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2017-08

Chan , J L , Kar , S , Vanky , E , Morin-Papunen , L , Piltonen , T , Puurunen , J , Tapanainen , J S , Maciel , G A R , Hayashida , S A Y , Soares , J M , Baracat , E C , Mellembakken , J R & Dokras , A 2017 , ' Racial and ethnic differences in the prevalence of metabolic syndrome and its components of metabolic syndrome in women with polycystic ovary syndrome : a regional cross-sectional study ' , American Journal of Obstetrics and Gynecology , vol. 217 , no. 2 , ARTN 189.e1-8 . <https://doi.org/10.1016/j.ajog.2017.04.007>

<http://hdl.handle.net/10138/297922>

<https://doi.org/10.1016/j.ajog.2017.04.007>

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GYNECOLOGY

Racial and ethnic differences in the prevalence of metabolic syndrome and its components of metabolic syndrome in women with polycystic ovary syndrome: a regional cross-sectional study

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BACKGROUND: Polycystic ovary syndrome is a heterogeneous disorder and its presentation varies with race and ethnicity. Reproductive-age women with polycystic ovary syndrome are at increased risk of metabolic syndrome; however, it is not clear if prevalence of metabolic syndrome and clustering of its components differs based on race and ethnicity. Moreover, the majority of these women do not undergo routine screening for metabolic syndrome.

OBJECTIVE: We sought to compare the prevalence of metabolic syndrome and clustering of its components in women with polycystic ovary syndrome in the United States with women in India, Brazil, Finland, and Norway.

STUDY DESIGN: This is a cross-sectional study performed in 1089 women with polycystic ovary syndrome from 1999 through 2016 in 5 outpatient clinics in the United States, India, Brazil, Finland, and Norway. Polycystic ovary syndrome was defined by the Rotterdam criteria. Main outcome measures were: metabolic syndrome prevalence, blood pressure, body mass index, fasting high-density lipoprotein cholesterol, fasting triglycerides, and fasting glucose. Data from all sites were reevaluated for appropriate application of diagnostic criteria for polycystic ovary syndrome, identification of polycystic ovary syndrome phenotype, and complete metabolic workup. The US White women with polycystic ovary syndrome were used as the referent group. Logistic regression models were used to evaluate associations between race and metabolic syndrome prevalence and its components and to adjust for potential confounders, including age and body mass index.

RESULTS: The median age of the entire cohort was 28 years. Women from India had the highest mean Ferriman-Gallwey score for clinical hyperandrogenism (15.6 ± 6.5 , $P < .001$). The age-adjusted odds ratio for metabolic syndrome was highest in US Black women at 4.52 (95%

confidence interval, 2.46–8.35) compared with US White women. When adjusted for age and body mass index, the prevalence was similar in the 2 groups. Significantly more Black women met body mass index and blood pressure criteria ($P < .001$), and fewer met fasting triglycerides criteria ($P < .05$). The age- and body mass index–adjusted prevalence of metabolic syndrome was highest in Indian women (odds ratio, 6.53; 95% confidence interval, 3.47–12.30) with abnormalities in glucose and fasting high-density lipoprotein cholesterol criterion and in Norwegian women (odds ratio, 2.16; 95% confidence interval, 1.17–3.98) with abnormalities in blood pressure, glucose, and fasting high-density lipoprotein cholesterol criterion. The Brazilian and Finnish cohorts had similar prevalence of metabolic syndrome and its components compared to US White women.

CONCLUSION: Despite a unifying diagnosis of polycystic ovary syndrome, there are significant differences in the prevalence of metabolic syndrome and clustering of its components based on race and ethnicity, which may reflect contributions from both racial and environmental factors. Our findings indicate the prevalence of metabolic syndrome components varies in women with polycystic ovary syndrome, such that compared to White women from the United States, Black US women had the highest prevalence, whereas women from India and Norway had a higher prevalence of metabolic syndrome independent of obesity. The differences in clustering of components of metabolic syndrome based on ethnicity highlight the need to routinely perform complete metabolic screening to identify specific targets for cardiovascular risk reduction strategies in these reproductive-age women.

Key words: ethnicity, metabolic syndrome, polycystic ovary syndrome, race

Cite this article as: Chan JL, Kar S, Vanky E, et al. Racial and ethnic differences in the prevalence of metabolic syndrome and its components of metabolic syndrome in women with polycystic ovary syndrome: a regional cross-sectional study. *Am J Obstet Gynecol* 2017;217:189.e1-8.

0002-9378/\$36.00

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<http://dx.doi.org/10.1016/j.ajog.2017.04.007>

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting reproductive-age women.^{1,2} In addition to its clinical manifestations of oligomenorrhea, androgen excess, and polycystic-appearing ovaries on ultrasound,³ PCOS is also associated with an increased prevalence of metabolic syndrome (MetSyn).^{4,5} MetSyn comprises a constellation of factors that increase the risk for cardiovascular disease, diabetes,

stroke, and diseases related to atherosclerosis.^{6,7}

Several studies addressed population differences in the clinical presentation of PCOS, including differences in serum androgen concentrations,⁸⁻¹⁰ prevalence of menstrual dysfunction,^{11,12} appearance of polycystic ovaries on ultrasound,^{8,11} and insulin resistance.^{11,13-15} Women with PCOS living in the United States have a high prevalence of MetSyn (43-46%),^{16,17} with high body mass index

TABLE 1
Recruitment specifics for each study site

Study site	Recruitment dates	Recruitment site	Clinical hyperandrogenism FG score	Biochemical hyperandrogenism	Testosterone assay	Transvaginal ultrasound probe resolution
United States	2009 through 2014	Outpatient gynecology/PCOS center	≥ 8	Total testosterone ≥ 55 ng/dL	Liquid chromatography mass spectrometry	5–9 MHz
India ^a	2009 through 2013	Outpatient gynecology private practice setting	≥ 8	—	—	5–13 MHz
Brazil	1999 through 2015	Outpatient gynecology/endocrine health unit	≥ 8	Total testosterone > 50 ng/dL	Electrochemiluminescence immunoassay	5–9 MHz
Finland	2004 through 2010	Outpatient gynecology clinic	≥ 8	Total testosterone ≥ 66.3 ng/dL or free androgen index ≥ 5.6	Liquid chromatography mass spectrometry	4–8 MHz
Norway	1999 through 2016	Outpatient gynecology/infertility clinics	≥ 8	Total testosterone > 72.1 ng/dL Androgen index ≥ 0.6	Radioimmunoassay employing double antibody technique	6 MHz

FG, Ferriman-Gallwey; PCOS, polycystic ovary syndrome.

^a Serum androgens were not routinely measure.

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(BMI) and low serum high-density lipoprotein cholesterol (HDL-C) levels as the predominant components. The prevalence of MetSyn in South Asian PCOS populations was reported to be 37.5%, with central obesity as one of the significant predictors of MetSyn.¹² Although studies from different parts of the world describe a higher prevalence of MetSyn in PCOS compared to geographically matched controls,⁵ few studies have directly compared the prevalence of MetSyn and its components in different races. One study reported that White women had higher blood pressure (BP) and worse lipid profiles compared to Middle Eastern women residing in Denmark.¹⁵ In 1 US-based PCOS cohort of 11,035 subjects, Blacks and Hispanics were more likely to be obese; Asians and Hispanics were more likely to have diabetes; and Blacks were more likely to be hypertensive.¹⁸ Although these Danish and US cohorts indicate ethnic differences in metabolic risk factors associated with PCOS, neither of these studies comprehensively examined prevalence of MetSyn as an outcome.

The Amsterdam European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine—sponsored Consensus Workshop Group concluded that “ethnic origin and culture contribute to the differing manifestations of PCOS”¹⁹ and must be considered when treating patients, especially when applying thresholds for metabolic screening. However, despite these recommendations, there are few population-based studies of PCOS including several races/ethnicities to increase our understanding of the possible role that racial and environmental factors might play in the expression of MetSyn in this high-risk group. International medical societies recommend screening all women with PCOS for cardiometabolic risk.⁶ However, in a recent survey of US gynecologists the majority reported that they do not screen women with PCOS for lipid and glucose abnormalities.²⁰ Given this, our primary aim was to compare the prevalence of MetSyn and to examine the clustering of its components in women with PCOS from the United States,

India, Brazil, Finland, and Norway. Although all these women shared the diagnosis of PCOS, we hypothesized that racial differences in the prevalence of MetSyn and clustering of associated symptoms exist, suggesting both racial and environmental modifiers of the phenotype across groups.

Materials and Methods

A cross-sectional study was performed using deidentified data from women between the ages of 20–50 years diagnosed with PCOS from 5 urban centers in the United States, India, Brazil, Norway, and Finland. Subjects were identified in databases maintained at each site as shown in Table 1. The institutional review boards at each study site approved this study. Women were included if they had PCOS as defined by presence of at least 2 of the 3 Rotterdam criteria³; they were required to have data on oligomenorrhea/amenorrhea and clinical or biochemical hyperandrogenism and have complete MetSyn data. PCOS diagnosis information, laboratory tests, and physical examination measurements were obtained from each

subject's initial visit. All data were reassessed retrospectively by lead author (J.L.C.) to confirm that each subject met the Rotterdam criteria and only subjects that met these criteria on reevaluation were included in this analysis. Oligomenorrhea was defined as an intermenstrual interval of >35 days and <8 menstrual bleeds in a year. Amenorrhea was defined as absent menstrual bleeding in the past 90 days. Clinical and biochemical hyperandrogenism criteria used for diagnosis at each study site is shown in Table 1. Descriptions of the assays used for testosterone measurements are also listed in Table 1. Each site had established upper limits for total testosterone that was used to define biochemical hyperandrogenism cut-offs for inclusion. In the data set from India, clinical hyperandrogenism was primarily used to establish diagnosis due to cost issues related to measuring androgen levels. Race and ethnicity were self-reported and collected at the time of recruitment. Subjects were excluded if they had elevated thyroid-stimulating hormone or prolactin levels, or if they had congenital adrenal hyperplasia, Cushing syndrome, androgen-secreting tumors, or other related disorders as per the Rotterdam definition. Women who were pregnant or breast-feeding were also excluded. All study sites were asked to provide information on medical and gynecologic histories, physical examinations, and transvaginal ultrasound data. Additional outcomes recorded included: age, BP, height, weight, fasting total cholesterol, fasting triglycerides (TG), fasting HDL-C, and fasting glucose. Blood samples in all cases were obtained after an overnight fast. Clinical hyperandrogenism was defined as a Ferriman-Gallwey (FG) score ≥ 8 . Polycystic-appearing ovaries were defined as the presence of at least 1 ovary with ≥ 12 follicles measuring 2–9 mm in diameter and/or ovarian volume >10 mm³. Resolutions of the transvaginal ultrasound probes used to evaluate ovaries at each study site are detailed in Table 1.

MetSyn was defined by the American Heart Association (AHA)/National Heart, Lung, and Blood Institute (NHLBI) consensus criteria²¹ as defined by ≥ 3 of the following criteria: obesity,

elevated TG (≥ 150 mg/dL), low HDL-C (≤ 50 mg/dL), elevated BP ($\geq 130/\geq 85$ mm Hg) or taking antihypertensive medications, elevated fasting glucose (≥ 100 mg/dL), and carried a diagnosis of preexisting diabetes or were taking medications for diabetes. Obesity was based on ethnic variations and defined as an elevated BMI of ≥ 30 kg/m² in non-Indian populations and ≥ 25 kg/m² in the Indian population, as the risk of type 2 diabetes and cardiovascular disease is increased at lower BMI targets in Asian Indians than in Whites.²²

Statistical analysis

Data from all sites were examined for completion of diagnostic criteria for PCOS and only those subjects with complete metabolic workups were included in this study. Demographic characteristics were compared among groups using analysis of variance for parametric continuous variables and Kruskal-Wallis tests for nonparametric variables. Pairwise comparisons with the US White group used as the referent group were performed using Student *t* tests or Wilcoxon rank sum tests as appropriate for continuous variables. The χ^2 tests were used to compare proportions. A subanalysis was performed including women who met the hyperandrogenic phenotype. Logistic regression models were used to evaluate associations between race and MetSyn prevalence and its components and to adjust for potential confounders such as age. In a secondary analysis we adjusted for BMI to determine if the prevalence of MetSyn was related to the high prevalence of obesity in the study population. All *P* values were 2-sided and a statistical significance level alpha of 0.05 was used. Analyses were performed using software (STATA, Version 13.0; StataCorp, College Station, TX).

Results

In total, 1089 women met our inclusion criteria including 184 non-Hispanic US White subjects, 100 non-Hispanic US Black subjects, 220 Indian subject, 233 Brazilian subjects, 94 Finnish subjects, and 258 Norwegian subjects. The demographic and clinical characteristics

of this study population are shown in Table 2. The median age of the cohort was 28 years (interquartile range, 24–33 years). Of the women, 54% met all 3 Rotterdam criteria and 73% met National Institutes of Health criteria for PCOS. Compared to the US White group, women from Finland and Norway had a lower prevalence of clinical and/or biochemical hyperandrogenism ($P < .001$). The mean FG score was highest in the Indian population (15.6, $P < .001$) and lowest in the Norwegian group (4.3, $P < .001$) compared to the US White women (11.1). All of the women in the Finnish group had documented polycystic-appearing ovaries on ultrasound (100%, $P < .001$).

The prevalence of MetSyn and its individual components were compared in the 6 groups. Table 2 demonstrates components of MetSyn and Table 3 demonstrates percentage prevalence of each component for the groups. Compared to the US White group, US Blacks had the highest prevalence of MetSyn (52.0% vs 28.3%, $P < .001$). The US Black women had the highest prevalence of abnormal BMI (74.0%, $P < .001$) and BP criterion (59.0%, $P < .001$), however, they had the lowest prevalence of TG criterion (10.0%, $P = .02$). Indian women had a higher unadjusted prevalence of MetSyn than US White women (38.2% vs 28.3%, $P = .036$) and had different components contributing to the elevated prevalence of MetSyn, namely higher prevalence of obesity (62.3% vs 47.3%, $P = .003$), elevated fasting glucose (28.6%, $P < .001$), and low HDL-C (97.3%, $P < .001$). While Finland and Norway are geographically adjacent, the prevalence of MetSyn differed such that Norwegians had a significantly higher prevalence (41.1%, $P < .01$) whereas women from Finland had a similar prevalence compared to US White women (27.7%). Between these 2 Scandinavian countries, there was differential clustering of MetSyn components. Norwegian prevalence of MetSyn was associated with elevated BP, elevated fasting glucose levels, and low HDL-C, whereas women in Finland had prevalence of MetSyn components similar to US White subjects.

PCOS is a heterogeneous condition and in some studies the prevalence of MetSyn

TABLE 2
Demographic characteristics of study population (n = 1089)

	US White, reference	US Black	India	Brazil	Finland	Norway
n	184	100	220	233	94	258
Median age, y (IQR)	29 (25–32)	29 (25.5–34)	25 (23–27) ^a	26 (23–30) ^b	33 (29–39) ^a	28.5 (25–32)
Presence of oligomenorrhea/amenorrhea	165 (89.7%)	84 (84%)	199 (90.5%)	205 (88%)	88 (93.6%)	232 (89.9%)
Presence of clinical or biochemical hyperandrogenism	162 (88.0%)	89 (89%)	201 (91.4%)	215 (92.3%)	60 (63.8%) ^a	180 (69.8%) ^a
Presence of polycystic-appearing ovaries on ultrasound	126 (68.5%)	76 (76%)	173 (78.6%) ^b	157 (67.4%) ^a	94 (100%) ^a	233 (90.3%) ^a
Total testosterone, mean (SD), ng/dL	53.2 (27.0)	63.4 (32.9)	— ^c	91.8 (41.4)	55.3 (30.3)	63.5 (31.7)
Ferriman-Gallwey score, mean (SD)	11.1 (7.4)	10.9 (7.0)	15.6 (6.3) ^a	12.2 (6.3)	7.8 (5.0) ^b	4.3 (4.2) ^a
Body mass index, mean (SD), kg/m ²	30.6 (8.1)	37.5 (9.4) ^a	26.7 (4.5) ^a	29.3 (6.9)	29.4 (7.1)	31.1 (7.0)
PCOS phenotype						
Frank PCOS ^d	85 (46.2%)	49 (49%)	133 (60.4%)	131 (56.2%)	54 (57.4%)	131 (50.8%)
Ovulatory PCOS ^e	19 (10.3%)	16 (16%)	21 (9.5%)	20 (8.6%)	6 (6.4%)	26 (10.1%)
NIH criteria ^f	58 (31.5%)	24 (24%)	47 (21.4%)	57 (24.5%)	0 (0%)	24 (9.3%)
Normoandrogenic PCOS ^g	22 (12.0%)	11 (11%)	19 (8.6%)	5 (2.1%)	34 (36.2%)	76 (29.5%)
TG, mean (SD), mg/dL	110.5 (63.5)	94.5 (63.6) ^b	131.0 (52.7) ^a	115.4 (68.8)	104.8 (55.0)	115.2 (72.3)
Systolic BP, mean (SD), mm Hg	123.4 (14.0)	130.1 (13.4) ^b	117.9 (10.7) ^a	119.8 (16.3) ^b	125.3 (13.8)	125.4 (15.4)
Diastolic BP, mean (SD), mm Hg	73.0 (9.0)	77.2 (9.1) ^b	71.4 (9.8)	75.3 (11.4) ^b	79.8 (9.4) ^a	82.8 (11.2) ^a
Fasting glucose, mean (SD), mg/dL	85.8 (18.2)	86.1 (14.3)	95.6 (19.3) ^a	90.4 (11.4) ^a	91.1 (13.9) ^a	93.4 (12.6) ^a
HDL-C, mean (SD), mg/dL	56.5 (19.2)	46.4 (11.7) ^a	39.4 (5.3) ^a	49.6 (15.8) ^a	53.2 (14.3)	48.6 (13.7) ^a

Data presented as n (%), unless otherwise specified.

BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; NIH, National Institutes of Health; PCOS, polycystic ovary syndrome; TG, triglycerides.

^a $P < .0001$ for pairwise comparison to US White group; ^b $P < .05$ for pairwise comparison to US White group; ^c Serum androgens were not routinely ordered in Indian population—clinical hyperandrogenism was used as criterion for this group; ^d Polycystic-appearing ovaries, hyperandrogenic, and oligoovulatory; ^e Hyperandrogenic, polycystic-appearing ovaries, regular cycles; ^f Oligoovulatory, hyperandrogenic, normal-appearing ovaries; ^g Oligoovulatory, polycystic-appearing ovaries, normoandrogenic.

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has been shown to be higher in the hyperandrogenic vs nonhyperandrogenic phenotypes.^{17,23} To determine if the prevalence of MetSyn is higher in women with the hyperandrogenic phenotype, we performed a subanalysis of these subjects (n = 793). The overall prevalence of MetSyn was similar in the hyperandrogenic group compared with the whole PCOS cohort (37.0% vs 32.4%, $P = .17$). When we examined each ethnic group, the hyperandrogenic phenotype in US Black (63 vs 52%, $P < .001$) and Finnish (37.0 vs 27.7%, $P = .02$) populations had a higher prevalence compared with the entire PCOS cohort.

In an age-adjusted analyses of subjects who met hyperandrogenic phenotype for PCOS (Table 4), US Black women

(adjusted odds ratio [OR], 4.52; 95% confidence interval [CI], 2.46–8.35; $P < .001$), Indians (adjusted OR, 2.04; 95% CI, 1.24–3.34; $P = .005$), and Norwegians (adjusted OR, 1.98; 95% CI, 1.16–3.24; $P = .007$) had an elevated odds of MetSyn compared with US White women. As prevalence of MetSyn appeared to vary significantly by race, we performed a secondary analysis to determine if prevalence of MetSyn was driven primarily by obesity (given the high prevalence of obesity in this study). We also adjusted for age, a known risk factor for MetSyn. Controlling for age and BMI, the odds of MetSyn in the US Black compared to US White population was no longer significantly elevated (adjusted OR, 1.72; 95% CI, 0.79–3.73; $P = .17$), suggesting that the prevalence of

MetSyn in this group is driven by elevated BMI. There was an elevated odds of MetSyn in Norwegians (adjusted OR, 2.19; 95% CI 1.18–4.06; $P = .002$) and Indians as compared with the US White population (adjusted OR, 6.53; 95% CI, 3.47–12.30; $P < .001$) after adjusting for age and BMI, suggesting that other components contributed to the prevalence of MetSyn in these 2 populations.

Comment

This is the first study to directly compare the prevalence of MetSyn and its components in young women with PCOS across 6 ethnic groups, spanning 4 continents. Our findings suggest that there is significant difference in the prevalence of MetSyn and clustering of its components

TABLE 3
Prevalence of metabolic syndrome in study population

	US White, reference	US Black	India	Brazil	Finland	Norway
n	184	100	220	233	94	258
Metabolic syndrome ^a	52 (28.3%)	52 (52.0%) ^b	84 (38.2%)	69 (29.6%)	26 (27.7%)	106 (41.1%) ^c
BMI criterion	87 (47.3%)	74 (74.0%) ^b	137 (62.3%) ^c	98 (42.1%)	45 (47.9%)	140 (54.3%)
TG $\geq$ 150 mg/dL	38 (20.7%)	10 (10.0%) ^c	59 (26.8%)	62 (26.6%)	11 (11.7%)	57 (22.1%)
BP criterion ^d	67 (36.4%)	59 (59.0%) ^b	37 (16.8%) ^b	82 (35.2%)	34 (36.2%)	136 (52.7%) ^c
Fasting glucose $\geq$ 100 mg/dL ^e	22 (12.0%)	22 (22.0%) ^c	63 (28.6%) ^b	41 (17.6%)	16 (17.0%)	56 (21.7%) ^c
HDL-C $\leq$ 50 mg/dL	77 (41.9%)	72 (72.0%) ^b	214 (97.3%) ^b	138 (59.2%) ^b	41 (43.6%)	154 (59.7%) ^b

Data presented as n (%), unless otherwise specified.

BMI, body mass index; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides.

^a Defined as having $\geq$ 3 of 5 criteria listed in table; ^b $P < .001$ for pairwise comparison to US White group; ^c $P < .05$ for pairwise comparison to US White group; ^d Includes women with preexisting diagnosis of hypertension or taking antihypertensives; ^e Includes women with preexisting diagnosis of diabetes or taking diabetes medications.

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in different regions of the world, despite a unifying diagnosis of PCOS. Specifically, it appears that US Black women have a higher prevalence of MetSyn related to obesity, while Norwegians and Indians have elevated odds of MetSyn independent of obesity when compared to the US White population. Our findings highlight the need for complete metabolic screening in reproductive-age women with PCOS to identify specific targets for intervention.

The largest meta-analysis of women with PCOS showed an elevated prevalence of MetSyn (OR, 2.88; 95% CI, 2.40–3.45, and BMI-matched studies OR, 2.20; 95% CI 1.36–3.56).⁵ This review included data from 10 countries, but did not include any studies from India, Brazil, or Scandinavia; did not perform a direct comparison between groups; and did not examine clustering of components of MetSyn. In our study, US Black women had the highest prevalence of MetSyn among all groups and a 4 times higher odds than US White women, driven mainly by elevated BMI. Previously, a cohort study of US women demonstrated a higher prevalence of MetSyn in non-Hispanic Black women (40%) as compared with 244 non-Hispanic White women (22.6%) with an elevated relative risk of 1.44 (95% CI 1.2–2.6).²⁴ All components of MetSyn were significantly different between

Black and White women residing in the United States, with all components significantly elevated except for TG levels that were significantly lower. These findings were similar to the study by Lo et al,¹⁸ as discussed in the “Introduction.” Collectively, given the constellation of obesity, hypertension, low HDL-C, and elevated fasting glucose, the US Black population with PCOS is at higher risk for 10-year general cardiovascular disease as compared to Whites.²⁴ As expected, the highest percentages of women with elevated BP were also the women who were obese. A principal component analysis carried out in 255 nondiabetic hyperandrogenic women demonstrated a clustering of BMI, hypertension, and hyperandrogenism in MetSyn, revealing an indirect link between BP and insulin resistance/MetSyn through BMI.²⁵

In our study comparing Whites residing in other world regions, we found the prevalence of MetSyn was increased in Norwegians with a prevalence of 41.4% and age-adjusted OR of 2.02 (95% CI, 1.26–3.24) compared to US White women. The Norwegian Nor-Trøndelag Health Study (HUNT 2) reported that the prevalence of MetSyn using Adult Treatment Panel III criteria among healthy women ages 20–49 years was 6–17%.²⁶ Although there is no published study comparing the prevalence of MetSyn in

women with PCOS from Norway and geographically matched controls, our data suggest a higher prevalence compared to the HUNT 2 study. While HUNT 2 participants were recruited via a health study from the general population, participants included in our study were recruited from gynecologic and infertility outpatient clinics, and could have contributed to the higher prevalence of MetSyn. When examining the components of MetSyn, Norwegian women had higher BP, higher fasting glucose levels, and lower HDL-C compared to the US White population. In the HUNT 2 study, female subjects with elevated BP ranged from 21.8% in the age group 20–29 years to 74.7% in the age group 40–49 years, indicating a high prevalence of hypertension in this population. The prevalence of elevated glucose and low HDL-C was higher in the PCOS Norwegian cohort in our study when compared to the similar age group in the HUNT study. The odds of MetSyn remained elevated in our Norwegian cohort even after adjusting for BMI, indicating that the prevalence may be increased by other factors discussed above. Overall, the clustering of MetSyn components in Norwegians was similar to the US Black cohort, except for the low TG levels observed in the latter group.

The prevalence of MetSyn in Brazilian women was similar to the US White women. A cross-sectional study of 102

TABLE 4

Odds ratios of metabolic syndrome by race in women with polycystic ovary syndrome compared with US White women

	Unadjusted OR (95% CI) ^a	Pvalue	Age-adjusted OR (95% CI)	Pvalue
US Black	4.54 (2.49–8.29)	<.001	4.52 (2.46–8.35)	<.001
India	1.58 (0.98–2.55)	.059	2.04 (1.24–3.34)	.005
Brazil	1.16 (0.72–1.88)	.55	1.31 (0.80–2.13)	.29
Finland	1.57 (0.81–3.05)	.18	1.25 (0.63–2.48)	.52
Norway	1.88 (1.15–3.05)	.01	1.98 (1.21–3.24)	.007
	BMI-adjusted OR (95% CI)	Pvalue	BMI and age-adjusted OR (95% CI)	Pvalue
US Black	1.70 (0.79–3.69)	.18	1.72 (0.79–3.73)	.17
India	5.34 (2.91–9.80)	<.001	6.53 (3.47–12.30)	<.001
Brazil	1.49 (0.82–2.72)	.19	1.66 (0.90–3.06)	.10
Finland	1.87 (0.83–4.22)	.13	1.57 (0.68–3.98)	.29
Norway	2.03 (1.11–3.71)	.02	2.16 (1.17–3.98)	.01

BMI, body mass index; CI, confidence interval; OR, odds ratio.

^a US White women as referent group.Chan et al. Racial differences in MetSyn in PCOS. *Am J Obstet Gynecol* 2017.

Brazilian PCOS patients reported a MetSyn prevalence of 28.4%,²⁷ similar to the prevalence in our study (29.6%). In the general urban Brazilian population the prevalence of MetSyn was 11.1% in women ≤ 36 years of age and 17.5% in women age 37–45 years²⁸ suggesting an increased risk in women with PCOS. A predominance of low HDL-C has also been described in the general Brazilian population.²⁷

In our study the prevalence of MetSyn was >6 -fold higher in the Indian cohort as compared with the US White population, after controlling for both BMI and age. This finding appeared to be driven by the elevated fasting glucose component. While South Asia has one of the highest prevalences of MetSyn, background rates vary according to degree of urbanization, region, and socioeconomic factors.²⁹ Increased rates of MetSyn in Indian women with PCOS compared to controls have been reported both in adolescents³⁰ and adults.³¹ Our Indian cohort had the highest fasting glucose levels, compared to other groups. A significantly increased prevalence of elevated fasting glucose, impaired glucose tolerance, MetSyn, and type 2 diabetes have been described in the South Asian general populations when compared with Whites.³² In one population-based cross-sectional study

the prevalence of MetSyn was 3-fold in South Asian compared with European women (30.8% vs 9.1%, $P < .0001$), with increased rates of impaired glucose tolerance (44.2% vs 21.3%, $P < .0001$), high BP (32.4% vs 20.7%, $P = .0002$), dyslipidemia (37.8% vs 20.7%, $P = .0003$), and central obesity (65.8% vs 30.1%, $P < .0001$)³³ indicating racial differences in metabolic risk. An age- and ethnicity-matched case-control study of women with PCOS residing in the United Kingdom found that compared to White women, South Asian women had similar fasting glucose concentrations, but had lower insulin sensitivities.¹¹ Comparisons between ethnically different populations residing in the same country reveal differences in genetic predispositions, whereas comparisons between racially similar groups residing in different countries may also reveal differences in environmental influences.

The prevalence of MetSyn in the Finnish cohort was similar to the US White population. A large proportion of Finnish subjects in our cohort did not meet the criteria for hyperandrogenism. When they were excluded from the analysis the prevalence of MetSyn increased to 37% supporting the data that the hyperandrogenic phenotype is associated with a higher prevalence of MetSyn.^{17,23}

However, the smaller sample size may have precluded us from finding a significant difference compared to the US White population. As expected, this prevalence was higher than the reported prevalence of 8–13% in young Finn females (mean age 24 years) and older adult women (ages 45–64 years) of 22%.³⁴ There was no difference in the clustering of MetSyn components between the Finnish cohort and the US Whites.

The main strength of our study was the review of all data by 1 author and application of the same diagnostic criteria for PCOS and MetSyn to all subjects included. In general, prevalence estimates of MetSyn for different racial and ethnic groups are difficult to compare in women with PCOS due to differences in diagnostic criteria (both for MetSyn and PCOS) and recruitment methods of subjects (clinic vs community based). We were able to obtain details of medical history and include women who were being treated or had a diagnosis of hypertension or diabetes (as per AHA/NHLBI criteria). Few studies have compared prevalence rates between >2 races or ethnicities. Guo et al³⁵ described differences in phenotypic characteristics of 547 Chinese women from the city of Jinan and 427 Dutch women from The Netherlands with

PCOS. Dutch women had significantly elevated BMI, waist circumference, and fasting glucose ($P < .001$), and lower HDL-C ($P < .001$) compared with Chinese women. The authors did not compare the prevalence of MetSyn and obesity could have contributed to the findings in the Dutch population. To accurately determine the impact of the hyperandrogenic phenotype on the prevalence of MetSyn, we only included women with PCOS recruited from clinical sites, and a single reviewer reconfirmed their diagnosis. On excluding the nonhyperandrogenic phenotype of menstrual irregularities and PCO morphology, we found an increase in prevalence of MetSyn in the Finnish and US Black women.

We recognize some limitations in our study. Recruitment of PCOS subjects was performed at 5 different sites, which may lead to selection bias and limit generalizability of our findings. As recruitment was performed from gynecology clinics, our results may not be generalizable on a wider population basis. Although we cannot control for specific referral biases at each site, our results are applicable to women seeking care for PCOS. We selected women from countries where there was limited published information on prevalence of MetSyn. As noted above, other studies have compared White populations with Chinese and Middle Eastern women.^{15,34} To standardize inclusion in our study, all centers were located in urban regions and data from each center were reassessed by a single reviewer to confirm that each subject met the Rotterdam criteria. While the variability in androgen assays and their limitations in measuring low levels of androgens as seen in females is well recognized, we did not reanalyze serum samples from all sites for androgens, but used cut-offs for each cohort depending on the assay used at their site and analyzed the data using either clinical or biochemical criteria as per the Rotterdam criteria. The Indian cohort only used the FG score. While it is possible to satisfy the hyperandrogenism criterion with either abnormal clinical or biochemical parameters, inclusion of subjects who meet only the clinical

criterion adds to the heterogeneity of the subjects included. This is a recognized limitation of the Rotterdam criteria, giving rise of different phenotypes. A cut-off FG score of ≥ 8 was used as criterion for clinical hyperandrogenism.³⁶ However, the Rotterdam criteria recognize that there is ethnic variation in hirsutism. Although the cut-off of 8 is appropriate for Whites and Blacks,³⁷ there is no validated population-based cut-off for FG score for Indians or South Americans based on 95th percentile values of unselected women of reproductive age.

Although there are other criteria for the diagnosis of MetSyn (including those provided by the World Health Organization and International Diabetes Federation [IDF]) we applied the AHA/NHLBI criteria as they are widely accepted in the United States, take into account ethnicity differences in central obesity, and correlate with increased risk of diabetes mellitus and cardiovascular disease. Although the AHA/NHLBI uses waist circumference to define abdominal obesity, we used BMI as a surrogate for waist circumference in our definition of MetSyn. Several studies demonstrated high correlation between waist circumference and BMI in patients with MetSyn³⁸ and BMI is a common measure of obesity. In the Atherosclerosis Risk in Communities Study, BMI was very highly correlated with waist circumference ($r = 0.88$) and anthropometric correlations with BMI employing dual-energy x-ray absorptiometry scanning also demonstrated a high degree of correlation with waist circumference ($r = 0.85$).³⁹ Both waist circumference and BMI have similar associations with incident diabetes.⁴⁰ Additionally, the worldwide IDF definition recommends that if BMI is >30 kg/m², central obesity can be assumed and waist circumference need not be measured.⁴¹ The Consensus Statement for Diagnosis of Obesity, Abdominal Obesity, and Metabolic Syndrome for Asian Indians and Recommendations for Physical Activity, Medical and Surgical Management states that BMI is the “most researched measure of generalized obesity and should be continued to be used using Asian Indian-specific cut-offs.”²²

Comment

In summary, after applying uniform diagnostic criteria for both PCOS and MetSyn in women with different racial and ethnic backgrounds, we report significant differences in the prevalence of MetSyn and clustering of its components, possibly reflecting contributions from both racial and environmental factors. Our data confirm presence of racial and ethnic differences in the clinical and cardiometabolic manifestations of PCOS and underscore the need to routinely screen for MetSyn. ■

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Received Dec. 16, 2016; revised March 16, 2017; accepted April 3, 2017.

This research was supported by the National Institutes of Health Reproductive Epidemiology Training Grant (T32 HD007440), Sigrid Juselius Foundation, and the Academy of Finland.

The authors report no conflict of interest.

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