP, respectively).

RESULTS

A total of 2916 papers were identified. Of these, 652 were removed because they were duplicates. A further 2220 articles were excluded after the title/abstract screen due to their irrelevant content. Nine more articles were also excluded after a full-text screening due to lack of relevant data. Thirty-five articles were included for the final analyses (FIGURE 1).

Clinical and biochemical hyperandrogenism

The data available from 26 studies regarding clinical and biochemical hyperandrogenism in various ethnic populations are summarized in TABLE 1. In two studies, it was shown that East Asian women with PCOS (eaPCOS) had lower mFG scores than White women with PCOS (wPCOS) (*Carmina et al., 1992*; *Guo et al., 2012*). In the other two studies comparing eaPCOS and wPCOS, eaPCOS appeared to have lower mFG scores, although this did not reach statistical significance (*Williamson et al., 2001*; *Legro et al., 2006*). The remaining studies did not show a difference in mFG scores between eaPCOS and wPCOS (*Welt et al., 2006*; *Wang et al., 2013*; *Afifi et al., 2017*). Except for one study in which Black women with PCOS (bPCOS) had higher mFG scores, the severity of hirsutism was comparable

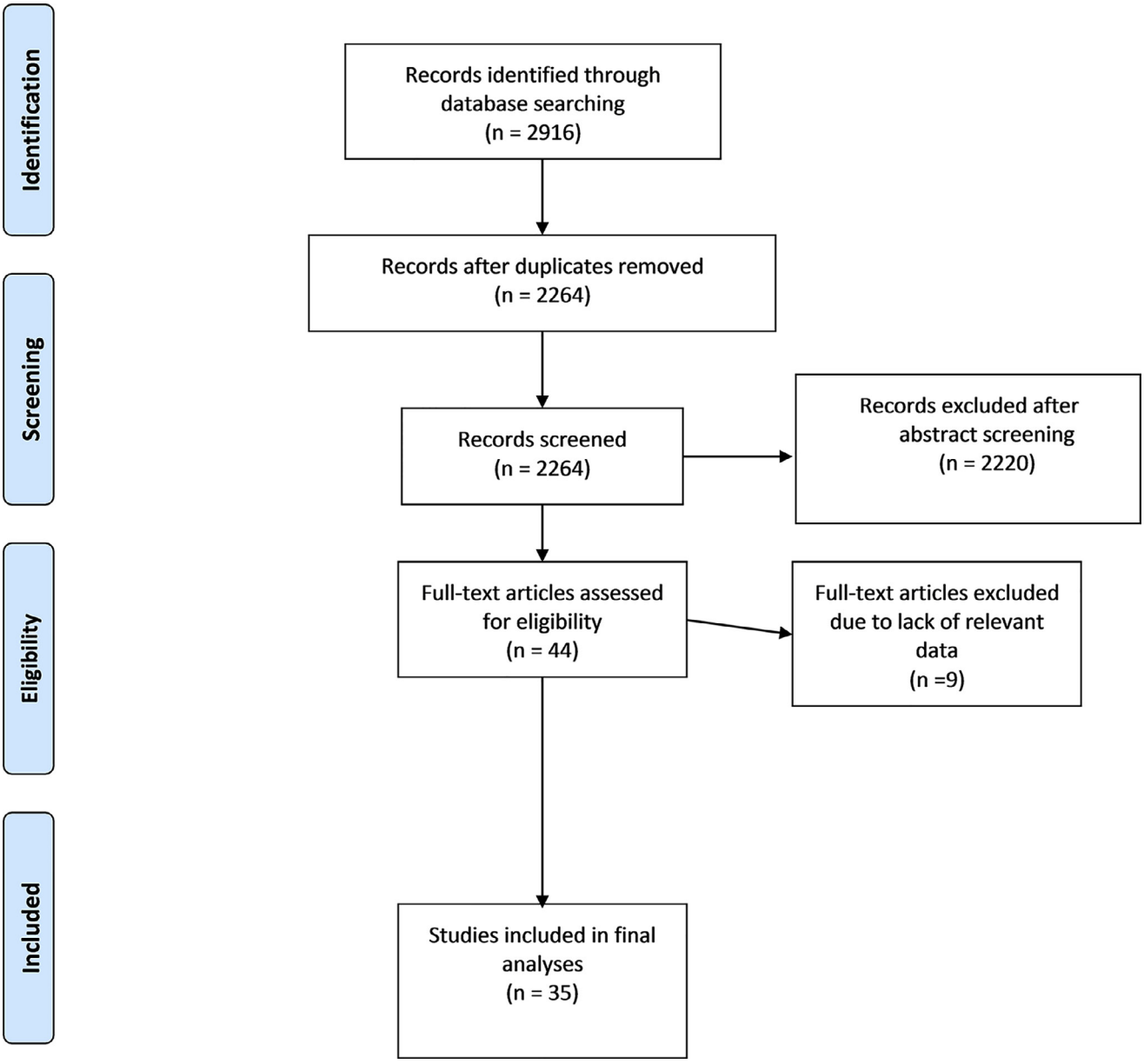

FIGURE 1 Summary of the literature search.

in bPCOS and wPCOS (*Afifi et al., 2017*). Although the hirsutism scores did not differ between Hispanic women with PCOS (hPCOS) and wPCOS in one study (*Welt et al., 2006*), it was in general found that hPCOS were more hirsute than wPCOS (*Afifi et al., 2017*; *Engmann et al., 2017*; *Sarkar et al., 2018*). South Asian women with PCOS (saPCOS) and Middle Eastern women with PCOS (mePCOS) had consistently higher mFG scores than their Caucasian counterparts (*Wijeyaratne et al., 2002*; *Glintborg et al., 2010*; *Mani et al., 2015*; *Afifi et al., 2017*; *Chan et al., 2017*). mFG scores varied even in different Caucasian groups (Icelandic Caucasian versus Boston Caucasian, White American versus Finnish and Norwegian). European Caucasians were less hirsute than their American counterparts (TABLE 1).

A comparison of total mFG scores was available in all studies, and two studies also reported on regional mFG score comparisons. Wang and colleagues showed that despite the similar total mFG scores, eaPCOS had less hair on the chest (*Wang et al., 2013*). Moreover, Afifi and co-workers found that while hPCOS and bPCOS had higher facial mFG scores, mePCOS and hPCOS had higher truncal and extremity mFG scores (*Afifi et al., 2017*). When compared with wPCOS, hirsutism started to present at earlier ages in saPCOS (approximately 18 versus approximately 22 years) (*Wijeyaratne et al., 2002*). Excess hair growth was an important reason for wPCOS to present to clinics and had greater impact on QoL in Brazilian than Austrian women (*Williamson et al., 2001*; *Hashimoto et al., 2003*).

Controversial results were available from seven studies that assessed acne prevalence among various ethnic groups. Acne was found to be more frequent in saPCOS than wPCOS in one study, whereas in another study the percentage of subjects with acne

TABLE 1 COMPARISON OF CLINICAL AND BIOCHEMICAL HYPERANDROGENISM BETWEEN VARIOUS ETHNIC GROUPS

Study (first author, year)	DC	Study population	Age (years)	mFG	Acne	Serum androgens	Comments
Carmina (1992)	NIH	25 Hispanic American 25 Japanese 25 Italian For each ethnic group 10 age-matched controls	30 ± 2 24 ± 1 24 ± 1	Patients: Hispanic American 12 ± 1 Japanese 3.5 ± 0.2 Italian 12.5 ± 1 Controls: All <8 Subjects with hirsutism: Hispanic American 60% Japanese ns Italian 75% Controls none		Serum T and DHEAS concentrations were similar in patients[a]	In spite of similar serum androgen concentrations, Japanese patients had a lower mFG score mFG scores of Japanese patients and controls were similar 3α-Androstanediol glucuronide, a marker of skin 5α-reductase activity, was lower in Japanese patients
Dunaif (1993)	NIH	13 Caribbean Hispanic 10 non-Hispanic White 5 Caribbean Hispanic control 8 non-Hispanic White control	25.1 ± 1 27 ± 2 28 ± 2 27 ± 1			Serum T, fT, A4, DHEAS and SHBG concentrations were similar in patients[a]	Similar androgen concentrations
Norman (1995)	NIH	11 Indian 11 White 11 Indian control 11 White control	~25 Age was similar for all groups			Serum T, A4 and DHEAS concentrations were similar Compared with obese White women, SHBG concentrations were higher in obese Indian patients	Similar androgen concentrations but fT concentrations were not assessed
Williamson (2001)	ns	112 White 16 Maori 15 Pacific Islander 19 Indian 4 Asian 6 other There was an inconsistency between number and percentage of PCOS patients	27.4 (all)	White 8.3 ± 9.0 Maori 10.5 ± 9.8 Pacific Islander 9.1 ± 0.2 Indian 8.3 ± 8.2 Asian+other 3.1 ± 5.5	Acne was found in all ethnic groups except Pacific Islanders	Maori and Pacific Islander women had the highest T and fT concentrations, with the lowest SHBG[a] Adrenal androgen concentrations were similar	Hirsutism was an important admission reason for White and Maori women Asians had the lowest mFG score but this was not statistically significant
Kauffman (2002)	NIH	48 White 26 Mexican American 11 White control 8 Mexican American control	~26[b] ~30 ~25			Serum T, fT and DHEAS concentrations were similar in patients[a]	Despite greater insulin resistance in Mexican American patients, androgen concentrations were similar
Wijeyaratne (2002)	ns	47 South Asian 40 Caucasian 11 South Asian control 22 Caucasian control	26 ± 4 30.1 ± 5 31.3 ± 2 32.9 ± 3	South Asian 18 Caucasian 7.5 South Asian 8 Caucasian 1.5	South Asian 66% Caucasian 30%	Serum T values were similar but SHBG concentrations were lower in South Asian women with PCOS[a] SHBG concentrations were similar in controls	Despite comparable T concentrations, South Asian women with PCOS had higher mFG scores and acne was more frequent in South Asian women Compared with White controls, South Asian controls also had higher mFG scores Hirsutism started to present at earlier ages in South Asian patients (~18 versus ~22 years)
Carmina (2003)	NIH	20 non-Hispanic White American 20 Italian	29 ± 2 26.6 ± 2			Serum T, fT and DHEAS concentrations were similar	Similar androgen concentrations
Hashimoto (2003)	NIH	102 Brazilian (predominantly Black) 31 Austrian	25.5 ± 3.9 23.8 ± 4.7				Brazilians were more hirsute, and hirsutism had a greater impact on the quality of life in Brazilian patients

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TABLE 1 *(continued)*

Study (first author, year)	DC	Study population	Age (years)	mFG	Acne	Serum androgens	Comments
Wijeyaratne (2004)	ns	74 Sri Lankan 47 British Asian 40 White 45 Sri Lankan control 11 British Asian control 22 White control	27.3 ± 1.7 26 ± 4 30.1 ± 0.5 33 ± 4.7 31.3 ± 2 32.8 ± 3			Serum T was similar SHBG was lower in Sri Lankan patients but similar in controls Despite similar T concentrations, FAI was greater in Sri Lankan patients	South Asian patients with PCOS had higher FAI measures
Ehrmann (2005)	NIH	303 White 51 Black 38 Other	28.8 ± 0.3 27.6 ± 0.8 26.7 ± 0.9			SHBG concentrations in White women with PCOS were higher but the difference was not statistically significant[a] DHEAS concentrations were comparable	Similar androgen concentrations
Kumar (2005)	NIH	186 White 27 Black 94 White control 88 Black control	27.3 ± 6.6 28.7 ± 6.2 28.7 ± 9.1 30.2 ± 9.1	White 7.7 ± 4.5 Black 8.3 ± 4.7 White 0.2 ± 0.4 Black 0.2 ± 0.4		Serum T, fT, DHEAS and SHBG concentrations were similar in PCOS patients[a] White controls had higher DHEAS concentrations	The severity of hirsutism was similar
Kauffman (2006)	R	111 White 50 Mexican American	27.3 26.9			Serum T and fT concentrations were similar Mexican American women had lower DHEAS concentrations[a]	In an age- and BMI-matched cohort, DHEAS concentrations were lower in Mexican American women
Legro (2006)	NIH	435 Caucasian 109 African American 17 Asian 72 American Indian or Alaska Native	28.2 ± 3.9 27.9 ± 4.3 30.4 ± 3.0 27.6 ± 4.1	Caucasian 14.5 ± 8.0 African American 13.9 ± 7.5 Asian 12.5 ± 7.2 American Indian or Alaska Native 15.1 ± 8.2		T concentrations were higher in Caucasian and African American women[a] FAI and SHBG concentrations were comparable	mFG scores of Asian women with PCOS were lower but this was not statistically significant
Welt (2006)	NIH	105 Iceland Caucasian 172 Boston Caucasian 44 Boston African American 25 Boston Hispanic 21 Boston Asian 32 Iceland controls	30.2 ± 6.2 28.8 ± 5.5 28.4 ± 6.7 26.3 ± 5.2 25.5 ± 5.3 32.2 ± 5.5	Iceland Caucasian 7.1 ± 6.0 Boston Caucasian 15.4 ± 8.5 Boston African American 18.5 ± 8.9 Boston Hispanic 18.2 ± 9.4 Boston Asian 15.7 ± 11.0 Iceland controls 3.0 ± 1.4	Iceland Caucasian 62.1% Boston Caucasian 84.8% Boston African American 86.0% Boston Hispanic 87.0% Boston Asian 85.7%	When compared with Boston Caucasians, A4 concentrations were higher in Icelandic women with PCOS, and T, fT and DHEAS concentrations were lower While SHBG concentrations were lower in African Americans and Hispanics, fT concentrations were highest in these ethnic groups	Icelandic Caucasian PCOS participants had a lower mean mFG score than Boston Caucasian participants The percentage of participants with acne was lower in Icelandic Caucasians with PCOS
Glintborg (2010)	R	784 Caucasian 190 Middle Eastern	32 25	Caucasian 11 Middle Eastern 16		Serum T, SHBG and fT concentrations were higher in Caucasian women but DHEAS concentrations were lower[a]	Despite lower androgen concentrations, Middle Eastern women with PCOS were more hirsute

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TABLE 1 *(continued)*

Study (first author, year)	DC	Study population	Age (years)	mFG	Acne	Serum androgens	Comments
Kauffman (2011)	R	120 White 71 Mexican American	27.4 26.8			Serum T, SHBG concentrations and FAI were similar but DHEAS concentrations were lower in Mexican American patients[a]	In an age- and BMI-matched cohort, Mexican American patients had lower DHEAS concentrations
Ladson (2011)	NIH	43 Black 77 White 87 Black control 35 White control	27.9 ± 5.0 26.0 ± 6.9 Age not specified	Black 17.6 ± 9.2 White 20.2 ± 8.0		Serum T and SHBG concentrations were comparable[a]	No difference in hirsutism scores and androgen concentrations
Guo (2012)	R	547 Chinese 427 Dutch	28.3 ± 3.4 29.0 ± 5.2	Chinese 3.6 ± 4.9 Dutch 5.2 ± 5.4		No difference in terms of the prevalence of biochemical hyperandrogenism	Chinese women were less hirsute
Wang (2013)	R	121 Caucasian 28 Asian	28.0 ± 5.4 29.6 ± 5.9	Caucasian 8.6 ± 6.5 Asian 7.4 ± 4.0	Caucasian 67.9% Asian 73.9%	Serum T, fT, DHEAS and A4 concentrations were measured The frequency of individuals with elevated androgen concentrations was comparable	The total mFG score was similar but Asian women had less hair in the chest region The prevalence of acne was similar
Hilman (2014)	R	413 non-Hispanic White 106 non-Hispanic Black	25.0 ± 6.7 26.3 ± 7.3			While serum T and fT concentrations were higher, serum DHEAS concentrations were lower in Black women[a]	Differences in androgen concentrations
Mani (2015)	ns	929 White 381 South Asian	27.1 ± 7.4 24.3 ± 6.7	Participants with hirsutism: White 77.4% South Asian 88.5%	White 23.9% South Asian 16.8%		Hirsutism was more common in South Asian women Acne was more common in White women
Chang (2016)	R	62 Black 32 White 23 Hispanic 113 Black control 54 White control 37 Hispanic control	41 41 39 40 40 39			Serum T, fT and SHBG concentrations were comparable across ethnic groups[a]	Similar androgen concentrations
Afifi (2017)	R	9 Middle Eastern 16 Ashkenazi Jewish 110 Caucasian 37 East Asian 5 South Asian 29 Hispanic 15 African American 2 Native American 20 Other	28.4 ± 7.5 28 ± 5.4 28.2 ± 6.0 27.1 ± 5.4 23 ± 6.3 28.9 ± 6.4 30.9 ± 6.8 23 ± 6.3 28.3 ± 5.3	Middle Eastern 12.3 ± 8.6 Ashkenazi Jewish 7.4 ± 5.3 Caucasian 7.4 ± 5.7 East Asian 7.9 ± 6.4 South Asian 9.6 ± 1.5 Hispanic 12.6 ± 7.5 African American 9.4 ± 4.4 Native American 4 ± 4.2 Other 9.1 ± 6.6			Hispanic, Middle Eastern, South Asian and African American women with PCOS had higher mFG scores Hispanic and African American women had higher facial mFG scores Middle Eastern and Hispanic patients had higher truncal and extremity mFG scores
Chan (2017)	R	184 American White 100 American Black 220 Indian 233 Brazilian 94 Finnish 258 Norwegian	29 29 25 26 33 28.5	Median mFG: American White 11.1 American Black 10.9 Indian 15.6 Brazilian 12.2 Finnish 7.8 Norwegian 4.3		Serum T concentrations were similar	Indian women were more hirsute and Norwegian and Finnish women with PCOS were less hirsute

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TABLE 1 *(continued)*

Study (first author, year)	DC	Study population	Age (years)	mFG	Acne	Serum androgens	Comments
Engmann (2017)	R	476 non-Hispanic White 98 non-Hispanic Black 128 Hispanic American	28.8 ± 4.2 28.7 ± 4.9 29.2 ± 4.1	Non-Hispanic White 17.0 ± 8.7 Non-Hispanic Black 15.8 ± 8.5 Hispanic American 17.6 ± 7.5 Participants with hirsutism: Non-Hispanic White 86.8% Non-Hispanic Black 82.7% Hispanic American 93.8%	Non-Hispanic White 35.2% Non-Hispanic Black 25.5% Hispanic American 64.1	Serum T and A4 concentrations were comparable[a] Hispanic women had higher FAI and lower SHBG measures	Hispanic women were more hirsute and had a severe hyperandrogenic profile Acne scores were higher in Hispanic women
Sarkar (2018)	R	256 non-Hispanic American 47 Hispanic American	28.1 28.5	Participants with hirsutism: Non-Hispanic American 49% Hispanic American 75.6%	Non-Hispanic American 63.4% Hispanic American 70.5%	Serum T, A4, DHEAS, SHBG and FAI measures were comparable	Hirsutism was more common in Hispanic women The prevalence of acne was similar

Age: values are mean ± SD, mean or median; mFG: values are mean ± SD.

[a] The measurements were made in the same laboratory.

[b] In this study age was not reported for whole PCOS cohort; however, the mean age of White and Mexican American participants with PCOS was approximately 26 years. White healthy controls were older than Mexican American healthy controls.A4, androstenedione; BMI, body mass index; DC, diagnostic criteria; DHEAS, dehydroepiandrosterone sulfate; FAI, free androgen index; fT, free testosterone; mFG, modified Ferriman–Gallwey score; NIH, National Institutes of Health criteria; ns, not specified; PCOS, polycystic ovary syndrome; R, Rotterdam criteria; SHBG, sex hormone-binding globulin; T, total testosterone.

was higher in wPCOS compared with saPCOS (*Wijeyaratne et al., 2002*; *Mani et al., 2015*). Acne scores in hPCOS were higher than in wPCOS in one study (*Engmann et al., 2017*) but the prevalence of acne was similar in another (*Sarkar et al., 2018*). A direct comparative study of wPCOS and eaPCOS showed that these two groups had similar frequencies of acne (*Wang et al., 2013*). Welt and colleagues found a lower prevalence of acne in Icelandic Caucasians than Boston Caucasians (*Welt et al., 2006*).

Androgen concentrations were assessed in 23 studies. In 15 out of the 23, hormone measurements were made in the same laboratory. Twelve studies did not reveal any differences in serum androgen based on ethnicity (TABLE 1) (*Carmina et al., 1992*; *Dunaif et al., 1993*; *Kauffman et al., 2002*; *Carmina et al., 2003*; *Ehrmann et al., 2005*; *Kumar et al., 2005*; *Ladson et al., 2011*; *Guo et al., 2012*; *Wang et al., 2013*; *Chang et al., 2016*; *Chan et al., 2017*; *Sarkar et al., 2018*). In two studies that assessed wPCOS and saPCOS, serum testosterone concentrations were comparable but sex hormone-binding globulin (SHBG) concentrations were lower and free androgen index was higher in saPCOS (*Wijeyaratne et al., 2002*; *Wijeyaratne et al., 2004*). In contrast, another study reported higher SHBG concentrations in obese saPCOS than obese wPCOS (*Norman et al., 1995*). Looking at dehydroepiandrosterone sulphate (DHEAS) concentrations in comparison to wPCOS, some studies noted lower DHEAS concentrations in hPCOS (*Kauffman et al., 2006*; *Kauffman et al., 2011*) and bPCOS (*Hillman et al., 2014*), and higher concentrations in mePCOS (*Glintborg et al., 2010*). Legro and colleagues found that, compared with eaPCOS, testosterone concentrations were higher in wPCOS and bPCOS but the free androgen index and SHBG measures were similar (*Legro et al., 2006*). Differences were reported even within various Caucasian populations. Whereas serum testosterone, free testosterone and DHEAS concentrations were lower, serum androstenedione measures were higher in Icelandic Caucasian women with PCOS when compared with Boston Caucasian women with PCOS (*Welt et al., 2006*).

Menstrual disturbances

The data regarding menstrual disturbances among various ethnic populations are summarized in TABLE 2. There were only seven studies that compared menstrual patterns in women with PCOS in different ethnic groups. Generally, no differences were noted (*Hashimoto et al., 2003*; *Hillman et al., 2014*; *Mani et al., 2015*; *Chan et al., 2017*). However, Wijeyaratne and colleagues showed that menstrual irregularities tended to be seen at earlier ages in saPCOS (*Wijeyaratne et al., 2002*). Furthermore, two studies indicated that, compared with wPCOS, the prevalence of menstrual disturbance was higher in eaPCOS (*Guo et al., 2012*; *Wang et al., 2013*).

PCOM

In 10 studies, ovarian morphology was compared between different ethnic groups. The data regarding ovarian morphology among various ethnic populations are summarized in TABLE 3. Despite the selection of different criteria to determine PCOM and PCOS, in most studies there was no difference between ethnic groups in terms of ovarian morphology. Although eaPCOS had a lower ovarian volume and follicle count, the prevalence of PCOM did not differ (*Legro et al., 1999*; *Welt et al., 2006*). However, Wang and co-workers determined no difference between eaPCOS and wPCOS in ovarian volume and follicle number (*Wang et al., 2013*). Interestingly, the frequency of PCOM, ovarian volume and follicle number

TABLE 2 COMPARISON OF MENSTRUAL DISTURBANCES BETWEEN VARIOUS ETHNIC GROUPS

Study (first author, year)	DC	Study population	Age (years) mean± SD, mean or median	Criteria	Comments
Wijeyaratne (2002)	ns	47 South Asian 40 Caucasian 11 South Asian control 22 Caucasian control	26 ± 4 30.1 ± 5 31.3 ± 2 32.9 ± 3	Menstrual disturbance: cycle length >35 days and lack of ovulation	Age at menarche and number of periods per year were similar (~13 years and ~5 periods/year, respectively) Menstrual irregularity tended to be seen in earlier ages in South Asian women (16.2 versus 18.4 years)
Hashimoto (2003)	NIH	102 Brazilian (predominantly Black) 31 Austrian	25.5 ± 3.9 23.8 ± 4.7		Menstrual disturbance frequencies were similar (~70%) but had a greater impact on quality of life in Brazilian women
Guo (2012)	R	547 Chinese 427 Dutch	28.3 ± 3.4 29.0 ± 5.2	Oligomenorrhoea: cycles between 35 and182 days Amenorrhoea: cycles ≥182 days	Chinese women presented more often with amenorrhoea (75% versus 27%)
Wang (2013)	R	121 Caucasian 28 Asian	28.0 ± 5.4 29.6 ± 5.9		Oligomenorrhoea was more frequent in Asian women
Hilman (2014)	R	413 non-Hispanic White 106 non-Hispanic Black	25.0 ± 6.7 26.3 ± 7.3	Menstrual disturbance: 9 or fewer menses/year	Menses per year were similar (~4 ± 3 menses/year)
Mani (2015)	ns	929 White 381 South Asian	27.1 ± 7.4 24.3 ± 6.7	Oligomenorrhoea: 9 or fewer menses/year Amenorrhoea: not specifically stated	Whereas oligomenorrhoea was more common in South Asian women, the percentage of women with amenorrhoea was higher in White women even though the menstrual disturbance rate was similar
Chan (2017)	R	184 American White 100 American Black 220 Indian 233 Brazilian 94 Finnish 258 Norwegian	29 29 25 26 33 28.5	Oligomenorrhoea: intermenstrual interval of >35days and <8 menstrual bleeds/year Amenorrhoea: absent menstrual bleeding in the past 90 days	The frequency of oligomenorrhoea/amenorrhoea was similar

DC, Diagnostic criteria; NIH, National Institutes of Health criteria; ns, not specified; R, Rotterdam criteria.

differed in various Caucasian populations. Icelandic subjects with PCOS had smaller ovaries and fewer follicles (although the frequency of PCOM was similar) and the prevalence of PCOM was higher in Norwegian and Finnish women with PCOS when compared with American White participants (*Welt et al., 2006*; *Chan et al., 2017*). In the only study that compared the prevalence of PCOM between wPCOS and mePCOS, Glintborg and colleagues found a higher frequency of PCOM in Caucasians (*Glintborg et al., 2010*).

Metabolic and cardiovascular comorbidities

Thirty studies evaluated and compared the metabolic and cardiovascular properties of individuals with PCOS belonging to different ethnicities. There was wide variability in the metabolic and cardiovascular comorbidities between different ethnic groups (TABLE 4). When compared with wPCOS, hPCOS and bPCOS were more obese. saPCOS and eaPCOS had lower BMI measures (*Carmina et al., 1992*; *Williamson et al., 2001*; *Wijeyaratne et al., 2002*; *Wijeyaratne et al., 2004*; *Al-Fozan et al., 2005*; *Legro et al., 2006*; *Lo et al., 2006*; *Welt et al., 2006*; *Koval et al., 2010*; *Ladson et al., 2011*; *Guo et al., 2012*; *Hillman et al., 2014*; *Mani et al., 2015*; *Chang et al., 2016*; *Chan et al., 2017*; *Sarkar et al., 2018*). However, WHR, an indicator of central adiposity, was higher in saPCOS and eaPCOS (*Wijeyaratne et al., 2002*; *Wijeyaratne et al., 2004*; *Guo et al., 2012*). mePCOS had similar or lower BMI values compared with wPCOS (*Al-Fozan et al., 2005*; *Glintborg et al., 2010*). The results were contradictory in terms of obesity among various Caucasian populations. While Northern Europeans had a similar BMI to American White participants, Southern Europeans were leaner (*Carmina et al., 2003*; *Welt et al., 2006*; *Essah et al., 2008*; *Chan et al., 2017*).

Considering glucose metabolism, when compared with wPCOS, hPCOS and bPCOS were more insulin resistant (*Dunaif et al., 1993*; *Kauffman et al., 2002*; *Ehrmann et al., 2005*; *Kauffman et al., 2006*; *Welt et al., 2006*; *Kauffman et al., 2011*; *Ladson et al., 2011*; *Hillman et al., 2014*; *Engmann et al., 2017*; *Sarkar et al., 2018*). Moreover, Hispanic ethnicity was determined as an independent risk factor for non-alcoholic steatohepatitis (*Sarkar et al., 2018*). Despite lower or comparable BMI values, saPCOS and mePCOS also had higher glucose concentrations in different settings (*Wijeyaratne et al., 2004*; *Al-Fozan et al., 2005*; *Glintborg et al., 2010*; *Mani et al., 2015*; *Chan et al., 2017*). Conflicting results were available for eaPCOS. In general, eaPCOS were leaner but more prone to central adiposity. Three studies revealed no difference between eaPCOS and wPCOS. While Carmina and colleagues used the percentage ideal body weight for comparison, BMI values were measured in other studies (*Carmina et al., 1992*; *Guo et al., 2012*; *Wang et al., 2013*). In the study conducted by Legro and co-workers, it was shown that eaPCOS tended to have lower HOMA-IR measures (*Legro et al., 2006*). Nevertheless, in the largest study based on a health database review including 3778 wPCOS, 552 bPCOS, 1117 eaPCOS, 1324 hPCOS and 432 individuals with PCOS belonging to other ethnic groups, Lo and colleagues showed that, after adjustment for BMI and age, eaPCOS had an increased risk of diabetes mellitus (*Lo et al., 2006*). Four studies evaluating acanthosis nigricans reported that this finding was

TABLE 3 COMPARISON OF OVARIAN MORPHOLOGY BETWEEN VARIOUS ETHNIC GROUPS

Study (first author, year)	DC	Study population	Age (years)	PCO criteria	Percentage of PCOS women with PCO	Comments
Carmina (1992)	NIH	25 Hispanic American 25 Japanese 25 Italian For each ethnic group 10 age-matched controls	30 ± 2 24 ± 1 24 ± 1	10 or more cysts 2–8 mm in diameter arranged either peripherally around a dense core of stroma or scattered throughout an increased amount of stroma	Hispanic American 80% Japanese 68% Italian 76%	Similar frequency of PCO (~75%)
Wijeyaratne (2002)	ns	47 South Asian 40 Caucasian 11 South Asian control 22 Caucasian control	26 ± 4 30.1 ± 5 31.3 ± 2 32.9 ± 3	10 or more cysts 2–8 mm in diameter with a thickened echo dense stroma		Mean ovarian volumes were comparable (~12 ml)
Legro (2006)	NIH	435 Caucasian 109 African American 17 Asian 72 American Indian or Alaska Native	28.2 ± 3.9 27.9 ± 4.3 30.4 ± 3.0 27.6 ± 4.1	Multiple cysts (≥10) of 2–8 mm in diameter distributed evenly around the ovarian periphery with an increased amount of stroma, or multiple small cysts 2–4 mm in diameter distributed throughout abundant stroma	Caucasian 89.4% African American 97.2% Asian 100% American Indian or Alaska Native 100% Mean right ovarian volume (ml): Caucasian 12.1 ± 6.7 African American 13.4 ± 9.2 Asian 10.9 ± 5.5 American Indian or Alaska Native 10.1 ± 4.3 Mean left ovarian volume (ml): Caucasian 11.6 ± 6.7 African American 11.3 ± 6.1 Asian 7.7 ± 5.3 American Indian or Alaska Native 8.7 ± 4.3	PCO was less frequent in Caucasian women with PCOS Asians and Native Americans had lower ovarian volumes Right and left ovary volumes were different
Welt (2006)	NIH	105 Iceland Caucasian 172 Boston Caucasian 44 Boston African American 25 Boston Hispanic 21 Boston Asian 32 Iceland controls	30.2 ± 6.2 28.8 ± 5.5 28.4 ± 6.7 26.3 ± 5.2 25.5 ± 5.3 32.2 ± 5.5	Presence of ≥12 follicles in each ovary measuring 2–9 mm in diameter, and/or increased ovarian volume (>10 ml)	Iceland Caucasian 92.5% Boston Caucasian 99.3% Boston African American 97.4% Boston Hispanic 95.0% Boston Asian 100% Maximum ovarian volume (ml): Iceland Caucasian 12.2 ± 5.6 Boston Caucasian 15.8 ± 7.2 Boston African American 18.2 ± 7.4 Boston Hispanic 14.4 ± 4.4 Boston Asian 13.3 ± 3.8 Maximum follicle no (count): Iceland Caucasian 11.6 ± 3.9 Boston Caucasian 14.5 ± 3.8 Boston African American 14.8 ± 4.6 Boston Hispanic 13.7 ± 3.8 Boston Asian 12.0 ± 2.9	When compared with Boston Caucasian subjects, Icelandic women with PCOS had smaller ovaries and fewer follicles but the frequency of PCO was similar Ovarian volume and follicle number were lower in Asian women
Glintborg (2010)	R	784 Caucasian 190 Middle Eastern	32 25	10 or more cysts 2–8 mm in diameter with a thickened echo-dense stroma	Caucasian 47% Middle Eastern 29%	PCO was less frequent in Middle Eastern patients
Ladson (2011)	NIH	43 Black 77 White 87 Black control 35 White control	27.9 ± 5.0 26.0 ± 6.9 Age not specified			Left and right ovarian volumes were comparable
Guo (2012)	R	547 Chinese 427 Dutch	28.3 ± 3.4 29.0 ± 5.2	Presence of ≥12 follicles in each ovary measuring 2–9 mm in diameter, and/or increased ovarian volume (>10 ml)		The prevalence of PCO did not differ
Wang (2013)	R	121 Caucasian 28 Asian	28.0 ± 5.4 29.6 ± 5.9	Presence of ≥12 follicles in each ovary measuring 2–9 mm in diameter, and/or increased ovarian volume (>10 ml)	Percentage of PCOS women with antral follicle count ≥12: Caucasian 85.1% Asian 82.1% Percentage of PCOS women with ovarian volume ≥10 ml: Caucasian 44.6% Asian 50.0%	Both groups had similar ovarian morphology

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TABLE 3 *(continued)*

Study (first author, year)	DC	Study population	Age (years)	PCO criteria	Percentage of PCOS women with PCO	Comments
Chan (2017)	R	184 American White 100 American Black 220 Indian 233 Brazilian 94 Finnish 258 Norwegian	29 29 25 26 33 28.5	Presence of ≥12 follicles in each ovary measuring 2–9 mm in diameter, and/or increased ovarian volume (>10 ml)	American White 68.5% American Black 76% Indian 78.6% Brazilian 67.4% Finnish 100% Norwegian 90.3%	When compared with American White patients with PCOS, the prevalence of PCO was higher in Indian, Finnish and Norwegian participants
Engmann (2017)	R	476 non-Hispanic White 98 non-Hispanic Black 128 Hispanic American	28.8 ± 4.2 28.7 ± 4.9 29.2 ± 4.1	Presence of ≥12 follicles in each ovary measuring 2–9 mm in diameter, and/or increased ovarian volume (>10 ml)	Non-Hispanic White 99.4% Non-Hispanic Black 99.0% Hispanic American 100%	Frequency of PCO, mean right ovarian volume and mean left ovarian volume were comparable

Age: values are mean ± SD, mean or median.

DC: diagnostic criteria; NIH, National Institutes of Health criteria; ns, not specified; PCO, polycystic ovarian morphology; PCOS, polycystic ovary syndrome; R, Rotterdam criteria.

more common in ethnic populations that were more insulin resistant (hPCOS and saPCOS; TABLE 4) (*Wijeyaratne et al., 2002*; *Welt et al., 2006*; *Mani et al., 2015*; *Sarkar et al., 2018*).

Seventeen studies evaluated lipids in different ethnic groups with PCOS. It was not the ethnicity but the fat mass (especially the central fat mass) that determined serum triglyceride and high-density lipoprotein (HDL) concentrations. In association with BMI or WHR, serum triglyceride concentrations were higher and serum HDL concentrations were lower in more obese (especially centrally obese) ethnic groups (*Williamson et al., 2001*; *Carmina et al., 2003*; *Wijeyaratne et al., 2004*; *Essah et al., 2008*; *Engmann et al., 2017*; *Sarkar et al., 2018*). Exceptionally, bPCOS had a more favourable lipid profile. In particular, serum triglyceride concentrations were lower in bPCOS. Moreover, bPCOS had higher HDL concentrations when compared with their White counterparts (*Koval et al., 2010*; *Ladson et al., 2011*). Conversely, Hilman and colleagues reported lower HDL concentrations in bPCOS even after adjusting for BMI and age (*Hillman et al., 2014*) (TABLE 4).

Although bPCOS had a low prevalence of dyslipidaemia, they presented with higher blood pressure. When compared with wPCOS, bPCOS had higher SBP and DBP values (*Lo et al., 2006*; *Hillman et al., 2014*; *Chang et al., 2016*; *Chan et al., 2017*). Blood pressure measurements were higher among European White women, followed by American White participants, with the values for other ethnic groups (saPCOS, mePCOS and eaPCOS) being lower than in White participants (*Wijeyaratne et al., 2002*; *Welt et al., 2006*; *Essah et al., 2008*; *Glintborg et al., 2010*; *Guo et al., 2012*; *Mani et al., 2015*; *Chan et al., 2017*) (TABLE 4).

Sub-infertility and pregnancy obstetric complications

No data currently exist regarding fertility outcomes in PCOS across various ethnic groups. In the only study that assessed the risk of gestational diabetes mellitus during pregnancy in PCOS including diverse ethnic groups (White, Black, Hispanic, Asian and others), Lo and co-workers reported East Asian ethnicity as a predictor for gestational diabetes mellitus with an odds ratio of 3.5 (95% confidence interval 2.3–5.5) in relation to the White population (*Lo et al., 2017*).

Mood disorders and QoL

Only two studies compared QoL parameters across different ethnicities. Hashimoto and colleagues compared Brazilian (Predominantly black) women with PCOS and Austrian women with PCOS. The rates of infertility and menstrual disturbances were similar. Hirsutism and obesity were more common among Brazilian participants. Overall, Brazilian women with PCOS had lower QoL scores. When compared with Austrian women with PCOS, hirsutism, infertility and menstrual disturbances had a more negative impact on QoL in Brazilian women with PCOS. Austrian women with PCOS were leaner. However, despite lower BMI measures, obesity had a greater impact on QoL in Austrian women with PCOS (*Hashimoto et al., 2003*). In the other study, Jones and co-workers compared saPCOS and wPCOS for health-related QoL scores and did not find any differences in mean scores (*Jones et al., 2010*). Although it was not a direct comparison of different ethnic groups, Schmid and co-workers illustrated a decreased QoL in Moslem immigrants in Austria. Moslem women had more concerns about infertility (*Schmid et al., 2004*).

Treatment outcomes

No studies were found regarding treatment outcomes of PCOS in different ethnic populations.

DISCUSSION

For this review, the literature was systematically searched to identify ethnic differences in the clinical presentation of PCOS and it was found that the phenotype of PCOS varies widely depending on the ethnicity.

Clinical hyperandrogenism is included in the definition of PCOS in all three sets of recommended diagnostic criteria (*Zawadzki, 1992*; *Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004*; *Azziz et al., 2006*). Hirsutism is used to define clinical hyperandrogenism, although acne or androgenic alopecia can accompany hirsutism in PCOS. Along with serum androgen concentrations, individual sensitivity of the pilosebaceous unit to androgens determines the degree of hair growth (*Yilmaz and Yildiz, 2019*). The mFG system is the gold standard method

TABLE 4 COMPARISON OF METABOLIC AND CARDIOVASCULAR RISK FACTORS BETWEEN VARIOUS ETHNIC GROUPS

Study (first author, year)	DC	Study population	Age (years)	Obesity	IR/prediabetes/diabetes	Acanthosis nigricans	Dyslipidaemia	Hypertension	Comments
Carmina (1992)	NIH	25 Hispanic American 25 Japanese 25 Italian For each ethnic group 10 age-matched controls	30 ± 2 24 ± 1 24 ± 1	Percentage of ideal body weight: Hispanic American 122% Japanese 111% Italian ns	FIC were lower in Japanese Similar IR				Hispanic patients were more obese FIC were lower in Japanese women Despite lower weight in Japanese women, all groups were similar in terms of IR
Dunaif (1993)	NIH	13 Caribbean Hispanic 10 non-Hispanic White 5 Caribbean Hispanic control 8 non-Hispanic White control	25.1 ± 1 27 ± 2 28 ± 2 27 ± 1	mBMI: Hispanic 35.6 ± 1.5 White 37.1 ± 1.8	In the euglycaemic clamp test, Caribbean Hispanic women had lower IS than non-Hispanic White women				In an age-, weight- and body composition-matched cohort, Caribbean Hispanic patients were more insulin resistant
Norman (1995)	NIH	11 Indian 11 White 11 Indian control 11 White control	~25 Age was similar for all groups						In an age- and BMI-matched cohort, Indian PCOS patients had higher insulin responses than White patients on an OGTT
Ehrmann (1999)	NIH	63 Caucasian 44 African American 10 Asian 5 Hispanic	ns		Frequency of IGT or type 2 DM: Caucasian 41% African American 50% Asian 40% Hispanic 50%				The study was not specifically designed to assess ethnic differences Numbers of Asian and Hispanic participants were low African Americans had a slight preponderance of type 2 DM No difference between ethnicities in terms of glucose tolerance
Williamson (2001)	ns	112 White 16 Maori 15 Pacific Islander 19 Indian 4 Asian 6 other There was an inconsistency between number and percentage of PCOS patients	27.4	mBMI: White 27.5 ± 6.6 Maori 32.3 ± 4.3 Pacific Islander 34.0 ± 6.0 Indian 28.7 ± 7.4 Asian+other 24.3 ± 4.6	FIC were higher in Maori and Pacific Islander		Maori and Pacific Islander women had higher TG and lower HDL concentrations	SBP and DBP were similar	Maori and Pacific Islander women had the worst metabolic profile while Asian women had a mild metabolic phenotype
Kauffman (2002)	NIH	48 White 26 Mexican American 11 White control 8 Mexican American control	~26[a] ~30 25	mBMI was higher in insulin-resistant Mexican American women with PCOS (40 versus 36)	FIC and HOMA-IR measures were higher in Mexican American women while glucose/insulin ratios were lower IR White 43.8% IR Mexican American 73.1%				After adjustment for BMI, Mexican American women still had higher FIC and HOMA-IR values but lower glucose/insulin ratios These ethnic difference were negligible at BMI values of ≤24 Ethnicity influenced the normative values of IR screening
Wijeyaratne (2002)	ns	47 South Asian 40 Caucasian 11 South Asian control 22 Caucasian control	26 ± 4 30.1 ± 5 31.3 ± 2 32.9 ± 3	mBMI: South Asian 30.6 ± 7.5 Caucasian 32.1 ± 5.9 WHR: South Asian 1.04 ± 0.02 Caucasian 0.92 ± 0.01	FIC in South Asian patients were higher IS calculated by the QUICKI method was lower in South Asians	South Asian 55% Caucasian 7%	Serum TC, TC/HDL and TG concentrations were similar	After adjustment for age, SBP and DBP were higher in Caucasians	Despite similar BMI and WHR, South Asians had lower IS than Caucasians Almost half of the South Asian women with PCOS had acanthosis nigricans

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TABLE 4 *(continued)*

Study (first author, year)	DC	Study population	Age (years)	Obesity	IR/prediabetes/diabetes	Acanthosis nigricans	Dyslipidaemia	Hypertension	Comments
Carmina (2003)	NIH	20 non-Hispanic White American 20 Italian	29 ± 2 26.6 ± 2	mBMI: White American 40.3 ± 1 Italian 29.7 ± 1 WHR: White American 0.85 ± 0.02 Italian 0.83 ± 0.04	FIC were higher in Americans American women had lower glucose/insulin ratios		TC and LDL were comparable Serum TG concentrations were higher in American women while HDL concentrations were lower	SBP and DBP were similar	After adjustment for BMI, American women still had a worse metabolic profile Consumption of saturated fat was higher in Americans
Hashimoto (2003)	NIH	102 Brazilian (predominantly Black) 31 Austrian	25.5 ± 3.923.8 ± 4.7	mBMI: Brazilian 27.5 ± 6.6 Austrian 23.7 ± 4.3					Austrian PCOS patients were leaner but obesity had a greater impact on the quality of life in Austrians
Wijeyaratne (2004)	ns	74 Sri Lankan 47 British Asian 40 White 45 Sri Lankan control 11 British Asian control 22 White control	27.3 ± 1.7 26 ± 4 30.1 ± 0.5 33 ± 4.7 31.3 ± 2 32.8 ± 3	mBMI: Sri Lankan 26.3 ± 0.9 British Asian 30.6 ± 7.5 White 32.1 ± 5.9 WHR: Sri Lankan 0.97 ± 0.01 British Asian 1.04 ± 0.02 White 0.92 ± 0.01	Sri Lankan women with PCOS had higher FPG and FIC but lower IS assessed by QUICKI		TC and TG concentrations were higher in Sri Lankan patients		South Asian women were younger Sri Lankan women had lower BMI Sri Lankan women had the highest homocysteine concentrations Despite lower BMI and comparable WHR, Sri Lankan women had a worse metabolic profile Sri Lankan women with PCOS may have increased cardiovascular disease risk compared with their White counterparts
Al-Fozan (2005)	ns	41 Western European 18 Middle Eastern 15 African American 9 East Indian 9 South American	33.3 ± 5.7 32.1 ± 4.9 33.8 ± 6.6 34.2 ± 4.8 28.8 ± 4.3	mBMI: Western European 30.2 ± 4.5 Middle Eastern 31.4 ± 5.0 African American 29.9 ± 4.8 East Indian 27.3 ± 5.5 South American 28.8 ± 4.3	Middle Eastern women had higher glucose and insulin concentrations than Western European women				Independent of BMI, Middle Eastern women had worse glucose tolerance than Western Europeans
Ehrmann (2005)	NIH	303 White 51 Black 38 Other	28.8 ± 0.3 27.6 ± 0.8 26.7 ± 0.9	mBMI: White 36.3 ± 0.5 Black 37.1 ± 1.2 Other 32.6 ± 1.1 WHR: White 0.87 ± 0.01 Black 0.91 ± 0.01 Other 0.88 ± 0.01	Black women had higher FIC, higher HbA_{1c} and were more IR by HOMA-IR				Black women with PCOS were more IR
Kumar (2005)	NIH	186 White 27 Black 94 White control 88 Black control	27.3 ± 6.6 28.7 ± 6.2 28.7 ± 9.1 30.2 ± 9.1	mBMI: White 36.0 ± 9.3 Black 36.0 ± 8.9 WHR: White 0.84 ± 0.08 Black 0.84 ± 0.10	FIC and FPG were similar				No differences in terms of carbohydrate metabolism

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TABLE 4 *(continued)*

Study (first author, year)	DC	Study population	Age (years)	Obesity	IR/prediabetes/diabetes	Acanthosis nigricans	Dyslipidaemia	Hypertension	Comments
Kauffman (2006)	R	111 White 50 Mexican American	27.3 26.9	mBMI: White 33.7 Mexican American 35.4	FPG concentrations were similar Mexican American patients had higher FIC and were higher IR				Mexican American patients had a worse metabolic profile
Legro (2006)	NIH	435 Caucasian 109 African American 17 Asian 72 American Indian or Alaska Native	28.2 ± 3.9 27.9 ± 4.3 30.4 ± 3.0 27.6 ± 4.1	mBMI: Caucasian 35.4 ± 8.8 African American 36.0 ± 8.4 Asian 29.1 ± 6.3 American Indian or Alaska Native 34.3 ± 8.0	Glucose/insulin ratios were lowest in Asian women, and Asian women tended to have more normal HOMA-IR values			mSBP: Caucasian 122.2 ± 13.7 African American 123.6 ± 12.6 Asian 111.4 ± 9.1 American Indian or Alaska Native 122.5 ± 15.0 mDBP: Caucasian 77.6 ± 9.9 African American 76.8 ± 10.5 Asian 73.1 ± 6.8 American Indian or Alaska Native 74.4 ± 9.2	Asian women with PCOS tended to be older and lighter After adjustment for weight, blood pressures were similar Asian women had a better metabolic profile
Lo (2006)	ns	3778 White 552 Black 1117 Asian 1324 Hispanic 432 other	32.6 ± 7.4 31.7 ± 7.9 32.2 ± 6.4 30.8 ± 6.7 31.7 ± 6.5	BMI ≥30: White 67.5% Black 80.3% Asian 45.1% Hispanic 73.8% Other 68.9%	DM: White 9.5% Black 8.9% Asian 11.9% Hispanic 11.9% Other 13.9%			HT: White 13.9% Black 21.7% Asian 14.2% Hispanic 12.2% Other 13.9%	Asian women with PCOS had the lowest BMI Black and Hispanic women were more obese After adjustment for BMI and age, Asian and Hispanic women had an increased risk of DM After adjustment for BMI, age and DM status, Black women had an increased risk of HT
Welt (2006)	NIH	105 Iceland Caucasian 172 Boston Caucasian 44 Boston African American 25 Boston Hispanic 21 Boston Asian 32 Iceland controls	30.2 ± 6.2 28.8 ± 5.5 28.4 ± 6.7 26.3 ± 5.2 25.5 ± 5.3 32.2 ± 5.5	mBMI: Iceland Caucasian 31.5 ± 7.7 Boston Caucasian 30.7 ± 9.2 Boston African American 36.3 ± 7.9 Boston Hispanic 32.3 ± 10.3 Boston Asian 26.3 ± 5.9	DM: Iceland Caucasian na Boston Caucasian 2% Boston African American 11.9% Boston Hispanic 4.3% Boston Asian 0% FIC and HOMA-IR measures were higher in African American and Hispanic women	Iceland Caucasian 47.4% Boston Caucasian 62.9% Boston African American 76.7% Boston Hispanic 69.6% Boston Asian 70%	TC, LDL and TG concentrations were comparable across all ethnic groups but HDL concentrations were lower in Icelandic Caucasians	mSBP of Icelandic PCOS subjects was higher	African American women had the highest BMI and Asian women had the lowest BMI African American and Hispanic participants had a worse metabolic profile The percentage of participants with acanthosis nigricans was lower in Icelandic Caucasians

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TABLE 4 *(continued)*

Study (first author, year)	DC	Study population	Age (years)	Obesity	IR/prediabetes/ diabetes	Acanthosis nigricans	Dyslipidaemia	Hypertension	Comments
Essah (2008)	NIH	106 American (92% White) 108 Italian	29.9 ± 7.5 24.7 ± 5.2	mBMI: American 36.1 ± 8.6 Italian 28.1 ± 5.8 BMI >30: American 73.6% Italian 30.6%			While HDL concentrations were lower, TC, LDL and TG concentrations were higher in American women	mSBP of Italian PCOS patients was higher	After adjustment for BMI and age, serum TG concentrations remained higher in American participants
Glintborg (2010)	R	784 Caucasian 190 Middle Eastern	32 25	mBMI: Caucasian 27.0 Middle Eastern 25.7	Middle Eastern women had higher FIC Middle Eastern PCOS patients had higher 2 h glucose and AUC insulin during OGTT		After adjustment for BMI and age, lipid profiles were comparable	mSBP and mDBP were higher in Caucasian women even after correcting for BMI and age	When compared with Middle Eastern women, Caucasian women with PCOS had higher IS but an increased cardiovascular disease risk
Koval (2010)	NIH	94 Caucasian 32 African American	30.5 ± 6.8 30.6 ± 7.6	mBMI: Caucasian 37.0 ± 7.1 African American 41.0 ± 9.6			After adjustment for BMI, age and HOMA-IR, African American women had higher HDL, lower TG and non-HDL cholesterol		African American women with PCOS had a more favourable lipid profile
Kauffman (2011)	R	120 White 71 Mexican American	27.4 26.8	mBMI: White 34.8 Mexican American 34.3	HOMA-IR, 2 h insulin concentrations and AUC insulin during OGTT were higher in Mexican American participants with PCOS Matsuda and Strumvoll IS index values were higher in Whites		TC, TG, HDL, LDL and non-HDL cholesterol concentrations were similar		In an age- and BMI-matched cohort, Mexican American women had higher IR but lipid concentrations were similar
Ladson (2011)	NIH	43 Black 77 White 87 Black control 35 White control	27.9 ± 5.0 26.0 ± 6.9 Age not specified	mBMI: Black 39.0 ± 9.3 White 37.7 ± 6.3 WHR: Black 0.88 ± 0.08 White 0.88 ± 0.06	FIC and HOMA-IR values were higher in Black participants		Black women with PCOS had higher HDL and lower TG concentrations	mSBP and mDBP were comparable	Lipid profile was more favourable in Black women with PCOS
Guo (2012)	R	547 Chinese 427 Dutch	28.3 ± 3.4 29.0 ± 5.2	mBMI: Chinese 25.3 ± 4.3 Dutch 26.3 ± 6.9 WHR: Chinese 0.85 ± 0.06 Dutch 0.82 ± 0.08	FPG was lower but FIC were higher in Chinese HOMA-IR values were similar		TC and TG concentrations were similar Chinese participants had higher LDL and lower non-HDL cholesterol concentrations	mSBP and mDBP were higher in Dutch women	Although mBMI values of Chinese women were lower, WHR of Chinese women was higher Chinese women were more prone to central obesity
Wang (2013)	R	121 Caucasian 28 Asian	28.0 ± 5.4 29.6 ± 5.9	mBMI: Caucasian 30.4 ± 8.1 Asian 30.1 ± 7.4	FPG, 2 h glucose concentrations and FIC were similar		TC, TG, HDL and LDL concentrations were similar		Groups were similar in terms of metabolic profile

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TABLE 4 *(continued)*

Study (first author, year)	DC	Study population	Age (years)	Obesity	IR/prediabetes/diabetes	Acanthosis nigricans	Dyslipidaemia	Hypertension	Comments
Hilman (2014)	R	413 non-Hispanic White 106 non-Hispanic Black	25.0 ± 6.7 26.3 ± 7.3	BMI >30: White 47% Black 72.3%	FIC and FPG were higher in Black women		TC, TG and HDL concentrations were lower in Black women	mSBP and mDBP were higher in Black women	Black women were more obese and had higher IR, had higher blood pressure values Despite the relatively favourable lipid profile, Black individuals with PCOS had a higher prevalence of metabolic syndrome and 10-year cardiovascular disease risk After adjustment for age and BMI, Black women had low HDL and high glucose concentrations
Mani (2015)	ns	929 White 381 South Asian	27.1 ± 7.4 24.3 ± 6.7	mBMI: White 31.5 ± 7.9 South Asian 29.3 ± 6.8	DM: White 5.6% South Asian 8.1%	White 3.1% South Asian 16.8%		mSBP and mDBP were higher in White women	South Asian women presented at earlier ages Despite lower BMI, acanthosis nigricans and DM were more common in South Asian women
Chang (2016)	R	62 Black 32 White 23 Hispanic 113 Black control 54 White control 37 Hispanic control	41 41 39 40 40 39	mBMI: Black 32.3 White 28.2 Hispanic 31.7 WHR: Black 0.87 White 0.83 Hispanic 0.86	FIC were lower in White women with PCOS even after adjustment for BMI Hispanic women had a higher frequency of IFG		Prevalence of hypertriglyceridaemia was higher in White women TC concentrations were lower in Black women	mSBP and the prevalence of HT were higher in Black individuals	Black and Hispanic women were more obese Black women had higher FIC Hypertension was more common in Black women Hispanic women had a higher frequency of IFG The lipid profile of Black women was more favourable Ethnicity influences cardiovascular risk factors in both individuals with and without PCOS but no synergistic effect on cardiovascular risk factors that varied by ethnicity was noted
Chan (2017)	R	184 American White 100 American Black 220 Indian 233 Brazilian 94 Finnish 258 Norwegian	29 29 25 26 33 28.5	Median BMI: American White 30.6 American Black 37.5 Indian 26.7 Brazilian 29.3 Finnish 29.4 Norwegian 31.1	Despite lower BMI, FPG concentrations were highest in Indian participants		When compared with American White women with PCOS, Black women had lower and Indian women had higher TG concentrations HDL concentrations were lower both in Indian and Black women	When compared with American White women with PCOS, Black participant had higher mSBP and mDBP mDBP was also higher in Brazilian, Finnish and Norwegian women with PCOS	Black individuals had the highest rate of obesity The prevalence of metabolic syndrome was higher in Black (52%) and Norwegian (41.1%) women compared with American White women (28.3%) In an age- and BMI-adjusted analysis, Indian and Norwegian women had elevated odds of metabolic syndrome
Engmann (2017)	R	476 non-Hispanic White 98 non-Hispanic Black 128 Hispanic American	28.8 ± 4.2 28.7 ± 4.9 29.2 ± 4.1	mBMI: non-Hispanic White 35.1 ± 9.8 non-Hispanic Black 35.7 ± 7.9 Hispanic American 36.4 ± 7.9	FIC, FPG and HOMA-IR measures were higher in Hispanic participants		TG concentrations were highest in Hispanic and lowest in Black women LDL concentrations were comparable	Black women had higher mSBP	Metabolic syndrome was more prevalent in Hispanic women Despite the comparable BMI and waist circumference, Hispanic women had the most severe metabolic disturbance

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TABLE 4 *(continued)*

Study (first author, year)	DC	Study population	Age (years)	Obesity	IR/prediabetes/diabetes	Acanthosis nigricans	Dyslipidaemia	Hypertension	Comments
Sarkar (2018)	R	256 non-Hispanic American 47 Hispanic American	28.1 28.5	median BMI: non-Hispanic American 26.0 Hispanic American 31.2	HOMA-IR measures were higher in Hispanic women	Non-Hispanic American 34.3% Hispanic American 65.2%	Whereas TG concentrations were higher, HDL concentrations were lower in Hispanic women		Hispanic women had an unfavourable metabolic profile Non-alcoholic steatohepatitis was more common in Hispanic women, and Hispanic ethnicity was an independent risk factor for this in multivariate analysis

Age: values are mean ± SD, mean or median.

[a] In this study age was not reported for whole PCOS cohort; however the mean age of White and Mexican American participants with PCOS was approximately 26 years. White healthy control participants were older than Mexican American healthy controls.AUC, area under the curve; BMI, body mass index (kg/m^2); DBP, diastolic blood pressure; DC, diagnostic criteria; DM, diabetes mellitus; FIC, fasting insulin concentration; FPG, fasting plasma glucose; HbA_{1c}, glycated haemoglobin; HDL, high-density lipoprotein; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; HT, hypertension; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; IR, insulin resistance; IS, insulin sensitivity; LDL, low-density lipoprotein; mBMI, mean body mass index (kg/m^2); mDBP, mean diastolic blood pressure; mSBP, mean systolic blood pressure; NIH, National Institutes of Health criteria; ns, not specified; OGTT, oral glucose tolerance test; PCOS, polycystic ovary syndrome; QUICKI, quantitative insulin sensitivity check index; R, Rotterdam criteria; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WHR, waist–hip ratio.

to diagnose and quantify hirsutism, scoring hair density in the nine body areas from 0 to 4. In the original study conducted in Caucasian women, a cut-off score of ≥8 was determined as defining hirsutism (*Hatch et al., 1981*). However, subsequent studies performed in diverse ethnic populations showed ethnic variations in the mFG cut-off. While lower cut-off values were recommended for East Asian women, higher mFG cut-off values have been proposed even in healthy Hispanic and Middle Eastern subjects owing to the higher hair density (*Escobar-Morreale et al., 2012*). The findings of this review suggest lower mFG scores in eaPCOS and higher mFG scores in hPCOS, saPCOS and mePCOS compared with Caucasians (FIGURE 2). All available data regarding bPCOS came from studies conducted in the USA and in these studies, in general, bPCOS had comparable mFG scores to their American non-Hispanic White counterparts. It is also worth emphasizing that there were differences in hirsutism even within Caucasian populations (European versus American) (TABLE 1).

Total mFG scores were used for the comparison of hirsutism between different ethnic groups in all but two studies. Although total mFG scores give an estimation of the total amount of body hair, excessive hair growth might occur only in some parts of the body. Some body areas may be more sensitive to androgen action and this might be more evident in some ethnic groups. In support of this idea, in the only two studies that also compared site-specific mFG scores, researchers pointed out ethnic differences in site-specific mFG scores (TABLE 1). mFG scores decrease with age (*Zhao et al., 2011*), but not all studies directly comparing different ethnicities in the current review were age matched, and age groups were heterogeneous (TABLE 1). This may lead to errors of interpretation. Moreover, there is no comparative study investigating how hair density changes with ageing in different ethnicities. Therefore, when using the mFG score to determine clinical androgen excess, the individual's ethnicity and age should be taken into consideration.

Acne can be observed in patients with hyperandrogenism. Although the available data are contradictory, some differences may exist in the biological characteristics of skin among various ethnic groups (*Davis and Callender, 2010*). For instance, the density of *Propionibacterium acnes* was found to be higher in African American individuals compared with Caucasian patients (*Warrier, 1996*). Hence, the prevalence of acne may differ in various ethnic groups. In this review, the results for acne were discordant and not sufficient to conclude whether ethnicity has any impact on the prevalence of acne among different ethnicities in PCOS. It should also be noted that there are no universally accepted visual tools to evaluate acne.

Evidence for ethnic differences in hyperandrogenemia was scarce and unclear. There are no studies specifically evaluating and rogens and their cut-off levels in different ethnic groups with different ages. Most studies had a limited sample size and did not assess the same androgens. Despite these limitations, androgen concentrations seemed to be similar in diverse ethnic populations, with a few exceptions for ethnic differences in SHBG and adrenal androgens (TABLE 1).

Ovulatory dysfunction is a diagnostic criterion for PCOS, and the clinical detection of ovulatory dysfunction is based on menstrual irregularity. Only seven studies were identified that compared the menstrual patterns of women with PCOS belonging to different ethnicities (TABLE 2). Menstrual disturbances appeared to be more common in eaPCOS. eaPCOS has a mild androgenic phenotype and menstrual disturbances may be a major complaint in clinical presentation. Considering that all studies enrolled patients presenting to clinics, this finding might be due to selection bias. Whether there are frank differences in menstrual irregularity between eaPCOS and other ethnic groups warrants further multiethnic comparative studies in unselected populations.

The 2003 Rotterdam consensus proposed PCOM as a diagnostic criterion for PCOS, defining it as the presence of 12 or more follicles in each

FIGURE 2 Variations in the clinical presentation of polycystic ovary syndrome patients belonging to different ethnicities. AN, acanthosis nigricans; BP, blood pressure; DHEAS, dehydroepiandrosterone sulphate; FAI, free androgen index; fT, free testosterone; GDM, gestational diabetes mellitus; HDL, high-density lipoprotein; IR, insulin resistance; SHBG, sex hormone-binding globulin; T, testosterone; TG, triglyceride.

ovary measuring 2–9 mm in diameter, and/or increased ovarian volume (>10 ml) on ultrasound (*Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004*). This criterion was also included in the Androgen Excess and PCOS (AE-PCOS) Society recommendations for the diagnosis of PCOS (*Azziz et al., 2006*). However, PCOM is not included as a diagnostic criterion by the National Institutes of Health (NIH) criteria (*Zawadzki, 1992*). Accordingly, using NIH criteria to diagnose PCOS may exclude some individuals with PCOM and may yield an underrepresentation of this group. In the current review, 15 studies had used NIH criteria. In general, the frequency of PCOM did not show a difference for different ethnic groups in the available studies. However, there were subtle differences in ovarian morphology even though the prevalence of PCOM was similar between ethnic groups. For instance, eaPCOS had lower follicle counts and ovarian volume in two studies (see TABLE 3). Further studies are needed to determine whether PCOM differs in different ethnic groups.

Obesity is prevalent in women with PCOS presenting to clinics. In this review, obesity was more frequent in hPCOS and bPCOS compared with Caucasian patients. On the other hand, eaPCOS and saPCOS had lower BMI values with increased central fat and a comparable or higher metabolic risk compared with Caucasian PCOS women. The most common method for assessing excessive fat is BMI calculation. A BMI value higher than 30 kg/m^2 was proposed to diagnose obesity in Caucasian populations. However, BMI is a crude indicator and does not reflect the increased metabolic and cardiovascular disease risk in certain ethnic populations (*Heymsfield et al., 2016*). Accordingly, different BMI thresholds were determined to define obesity in various ethnic groups. BMI cut-offs have been lowered to 25 and 23 kg/m^2 to reflect the risk in South Asian and East Asian populations, respectively (*Misra et al., 2009*; *Chen et al., 2010*). Considering the propensity of East Asian and South Asian individuals to develop central adiposity, the lowered thresholds of BMI may still not be appropriate for these ethnic populations. Therefore, for evaluating the increased adiposity in women of various ethnic origins with PCOS, the use of population-specific anthropometric measures such as WHR may provide a better assessment of metabolic risk.

Many women with PCOS are insulin resistant and the incidence of prediabetes and diabetes mellitus is increased in women with PCOS independent of age and BMI (*Moran et al., 2010*). Some ethnic groups have a propensity to insulin resistance and therefore prediabetes/diabetes mellitus (*Raygor et al., 2019*). Thus, one might expect variable degrees of insulin resistance in PCOS patients with different ethnicities. In this systematic review, it was found that hPCOS, bPCOS, mePCOS and saPCOS were more insulin resistant and predisposed to glucose intolerance compared with wPCOS. Moreover, the prevalence of acanthosis nigricans was higher in the ethnic groups with a higher level of insulin resistance. However, the methods to assess glucose homeostasis showed variations (TABLE 4). Other cardiovascular risk factors, including dyslipidaemia and hypertension, also varied among different ethnic populations. Dyslipidaemia was more prevalent in more obese ethnic groups. bPCOS had better lipid measures but higher blood pressure.

TABLE 5 AREAS FOR FUTURE RESEARCH REGARDING IMPACT OF ETHNICITY ON PCOS

- Development of age- and ethnicity-specific visual tools and cut-off values for assessment and definition of clinical hyperandrogenism, including hirsutism and acne
- Comparative analysis of biochemical hyperandrogenism in multiethnic cohorts with high-quality assays
- Assessment of phenotypic variation including prevalence of prediabetes/diabetes and risk of cardiovascular disease in multiethnic longitudinal studies of unselected populations
- Evaluation of the impact of ethnicity on fertility, obstetric and neonatal outcomes in comparative studies of women with PCOS
- Determination of the role of ethnicity on perception of PCOS and emotional well-being and quality of life
- Assessment of the role of ethnicity on long-term medical management of PCOS

PCOS, polycystic ovary syndrome.

High blood pressure values were also noted in European and American Caucasians when compared with saPCOS, mePCOS and eaPCOS (TABLE 4). Hence, the components of the metabolic syndrome were widely variable in women with PCOS of different ethnicities. The current data regarding the differences in clustering components of metabolic syndrome in different ethnic populations emphasize that ethnic variables should also be taken into consideration when evaluating patients' metabolic status.

PCOS is the main cause of anovulatory subfertility. Evidence suggests that both natural and assisted fecundity rates differ between various ethnic groups and that ethnicity may affect the success of fertility treatments and their outcomes (*Huddleston et al., 2010*; *Dimitriadis et al., 2017*). However, this literature search did not reveal any study comparing fertility outcomes across various ethnic groups that included only women with PCOS. Women with PCOS are at increased risk of pregnancy complications and adverse obstetric outcomes (*Roos et al., 2011*). The diverse reproductive and metabolic presentation of PCOS in diverse ethnic populations may persist during pregnancy and influence the obstetric and neonatal outcomes. Therefore, it can be expected that pregnancy-associated complications may vary in different ethnic groups. In the current review, only one study was found showing that eaPCOS had a higher risk of gestational diabetes mellitus during pregnancy compared with wPCOS (*Lo et al., 2017*).

Psychological disorders are common in PCOS and several symptoms related to PCOS may have a negative impact on QoL (*Dokras et al., 2018*). The patient's ethnic and cultural background may also affect the perception of the disorder (*Hashimoto et al., 2003*; *Schmid et al., 2004*). Two studies were found that assessed the QoL scores of PCOS patients with different ethnicities, and in a separate study individuals from different religions were compared (*Kumar et al., 2005*; *Jones et al., 2010*; *Wang et al., 2013*). More data are needed on the potential role of ethnicity in psychological disorders and QoL in patients with PCOS.

Lifestyle intervention is the first-line treatment for PCOS, and medical treatment aims to improve reproductive and metabolic dysfunction (*Teede et al., 2018*). There was no study that compared the outcomes of lifestyle intervention and medical treatment among different ethnic populations with PCOS. Ethnic variations can be important for treatment outcomes. For instance, interindividual variations in metformin response due to genetic heterogeneity have been reported in patients with diabetes (*Mofo Mato et al., 2018*). Moreover, the ethnic or cultural background of an individual may affect drug preferences. Rocca and colleagues reported significant ethnic disparities in use of the contraceptive pill (*Rocca and Harper, 2012*). Accordingly, the potential influence of ethnicity on response to lifestyle interventions or medical treatment in PCOS is an area of interest for future research.

Overall, ethnicity plays an important role in the phenotypic presentation of PCOS and its individual components. For example, independent of PCOS, mFG cut-off scores for defining hirsutism and the severity of hirsutism vary by ethnicity. Scores of ≥4 and ≥6 define hirsutism in White and Black women and Han Chinese women, respectively. Accordingly, in 2018, the International PCOS Network suggested that ethnic variation should be considered in the management of PCOS (*Teede et al., 2018*). However, the studies included in our review did not compare phenotypic variations in PCOS using ethnicity-specific recommendations. Future studies on the impact of ethnicity are needed to inform the guidelines (TABLE 5).

There are some limitations to the current systematic review. First, the review included studies that were performed in clinics. The clinical presentation and ethnic characteristics of PCOS may vary in unselected populations (*Ezeh et al., 2013*). Therefore these findings on clinical referral populations might not be able to be extrapolated to unselected populations. Second, in all studies, ethnicity was assessed by self-reported data. However, self-reported ethnicity might be subjective and biased. Using genetic ancestry instead of self-reported ethnicity may provide a better ethnic determination (*Louwers et al., 2014*). Finally, although in some studies the participants lived in the same environment, in others study participants were recruited from different countries. Considering the effect of environmental factors on PCOS, the disparities between different ethnic groups might not be attributable to ethnic factors *per se*.

CONCLUSION

Based on the limited data available, the clinical presentation of PCOS shows a wide variation among different ethnic populations. Larger multiethnic comparative studies specifically assessing the role of ethnicity in the diagnosis and management of PCOS are needed for developing ethnicity-specific guidelines.

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