Cutaneous Findings and Systemic Associations in Women With Polycystic Ovary Syndrome

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IMPORTANCE Understanding of the associations among cutaneous findings, systemic abnormalities, and fulfillment of the diagnostic criteria in women suspected of having polycystic ovary syndrome (PCOS) is incomplete.

OBJECTIVE To identify cutaneous and systemic features of PCOS that help distinguish women who do and do not meet the diagnostic criteria.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cross-sectional study of a racially diverse referred sample of women seen at the University of California, San Francisco, Polycystic Ovary Syndrome Multidisciplinary Clinic over a 6-year period between May 18, 2006, and October 25, 2012. Participants were 401 women referred for suspected PCOS. In total, 68.8% (276 of 401) met the Rotterdam PCOS diagnostic criteria, while 12.0% (48 of 401) did not. Overall, 11.5% (46 of 401) had insufficient data to render a diagnosis, 1.7% (7 of 401) were excluded from the study, and 6.0% (24 of 401) refused to participate in the study.

EXPOSURE Comprehensive skin examination and transvaginal ultrasonography. All patients were tested for levels of total testosterone, free testosterone, dehydroepiandrosterone (DHEAS), androstenedione, luteinizing hormone, and follicle-stimulating hormone. Levels of serum cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides were obtained, in addition to 0-hour and 2-hour oral glucose tolerance test (OGTT) results, with measurement of glucose and insulin levels.

MAIN OUTCOMES AND MEASURES Findings from comprehensive skin examination, laboratory testing, and transvaginal ultrasonography.

RESULTS In total, 401 women with suspected PCOS were included in the study. The median patient age was 28 years. Compared with women who did not meet the diagnostic criteria for PCOS, women who met the criteria had higher rates of hirsutism (53.3% [144 of 270] vs 31.2% [15 of 48], P = .005) (with higher mean modified Ferriman-Gallwey scores of 8.6 vs 5.6, P = .001); acne (61.2% [164 of 268] vs 40.4% [19 of 47], P = .004), and acanthosis nigricans (AN) (36.9% [89 of 241] vs 20.0% [9 of 45], P = .03). Cutaneous distributions also varied. Women who met the PCOS criteria demonstrated more severe truncal hirsutism and higher rates of axillary AN. Women who met the PCOS criteria had elevated total testosterone levels (40.7% [105 of 258] vs 4.3% [2 of 47], P < .001). Among women with PCOS, the presence of hirsutism (43.9% [54 of 123] vs 30.9% [34 of 110], P = .04) or AN (53.3% [40 of 75] vs 27.0% [40 of 148], P < .001) was associated with higher rates of elevated free testosterone levels as well as several metabolic abnormalities, including insulin resistance, dyslipidemia, and increased body mass index. Although the prevalence of acne was increased among women with PCOS, there were minimal differences in acne types and distribution between the women meeting vs not meeting the PCOS criteria.

CONCLUSIONS AND RELEVANCE Hirsutism and AN are the most reliable cutaneous markers of PCOS and require a comprehensive skin examination to diagnose. When present, hirsutism and AN should raise clinical concern that warrants further diagnostic evaluation for metabolic comorbidities that may lead to long-term complications. Acne and androgenic alopecia are prevalent but unreliable markers of biochemical hyperandrogenism among this population.

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Polycystic ovary syndrome (PCOS) affects 2% to 7% of women in the general population.² The diagnostic criteria for PCOS continue to evolve, but the 2003 Rotterdam consensus criteria remain widely used.² In addition to the exclusion of other disorders, these criteria require at least 2 of the following findings for diagnosis: oligoanovulation, polycystic ovaries on transvaginal ultrasonography, and clinical signs or biochemical evidence of hyperandrogenism (HA). The pathogenesis underlying these clinical features is poorly understood. Gonadotropic dysregulation, genetics, and environmental factors have been implicated.³

It is estimated that 72% to 82% of women with PCOS are seen with cutaneous signs classically associated with HA such as acne, hirsutism, and androgenic alopecia (AGA).¹,⁴,⁵ Hyperandrogenism may also manifest as acanthosis nigricans (AN) or seborrheic dermatitis.⁶,⁷ Patients with PCOS are frequently first seen by a dermatologist.⁸

Polycystic ovary syndrome is associated with cardiovascular risk factors as well as long-term complications, including obesity, infertility, malignancy, and insulin resistance.²,⁹-¹³ Other associations include obstructive sleep apnea, nonalcoholic steatohepatitis, and psychiatric illnesses, such as depression, anxiety, and eating disorders.¹³ However, understanding regarding the cutaneous features seen in PCOS and their associations with clinically measurable endocrine and metabolic abnormalities requires further development.³,⁴,¹⁴-¹⁷ Incomplete cutaneous examinations, few patients, racially homogeneous cross-sections, and an absence of comparison groups have limited the generalizability of these findings.

In addition, it is difficult for physicians to identify women with PCOS among those with similar features, such as acne, AGA, or hirsutism. This study aimed to identify the cutaneous, reproductive, and metabolic characteristics that distinguished patients meeting the diagnostic criteria for PCOS vs those not meeting the criteria among a high-risk population of women referred to a multidisciplinary PCOS clinic. To achieve this aim, this study systematically characterized the cutaneous, reproductive, and metabolic characteristics in a large, racially diverse cross-section of patients referred for suspected PCOS.

Methods

Study Design

This UCSF Committee for Human Research–approved, retrospective study consecutively recruited women suspected of having PCOS who were referred to the University of California, San Francisco, Polycystic Ovary Syndrome Multidisciplinary Clinic between May 18, 2006, and October 25, 2012. Any patient able to provide written informed consent who had discontinued hormonal contraception for at least 4 weeks was eligible for study inclusion. The Rotterdam consensus criteria were used to render diagnoses of PCOS.¹ In defining the Rotterdam criteria for the purposes of this study, clinical HA was defined as the presence of the cutaneous features of HA, and biochemical HA was defined as the presence of at least 1 serum androgen. Oligoanovulation was defined as fewer than 8 menstrual cycles per year. Referred women who did not meet the criteria for PCOS were assessed as well and served as a comparison group. Women having another endocrinopathy or taking combined oral contraceptives at the time of testing or evaluation were excluded from the study. Women with prior or current treatments for acne (topical or systemic medications, including isotretinoin), hirsutism (laser, electrolysis, or efomithine hydrochloride), or AGA (topical minoxidil) were included in the study. Scoring of their cutaneous findings was not adjusted for their treatment histories. Patients were instructed not to perform any type of hair removal for 1 week before clinical evaluation.

A reproductive endocrinologist (M.I.C. or H.H.) and dermatologist (L.T.Z. or K.S.) evaluated patients on the same day. Demographic information and detailed medical histories were obtained. Transvaginal ultrasonography was performed in all patients for assessment of antral follicle count and ovarian volume. A comprehensive dermatologic examination was performed on each patient, including evaluation for acne, hirsutism, AN, AGA, and seborrheic dermatitis. Acne lesions were counted and recorded as comedones, papulopustules, nodules, and postinflammatory erythematous macules or postinflammatory pigment alterations in each segment of the face (forehead, left cheek, right cheek, perioral or jawline region, and submental area). The Leeds technique²⁸ was used to grade acne burden on the back and chest. Hirsutism was evaluated by the modified Ferriman-Gallwey (MFG) score.¹⁹,²¹ A total MFG score of at least 8 was denoted as hirsutism. The axillae, central chest, inframammary region, inguinal creases, knuckles, and neck were examined for AN. Androgenic alopecia was graded by the degree and distribution of hair loss based on the scales by Ludwig²² and Olsen.²³

All patients were tested for levels of total testosterone, free testosterone, dehydroepiandrosterone (DHEAS), androstenedione, luteinizing hormone, and follicle-stimulating hormone. Rarely, Cushing syndrome needed to be ruled out with cortisol testing based on the clinical presentation. However, because of the challenging logistics of testing for Cushing syndrome, only women with suspicious presentations were tested. Levels of thyroid-stimulating hormone, prolactin, and 17-hydroxyprogesterone were evaluated to rule out alternative endocrine disorders. Laboratory values were obtained at the study clinic or from referring health care professionals. Normative values from each test’s laboratory were used to determine whether levels were normal or abnormal. Levels of serum cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides were obtained, in addition to 0-hour and 2-hour oral glucose tolerance test (OGTT) results, with measurement of glucose and insulin levels. The homeostatic model of insulin resistance (HOMA-IR)²⁴ was used to calculate insulin resistance for each participant with the following equation: (Glucose Level × Insulin Level) / 405, where the glucose level is expressed in milligrams per deciliter, and the insulin level is expressed in milliunits per liter.

Data Reporting and Statistical Analysis

Levels of DHEAS, total testosterone, and free testosterone, in addition to 2-hour OGTT results and findings of polycystic ovaries by ultrasonography, acne, AGA, and AN, were dichotomously reported as normal or abnormal or as present or absent. The mean values were used to compare levels of serum cholesterol, HDL-C,
Cutaneous Findings Associated With Polycystic Ovary Syndrome

Results

Demographics
In total, 401 women suspected of having PCOS were referred to our clinic during a 6-year period (May 18, 2006, to October 25, 2012). The median patient age was 28 years. Overall, 68.8% (276 of 401) met the Rotterdam PCOS diagnostic criteria, while 12.0% (48 of 401) did not. A total of 11.5% (46 of 401) had insufficient data to render a diagnosis, 1.7% (7 of 401) were excluded from the study, and 6.0% (24 of 401) refused to participate in the study. Women with missing information about menstrual patterns (n = 9), biochemical and clinical HA (n = 1), transvaginal ultrasonography (n = 24), or other dermatologic and biochemical evaluations were included in the study if they were able to meet the PCOS criteria but were excluded from the relevant subanalyses. Women meeting the criteria for PCOS had a younger mean age than women not meeting the criteria (28.1 vs 33.0 years, P = .002). There were no significant differences with respect to race, marital status, parity, level of education, household income, and the use of alcohol or tobacco between women who met the PCOS criteria and those who did not.

Overall Burden of Cutaneous Findings
Most women (91.7% [253 of 276]) meeting the criteria for PCOS had at least 1 skin finding. Those who met the criteria were found to have a higher burden of acne, hirsutism, and AN than women who did not meet the criteria (Table 1). On average, patients meeting the criteria for PCOS had more cutaneous findings (mean [SD], 1.97 [1.18] vs 1.25 [1.14], P < .001). Among women meeting the PCOS criteria, hirsutism was significantly associated with the presence of AN (P < .001), with one-quarter (25.0% [67 of 268]) of patients with either cutaneous manifestation having both.

Acne
Women who met the criteria for PCOS were more likely to have acne than women who did not meet the criteria (61.2% [164 of 268] vs 40.4% [19 of 47], P = .004) (Table 1). The mean Leeds scores for the back and chest were not significantly different. Analysis by acne lesion counts and types revealed minimal differences between the 2 groups. Women meeting the PCOS criteria had slightly increased mean numbers of comedones on the forehead (3.15 vs 3.84, P = .006) and the perioral or jawline regions (2.92 vs 2.62, P = .04). Comparison of regional burdens of other acne lesion types did not reveal significant differences. Among women meeting the criteria for PCOS, acne when present was associated with younger age (27.3 vs 29.2 years, P = .03) and with a slightly lower prevalence of biochemical androgen elevation (57.6% [87 of 151] vs 70.3% [64 of 91], P = .05) (Table 2).

Hirsutism
Women who met the criteria for PCOS were more likely to have hirsutism than women who did not meet the criteria (53.3% [144 of 270] vs 31.2% [15 of 48], P = .005) (Table 1). Women meeting the criteria had a higher mean total MFG score (8.6 vs 5.6, P = .001) (Table 3). Increased hair was noted on the chin, with a site-specific MFG score (range, 0–4) of 1.3 for women who met the PCOS criteria vs 0.9 for women who did not meet the criteria (P < .05). Most important, higher mean truncal MFG scores were noted in women with PCOS, including the chest (0.4 vs 0.1, P < .01), upper abdomen (0.7 vs 0.3, P < .01), lower abdomen (1.7 vs 1.0, P < .001), upper back (0.5 vs 0.2, P < .01), and lower back (0.9 vs 0.6, P < .01). No significant differences were noted for the upper lip, upper arms, and thighs. In patients meeting the criteria for PCOS, hirsutism when present was associated with a higher prevalence of elevated free testosterone (43.9% [54 of 123] vs 30.9% [34 of 110], P = .04) but not other androgen measurements. The presence of hirsutism was also associated with a higher mean HOMA-IR (4.18 vs 3.38, P = .002), body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) (32.3 vs 28.0, P < .001), and triglycerides level (114 vs 104 mg/dL, P = .04), as well as a lower HDL-C level (52 vs 59 mg/dL, P < .001) (Table 2).

Acanthosis Nigricans
Women who met the criteria for PCOS were more likely to have AN than women who did not meet the criteria (36.9% [89 of 241] vs 20.0% [9 of 45], P = .03) (Table 1), particularly in the axillae (32.4% [78 of 241] vs 13.3% [6 of 45], P < .01) (Table 4). Among women with PCOS, AN when present was associated with an increased prevalence of free testosterone elevation (53.3% [40 of 75] vs 27.0% [40 of 148], P < .001) but not other androgen measurements and with abnormal 2-hour OGTT results (31.7% [20 of 63] vs 9.1% [12 of 132], P < .001) (Table 2). Acanthosis nigricans in PCOS was also associated with an increased mean HOMA-IR (7.13 vs 2.05, P < .001) and BMI (36.4 vs 27.6, P < .001) and with higher levels of total cholesterol (197 vs 182 mg/dL, P = .02), LDL-C (115 vs 105 mg/dL, P = .02), and triglycerides (147 vs 91 mg/dL, P < .001), as well as a lower mean HDL-C level (49 vs 58, P < .001) (Table 2). Among women without PCOS, AN was associated with an increased BMI (29.0 vs 34.3, P = .04) and a higher prevalence of abnormal 2-hour OGTT results (8.3% [2 of 24] vs 50.0% [3 of 6], P = .02).

<table>
<thead>
<tr>
<th>Cutaneous Finding</th>
<th>Did Not Meet the Criteria No./Total No. (%)</th>
<th>Met the PCOS Criteria No./Total No. (%)</th>
<th>P Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne</td>
<td>19/47 (40.4)</td>
<td>164/268 (61.2)</td>
<td>.004</td>
</tr>
<tr>
<td>Hirsutism</td>
<td>15/48 (31.2)</td>
<td>144/270 (53.3)</td>
<td>.005</td>
</tr>
<tr>
<td>Acanthosis nigricans</td>
<td>9/45 (20.0)</td>
<td>89/241 (36.9)</td>
<td>.03</td>
</tr>
<tr>
<td>Androgenic alopecia</td>
<td>5/44 (11.4)</td>
<td>53/237 (22.4)</td>
<td>.10</td>
</tr>
<tr>
<td>Seborrheic dermatitis</td>
<td>8/45 (17.8)</td>
<td>73/240 (30.4)</td>
<td>.08</td>
</tr>
</tbody>
</table>

Abbreviation: PCOS, polycystic ovary syndrome. *χ² Test.
Table 2: Reproductive and Metabolic Characteristics of Women Clinically Suspected of Having PCOS Who Did or Did Not Meet the PCOS Criteria

<table>
<thead>
<tr>
<th>Met the PCOS Criteria</th>
<th>Did Not Meet the Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive Findings, No./Total No. (%)</td>
<td>Reproductive Findings, No./Total No. (%)</td>
</tr>
<tr>
<td>Age (mean, SD), y</td>
<td>29.7 (6.6)</td>
</tr>
<tr>
<td>Androgenic alopecia present</td>
<td>28.1 (6.5)</td>
</tr>
<tr>
<td>Acne present</td>
<td>28.1 (6.5)</td>
</tr>
<tr>
<td>Hirsutism present</td>
<td>28.1 (6.5)</td>
</tr>
<tr>
<td>PCOS criteria</td>
<td>28.1 (6.5)</td>
</tr>
<tr>
<td>Metabolic Findings</td>
<td>Metabolic Findings</td>
</tr>
<tr>
<td>BMI, mean (SD), kg/m²</td>
<td>27.3 (5.7)</td>
</tr>
<tr>
<td>Elevated total testosterone level</td>
<td>27.1 (5.5)</td>
</tr>
<tr>
<td>Elevated DHEAS level</td>
<td>27.1 (5.5)</td>
</tr>
<tr>
<td>Oligoanovulation</td>
<td>27.1 (5.5)</td>
</tr>
<tr>
<td>Polycystic ovaries</td>
<td>27.1 (5.5)</td>
</tr>
<tr>
<td>Reproductive Findings, No./Total No. (%)</td>
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</tr>
<tr>
<td>Age (mean, SD), y</td>
<td>29.7 (6.6)</td>
</tr>
<tr>
<td>Androgenic alopecia present</td>
<td>28.1 (6.5)</td>
</tr>
<tr>
<td>Acne present</td>
<td>28.1 (6.5)</td>
</tr>
<tr>
<td>Hirsutism present</td>
<td>28.1 (6.5)</td>
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<tr>
<td>PCOS criteria</td>
<td>28.1 (6.5)</td>
</tr>
<tr>
<td>Metabolic Findings</td>
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</tr>
<tr>
<td>BMI, mean (SD), kg/m²</td>
<td>27.3 (5.7)</td>
</tr>
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<td>Elevated DHEAS level</td>
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</tr>
<tr>
<td>Oligoanovulation</td>
<td>27.1 (5.5)</td>
</tr>
<tr>
<td>Polycystic ovaries</td>
<td>27.1 (5.5)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; DHEAS, dehydroepiandrosterone; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model of insulin resistance; LDL-C, low-density lipoprotein cholesterol; PCOS, polycystic ovary syndrome; OGTT, oral glucose tolerance test; SD, standard deviation.
Androgenic Alopecia
There was a suggestion of an increased prevalence of AGA among women who met the criteria for PCOS relative to those who did not, but this difference was not statistically significant (22.4% [53 of 237] vs 11.4% [5 of 44], P = .10) (Table 1). Of women with AGA meeting the PCOS criteria, 43.7% (31 of 71) demonstrated a diffuse pattern, with Ludwig grades of 1 (38.1% [16 of 42]), 2 (11.9% [5 of 42]), and 3 (7.1% [3 of 42]). Of women with AGA meeting the PCOS criteria, 56.3% (40 of 71) demonstrated frontal accentuation, with Olseng grades of 1 (81.1% [30 of 37]) and 2 (10.8% [4 of 37]). Among women meeting the criteria, AGA when present was inversely related to the prevalence of polycystic ovaries (86.4% [38 of 44] vs 92.4% [158 of 171], P = .05) (Table 2).

Reproductive and Metabolic Findings
Women meeting the PCOS criteria had a higher prevalence of at least 1 elevated biochemical androgen (total testosterone, free testosterone, or DHEAS) (62.5% [157 of 251] vs 20.9% [9 of 43], P < .001), oligoovulation (89.9% [240 of 267] vs 29.5% [13 of 44], P < .001), and polycystic ovaries (89.7% [226 of 252] vs 33.3% [12 of 36], P < .001), along with lower HDL-C levels (55.6 vs 61.9 mg/dL, P = .03) (Table 2). Among biochemical androgens, only the prevalence of elevated DHEAS level was similar between the 2 groups. There were also no significant differences in the HOMA-IR and the prevalence of abnormal 2-hour OGTT results, as well as levels of total cholesterol, LDL-C, and triglycerides. However, a suggestion toward greater insulin resistance among women meeting the PCOS criteria (mean HOMA-IR, 3.75 vs 1.94, P < .001) was notable. There was no difference in the rates of obesity (BMI, >30.0) between those who met the criteria for PCOS vs women who did not (44.5% [122 of 274] vs 43.8% [21 of 48], P > .99). The associations between cutaneous, reproductive, and metabolic findings are summarized in Table 2.

Discussion
This study demonstrates that cutaneous evidence of PCOS when present manifests across a clinical spectrum ranging from none to multiple findings, mirroring previously recognized clinical heterogeneity of PCOS subtypes defined by the Rotterdam criteria.2-25,26 Herein, 8.3% [23 of 276] of women meeting the PCOS criteria had none of the skin manifestations examined. Each finding has a characteristic distribution and is associated with systemic abnormalities, which are summarized in Table 5.

Table 5. Summary of Key Cutaneous Findings of PCOS Among a High-Risk Population

<table>
<thead>
<tr>
<th>Cutaneous Finding</th>
<th>Key Distribution</th>
<th>Systemic Association</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne</td>
<td>Face (forehead)</td>
<td>None</td>
<td>Increased prevalence among patients who meet PCOS diagnosis but no significant difference in distribution of lesions, not associated with biochemical hyperandrogenism, not a reliable marker of hyperandrogenism in PCOS</td>
</tr>
<tr>
<td>Hirsutism</td>
<td>Truncal is most specific (chest, abdomen, or back), less specific are chin and thigh, nonspecific are upper lip and upper arm</td>
<td>Elevated free testosterone level, increased insulin resistance, increased BMI, dyslipidemia (HDL-C, triglycerides)</td>
<td>Excellent marker for PCOS and warrants selective endocrine and metabolic diagnostic evaluation, requires a comprehensive skin examination</td>
</tr>
<tr>
<td>Acanthosis nigricans</td>
<td>Axillae</td>
<td>Elevated free testosterone level, increased insulin resistance, increased glucose intolerance, increased BMI, dyslipidemia (total cholesterol, LDL-C, HDL-C, or triglycerides)</td>
<td>Excellent marker for PCOS and warrants selective endocrine and metabolic diagnostic evaluation, requires a comprehensive skin examination</td>
</tr>
<tr>
<td>Androgenic alopecia</td>
<td>Scalp</td>
<td>Lower prevalence of polycystic ovaries, associated with clinical but not biochemical hyperandrogenism</td>
<td>Not a reliable marker for PCOS</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCOS, polycystic ovary syndrome.
As expected for the diagnostic criteria used, women who met the PCOS criteria had a higher prevalence of skin findings, elevated androgens, oligoovulation, and polycystic ovaries. Physical examination and studies that investigate these features help determine if a patient meets the Rotterdam criteria. Acne, hirsutism, and AN were the most common skin manifestations, while hirsutism and AN were the most sensitive and informative for PCOS diagnosis. In particular, findings of axillary AN and low HDL-C levels in combination may distinguish women most at risk for meeting the PCOS criteria among a suspected population and may help identify patients most in need of further diagnostic evaluation. Although not classically considered a sign of HA, AN was strongly associated with biochemical HA and a diagnosis of PCOS among the referral population (women suspected of having PCOS).

This study was intended to identify cutaneous and systemic features that distinguish women most at risk for having PCOS among a racially diverse, high-risk population. It has several important limitations. All women in this study were referred for clinically suspected PCOS, likely increasing the overall prevalence of cutaneous findings. In addition, the comparison group did not comprise a healthy control population but was composed of women with clinical suspicion of PCOS but ultimately found not to meet the diagnostic criteria. Therefore, this study was not designed to detect features that set women who meet the PCOS diagnostic criteria apart from healthy women. In addition, this study was likely underpowered to detect clinically relevant differences in insulin sensitivity between women meeting and those not meeting the criteria. Another limitation is that women continuing treatments for cutaneous manifestations of PCOS were not excluded. However, this study design may better mirror the common clinical scenario in which a dermatologist must, from a high-risk population, identify women who will likely meet the PCOS criteria. Finally, because some androgen measurements were derived from many different testing laboratories and because normal ranges vary between laboratories, only dichotomous (normal or abnormal) biochemical androgen results could be used, limiting the power of the study.

**Acne**
The prevalence of acne among women who did not meet the PCOS criteria in this study (40.4% [19 of 47]) was consistent with previously reported estimates of acne prevalence among adult women (6%-55%). In this study, women with PCOS had a prevalence of acne (61.2% [164 of 268]) in the range of previous reports (15%-95%). This result may reflect the study population’s broad racial distribution because race may affect acne prevalence.

Among women with PCOS, acne when present was not associated with metabolic dysregulation or increased serum androgens, corroborating the results of other studies and suggesting that the acne-androgen association is complex. Most important, acne does not uniformly indicate biochemical HA.

**Hirsutism**
Although hirsutism affects 5% to 15% of women in the general population, previous studies have reported a higher burden of hirsutism among women with PCOS, estimating its prevalence between 8.1% in one study and 77.5% in another study. The prevalence of hirsutism among women with PCOS in this study was 53.3% (144 of 270). A comprehensive skin examination was necessary to detect pronounced truncal hirsutism among women affected by PCOS (Table 3). Facial hirsutism may potentially not be a reliable marker of hirsutism in PCOS because of hair removal practices.

In patients with PCOS, hirsutism when present was associated with important reproductive and metabolic abnormalities, including elevated free testosterone levels, increased insulin resistance, lower HDL-C levels, and higher triglycerides levels. Therefore, hirsutism is a cogent indication for a reproductive and metabolic workup in women with PCOS.

**Acanthosis Nigricans**
Acanthosis nigricans is estimated to affect 20% of the US population. Previous studies have shown a broad range in the prevalence of AN among women with PCOS (2.5% in the United Kingdom, 5.2% in Turkey, and 17.2% in China). A comprehensive skin examination is necessary to detect AN in the axilla, where it is most frequently affected. The high rate seen in this study (36.9% [89 of 241]) may result from the inclusion of more body sites for evaluation, demographic differences, and the high prevalence of obesity and metabolic dysfunction in the United States.

Among women with PCOS, the finding that AN when present was associated with higher free testosterone levels may be explained by the association of AN with hyperinsulinemia, which can promote ovarian thecal androgen secretion and inhibit hepatic synthesis of sex hormone–binding globulin. In addition, among women with PCOS, AN was associated with substantial metabolic dysfunction (increased insulin resistance, glucose intolerance, BMI, and dyslipidemia), consistent with the observations that AN is a marker of metabolic derangement. Therefore, the presence of AN should raise clinical concern regarding a patient’s potential metabolic risk factors.

**Androgenic Alopeicia**
The 22.4% (53 of 237) prevalence of AGA among women meeting the PCOS criteria in this study (and that of a recently published study based on the same cross-section) is elevated relative to measurements in unselected populations of similar age but is less than the 35% prevalence reported in a Turkish study of women with PCOS. Among women meeting the criteria in this study, AGA was not associated with biochemical HA. These data support previous observations that AGA in PCOS is more tightly associated with clinical HA but not biochemical HA.

**Conclusions**
Cutaneous findings of PCOS when present manifest across a clinical spectrum ranging from complete absence to multiple skin findings. Although acne is a common cutaneous feature in women with PCOS, it did not distinguish between women suspected of having PCOS and those actually meeting the diagnostic criteria. Acne was also not associated with increased androgen levels, suggesting a complex acne-androgen association.
This study demonstrates that hirsutism and AN are the most useful cutaneous indicators of PCOS to distinguish patients most at risk for having PCOS among a suspected population. Most important, these cutaneous features manifest a characteristic distribution and systemic associations (Table 5). With regard to distribution, truncal hirsutism was found to be a better indicator of PCOS than facial hirsutism. Acanthosis nigricans, with more axillary involvement than neck involvement, was common in PCOS. Therefore, a comprehensive skin examination may be necessary to detect cutaneous evidence of PCOS.

This study found significant overlap among the reproductive and metabolic abnormalities associated with hirsutism and AN in women meeting the criteria for PCOS. The significant coincidence between hirsutism and AN may have contributed to the similarities in systemic findings. Alternatively, hirsutism and AN may be linked by an underlying mechanism that is distinct from the pathogenesis underlying acne and AGA, which are less likely to be associated with systemic abnormalities in PCOS. This study lends support to the concept that hyperinsulinemia, a likely driver of AN, is also an important element of PCOS-related pathogenesis, although it is not part of the current criteria.40 Most important, in the setting of suspected PCOS (with or without meeting the diagnostic criteria), hirsutism and AN warrant additional diagnostic evaluation because they are associated with increased glucose intolerance, BMI, free testosterone levels, and dyslipidemia.

REFERENCES
25. Hong JS, Kwon HH, Park SY, et al. Cutaneous manifestations of the subtypes of polycystic ovary


**NOTABLE NOTES**

**Dermatologic Ailments in the White House**

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American history encompasses a wide spectrum of dermatologic disease that has affected past presidents of the United States and their families. America’s founding father, George Washington, developed a carbuncle on his left hip during his first year as president. Although Kennedy exuded vitality with his youthful, tanned-like appearance, the hyperpigmentation of his face noted after the president’s fatal seizure in 1945, raising questions regarding melanoma as the possible culprit.1,2

John F. Kennedy was diagnosed as having Addison disease in 1947, years before serving as president. Although Kennedy exuded vitality with his youthful, tanned-like appearance, the hyperpigmentation of his face was actually a manifestation of his autoimmune condition. Lyndon B. Johnson underwent a clandestine procedure in 1967 to remove a basal cell carcinoma from his left ankle. Similarly, Ronald Reagan had basal cell carcinomas removed both during and in the years following his presidency; moreover, his daughter, Maureen Reagan, subsequently died as a result of melanoma metastases, affecting the brain.3

As revealed throughout American history, dermatology can indeed have an impact on anyone’s life, including the lives of prominent political leaders.

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