Aust N Z J Obstet Gynaecol 2001; 41: 2: 202–206

REPRODUCTIVE ENDOCRINOLOGY

The impact of ethnicity on the presentation of polycystic ovarian syndrome

Karen Williamson,[1] Alistair J Gunn,[2] Neil Johnson,[1] Stella R Milsom[1]

Department of Reproductive Medicine, National Women's Hospital,[1] Department of Paediatrics, Faculty of Medical and Health Sciences, University of Auckland,[2] Auckland, New Zealand

SUMMARY

The effect of ethnicity on the prevalence and presentation of polycystic ovarian syndrome (PCOS) was examined in a cross-sectional study of women with clinical – and ultrasound – diagnosed PCOS. European, Maori and Pacific Island women were seen in proportion to the general population, whereas Indian women were over-represented and Chinese women under-represented. European and Maori women were more likely to present with hirsutism than other ethnic groups (43% versus 25%, $p < 0.05$), while European women were less likely to present with infertility (46% versus 68%, $p < 0.01$). The Pacific Island women had little or no acne but other signs of PCOS were similar among ethnic groups. Although less than 10% of patients were referred with obesity, the majority of PCOS women were overweight on examination. Maori and Pacific Island women were more obese and had the highest rates of insulin resistance and lipid abnormalities. The adverse metabolic profile of many of these women, particularly the Maori and Pacific Islanders, is very likely to predispose them to early cardiovascular disease.

INTRODUCTION

Polycystic ovaries are now known to be a common ultrasonographic finding.[1] The majority of women with this ultrasound finding have associated biochemical and/or clinical abnormalities and are described as having polycystic ovarian syndrome (PCOS). The syndrome may include menstrual irregularity, symptoms of androgen excess, and subfertility. More recently, PCOS has been found to be associated with insulin resistance,[2] dyslipidaemia, and increased long-term risks of diabetes, hypertension and possibly ischaemic heart disease.[3] Obesity is not part of the syndrome but significantly exacerbates symptoms, probably by worsening the hyperinsulinism. Conversely, weight reduction reverses or reduces many of the symptoms and metabolic abnormalities associated with PCOS.[4,5]

Obesity, non-insulin dependent diabetes (NIDD) and ischaemic heart disease are common diseases in Maori and Pacific Islanders.[6] However, there are no data available concerning the prevalence of PCOS in Maori and Pacific Island women, and whether the presence of PCOS in these women is associated with evidence of increased cardiovascular risk. The aim of the present study was to examine the influence of ethnicity on prevalence, referral patterns, clinical presentation and metabolic risk associated with PCOS.

Address for correspondence

Dr Stella R Milsom
Dept of Reproductive Medicine
National Women's Hospital
Greenlane, Auckland
New Zealand.

Karen Williamson NZRN Research Nurse, Alistair J. Gunn FRACP Senior Research Fellow, Neil Johnson FRANZCOG Acting Senior Lecturer, Stella R Milsom FRACP Endocrinologist

METHODS

Subjects

Two hundred and one consecutive women presented to the gynae-endocrine clinic at National Women's Hospital with symptoms of hirsutism, acne, irregular menses and/or anovulatory infertility between January 1994 and December 1997. PCOS was confirmed either by ultrasound (n = 161) or by laparoscopy (n = 1). Women were excluded from the study if ultrasound did not show accepted features of PCOS (n = 28), or if ethnicity was not defined (n = 1) or the patient was already on hormonal medication (n = 10). Thus the study population was 162 women.

The reasons for referral were recorded as follows: hirsutism, acne, infertility, recurrent miscarriage, oligomenorrhoea, dysfunctional uterine bleeding (DUB), and weight gain. Infertility was defined as lack of conception after > 12 months of unprotected intercourse. Oligomenorrhoea was defined as < 11 spontaneous periods per year, regular cycles as 11–14 spontaneous periods per year and dysfunctional uterine bleeding as more than 15 spontaneous periods per year.

All patients were examined for the presence of excess body hair and the Ferriman-Gallwey (FG) score calculated.[1] Acne was recorded if present but not

graded. Any features on examination suggestive of cortisol excess or virilisation were noted. Height, weight, and supine blood pressure were recorded and body mass index calculated as: weight (kg) / height (m) squared.

Women were asked to self define ethnicity into one of seven groups: European, Maori, Pacific Island, Indian (including Fijian Indian), Chinese, other Asian, and others. An ethnicity distribution comparison was made between the clinical cohort and the 1996 NZ census figures for the 341,778 women aged 15–49 living in the Auckland and Northland Districts of New Zealand, the catchment area of the clinic.

Ultrasound

Transabdominal and/or transvaginal pelvic ultrasound examination was performed in all women using a 7.5 MHz trans-vaginal probe or 3.5 MHz linear array abdominal probe by two experienced radiologists. Ovaries were defined as polycystic if two or more of the following criteria were met: > 10 follicles, 2–8 mm in size, seen in a peripheral distribution in each ovary; increase in stromal density; and/or increased ovarian volume (> 8 ml).[1]

Hormone assays

Blood samples were performed after a 12-hour overnight fast and between days 1 and 10 of the cycle (unless the subject was amenorrhoeic). The following assays were performed in the National Women's Hospital laboratories: lutenising hormone (LH), follicle stimulating hormone (FSH), prolactin (PRL), total testosterone (T), dehydroepiandrosterone sulphate (DHEAS), androstenedione, 17-hydroxy-progesterone (17-OHP), sex hormone binding globulin (SHBG), fasting insulin, total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides. The inter- and intra-assay coefficient of variation for these assays is < 10%. In order to exclude secondary causes of PCOS, additional testing to exclude late onset congenital adrenal hyperplasia, Cushing's syndrome or a virilising lesion of the adrenal or ovary was performed if clinically indicated. No such patients were identified.

Statistical analysis

As the numbers of Chinese and Asian women were low (n = 0 and 4, respectively) the number of ethnic groups was reduced to five for the purpose of statistical analysis: European, Maori, Pacific Island, Indian (including Fijian Indian) and Other Asian (n = 4), Chinese (n = 0), Sri Lankan (n = 3), African Negro (n = 1), Iranian (n = 1), and Iraqi (n = 1). Analysis between groups was carried out by chi-squared tests for categorical variables. Continuous variables were tested using the Kruskal Wallis Test followed by post hoc use of the Wilcoxon Rank Sum test. The relationship between continuous variables such as body mass index (BMI) and laboratory values was determined by regression analysis.

RESULTS

The patient demographics (n = 162) are shown in Table 1. The ethnic composition is compared to the population of the hospital catchment area in Table 2. The majority of women with PCOS attending the clinic were European (69.2%), with Maori, Pacific Island, and Indian women being represented in smaller numbers (9.9%, 9.3% and 11.7%, respectively). Smaller ethnic groups constitute the remainder. The patients differed significantly from the ethnic distribution of the North Health referral population (p = 0.027). The largest difference seen was that Indian women were over-represented in the clinical group (11.7%) compared to the proportion of the North Health population (2.1%). No Chinese women with PCOS were identified within the study group compared with 4.5% Chinese women in the North Health population. The proportion of European, Maori and Pacific Island women presenting with PCOS was consistent with their representation in the North Health demographics.

Table 1 Demographics of the study population

Age (mean, range (yrs))	**27.4 (16–42)**
	%
Oligomenorrhoea	88.9
Hirsutism (FG ≥ 6)	91.0
Acne	30.9
Infertility	48.0
Recurrent miscarriage	2.5
DUB	2.5
Acanthosis nigricans	4.5
BMI (kg/m^2)	
< 20	7.7
20 – < 25	25
25 – <30	26.9
30 – <40	34.6
≥ 40	5.8

Infertility > 12 months duration; oligomenorrhoea (cycles > 35 days); DUB: dysfunctional uterine bleeding

Table 2 Comparison of ethnicity between the cohort with PCOS and women aged 15–49 years, resident in the North Health area

	PCOS	**North Health women aged 15–49 years**
	%	**%**
European	69.2	57.7
Maori	9.9	13.5
Pacific Island	9.3	9.8
Indian	11.7	2.1
Chinese	0	4.5
Other Asian	2.4	4.2
Other	3.7	8.1
Total (n)	**162**	**341,778**

The ethnic composition of the patients with PCOS was significantly different from the reference population with more Indian patients and fewer Chinese patients (p < 0.03, chi-squared).

Referral patterns

The reasons for referral by ethnic group are shown in Table 3. The principal reasons for referral were infertility, oligomenorrhoea, hirsutism, and acne. Most patients were referred with several complaints. Menstrual problems or subfertility or both were cited in 80–100% of referrals across ethnic groups, but were not equally distributed. Whereas oligo/amenorrhoea was common in all ethnic groups, non-European women presented more often for infertility than did European women (68% versus 46%, $p < 0.01$). In contrast, hirsutism was more often cited as a concern by European and Maori women than the other groups (43% versus 25%, $p < 0.05$). No Maori or Pacific Island women presented with acne (although 19% of Maori women were found to have evidence of acne on examination). Surprisingly, obesity was not perceived as a clinical issue in most cases, since it was mentioned in only 11.7% of referrals across ethnic groups.

Table 3 Referral patterns among different ethnic groups of women with PCOS, showing the percentage of each group presenting with each complaint

	Oligmenorrhoea %	Hirsute %	Acne %	Infertility %	Obesity %
European	45	43	18	46	14
Maori	44	44	0	63	0
Pacific Island	57	27	0	80	20
Indian	58	32	5	68	5
Other	50	10	10	60	10

European and Maori women were referred with hirsutism more often than other ethnic groups ($p < 0.05$), whereas non-European women were more likely to present with infertility ($p < 0.01$)

Clinical and laboratory characteristics

Hirsutism (FG > 6) was common in all ethnic groups even though it was only a significant reason for referral in European and Maori women. Acne was found on examination in all ethnic groups except the Pacific Island women. As predicted, the group as a whole had relatively increased levels of androgens, insulin, lipids, and plasma glucose (although no subject was frankly diabetic). Compared with the rest of the group, the Maori and Pacific Island women had the highest levels of total and free testosterone ($p < 0.05$), with the lowest SHBG ($p < 0.02$), the highest fasting insulin ($p = 0.05$), as well as higher levels of triglycerides ($p < 0.05$), the lowest cholesterol HDL levels ($p < 0.005$) with a strong trend to the worst cholesterol/HDL ratio ($p = 0.08$) (Table 4). As reported below, however, much of these differences appear to be related to their greater BMI. Their blood pressures and adrenal androgen levels were not significantly different from the other groups.

Weight

The group as a whole were overweight (mean BMI 28.6, range 16.9–46.5). The distribution of BMI for women in each ethnic group is shown in Figure 1. Obesity was significantly more common in Maori and Pacific Island women ($p < 0.002$ and $p < 0.001$, respectively, compared with European women). Pacific Island women had the largest proportion of morbid obesity (20%). There were no underweight (BMI < 19) Maori or Pacific Island women although a significant minority of other ethnic groups were underweight (9.2% of Caucasians, 5.6% of Indians, and 20% of the Other ethnic group). It is important to note that BMI reference tables have been derived from Caucasian populations.

Table 4 Clinical characteristics and laboratory values in different ethnic groups

	European	Maori	Pacific Island	Indian	Other
Hirsutism (FG Score < 6)	8.3 ± 9.0	10.5 ± 9.8	9.1 ± 7.2	8.3 ± 8.2	3.1 ± 5.5
Systolic BP (mmHg)	118 ± 19	121 ± 20	112 ± 16	116 ± 17	111 ± 12
Diastolic BP (mmHg)	74 ± 14	78 ± 13	75 ± 13	71 ± 10	67 ± 11
TG* (mmol L^{-1})	1.3 ± 1.0	2.0 ± 0.6	2.3 ± 1.7	1.3 ± 0.5	1.6 ± 0.6
Total testosterone (≤ 2.5nmol L^{-1})	2.2 ± 1.0	2.9 ± 1.1	2.2 ± 0.7	2.1 ± 0.6	2.3 ± 1.1
Total cholesterol (≤ 5.0 nmol L^{-1})	5.2 ± 1.1	5.3 ± 1.3	4.4 ± 0.5	5.1 ± 0.7	5.4 ± 0.7
HDL* (mmol L^{-1})	1.3 ± 0.3	1.0 ± 0.2	1.0 ± 0.3	1.2 ± 0.3	1.37 ± 0.4
LDL (mmol L^{-1})	3.3 ± 1.0	3.4 ± 1.2	2.7 ± 0.4	3.4 ± 0.6	3.4 ± 0.6
Fasting glucose mM (<6.0)	5.3 ± 2.0	5.0 ± 1.2	5.5 ± 0.9	5.1 ± 0.7	5.1 ± 0.4
Fasting insulin (mU/L)	17.9 ±1 7.0	33.4 ± 12.4	28.5 ± 26	27.8 ± 12.3	10.5 ± 0.7
Luteinising hormone (IU/L)	10.9 ± 7.2	11.3 ± 5.3	12.4 ± 5.5	10.3 ± 5.7	12.0 ± 6.6
BMI (kg/m^2) **	27.5 ± 6.6	32.3 ± 4.3	34.0 ± 6.0	28.7 ± 7.4	24.3±4.6
SHBG *** (nmol L^{-1})	55.6 ± 17.6	52.0 ± 23.8	39.6 ± 4.7	44.3 ± 15	49.7 ± 15.5

Data are mean ±SD. Reference values are given in brackets. * = $p < 0.05$. ** = $p < 0.0001$. *** = $p < 0.005$, between ethnic groups. Kruskal Wallis Test. Abbreviations: SHBG = sex hormone binding globulin; TG = triglycerides; HDL = high density lipoproteins; LDL = low density lipoproteins.

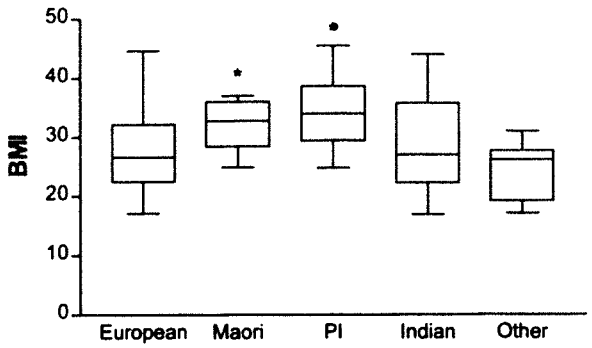

Figure 1 Box plot of BMI for different ethnic groups. The box extends from the 25th percentile to the 75th percentile, with a line at the median (the 50th percentile). The whiskers extend above and below the box to show the highest and lowest values. Ethnicity significantly affected BMI ($p < 0.001$). Overall, Maori and Pacific Island (PI) women were significantly more obese than European women ($p < 0.001$) or the group as a whole.

Relationship of BMI to clinical and laboratory characteristics

A significant correlation was observed between BMI and systolic and diastolic BP ($r = 0.52$, $p < 0.007$), FG score ($r = 0.16$, $p < 0.05$), SHBG ($r = 0.35$, $p < 0.001$), free testosterone ($r = 0.21$, $p < 0.02$), fasting insulin ($r = 0.57$, $p < 0.001$), total cholesterol ($r = 0.24$, $p < 0.04$), HDL cholesterol ($r = 0.51$, $p < 0.001$), cholesterol/HDL ratio ($r = 0.52$, $p < 0.001$) and triglycerides ($r = 0.57$, $p < 0.001$) within the group as a whole with increasingly adverse metabolic features as weight increased. Overweight women were much more likely to have hirsutism ($p < 0.001$, chi-squared) as well as a longer duration of infertility at the time of presentation ($p < 0.05$, Mann Whitney test). No statistically significant correlation was observed between BMI and DHEAS, androstenedione, testosterone, LH or FSH levels, but there was a trend for overweight women to have higher mean levels of serum LDL cholesterol ($p = 0.06$). There was no apparent relationship of increased weight to the presence or severity of acne or oligomenorrhoea or with the relatively infrequent complications of acanthosis nigricans and recurrent miscarriage.

DISCUSSION

The overall prevalence of PCOS in women of reproductive age is reported to be between 5 and 23%[1,7,8] in studies derived from predominantly European populations. However, recent papers have suggested that PCOS may be more common in specific ethnic groups. The prevalence of PCOS has been reported to be as high as 52% in women from the Indian subcontinent.[9] Similarly, Hispanic-American women were reported to have an increased prevalence of PCOS compared with Caucasian women or African-American women.[10]

In the present study the prevalence of clinical PCOS in Maori and Pacific Island women was similar to the reference North Health population. In contrast, Indian women were significantly over-represented, almost five times more than the proportion of Indian women within the catchment population. Clearly there are other possible reasons for apparent over-representation such as more ready access to, or willingness to use, tertiary healthcare. Nevertheless these figures are in accord with the study by Rodin et al in suggesting a very high prevalence of PCOS in women from the Indian subcontinent.[9] Finally, there were no women of Chinese descent with PCOS in this study cohort compared with an expected frequency of 4.5% in the reference population. To our knowledge there are no previous data on the frequency of PCOS in Chinese women.

The present data confirm the findings of other studies that irregular periods, hirsutism, acne, subfertility, metabolic abnormalities, and elevated serum androgen levels are frequently found in women with PCOS, and that these features correlate with weight.[11] Recurrent miscarriage has also been reported to be more common with PCOS and may be related to higher androgen levels,[12] but was relatively uncommon in our study population.

The clinical presentation of PCOS may differ between ethnic groups. Japanese women with PCOS tend to be less obese, less hirsute, and have lower fasting insulin levels than American or Italian women with PCOS, although no difference was found in regard to insulin resistance.[13] In Caribbean-Hispanic women, PCOS and ethnicity were associated with independent and additive decreases in insulin sensitivity.[10] Norman et al found Indian women with PCOS to be more insulin resistant than case matched white controls, based on glucose tolerance tests.[14]

Within the present cohort, menstrual irregularity was a common presenting feature in all ethnic groups but infertility was a more common problem in the non-Europeans, particularly the Pacific Island and Indian women. One contributing factor is likely to be excess weight, as suggested by a significantly greater duration of infertility with greater obesity. Consistent with this, previous studies have demonstrated that weight loss is associated with substantially improved conception rates.[5] Hirsutism was common in all the groups (seen in approximately two-thirds of patients); in contrast although acne was also common, it was never found in the Pacific Island women. Maori, Pacific Island and Indian women demonstrated the highest prevalence of obesity, but this was seldom mentioned as an issue in the referral letter. It is not clear whether this was due to a reluctance to offend patients or a failure to appreciate the critical significance of increased bodyweight for the management of PCOS on the part of both the patients and practitioners.

Across the group, there were the expected findings of elevated androgens, LH, insulin, total cholesterol,

and LDL cholesterol compared to reference control population (Milsom et al, unpublished data). Maori and Pacific Island women had significantly more adverse metabolic features, with the highest levels of androgens, triglycerides, LDL cholesterol, fasting insulin, systolic and diastolic blood pressure, and lowest HDL within the group. These are all well identified cardiac risk factors and as such should be of considerable concern given that Maori women are known to be at increased risk of both non-fatal and fatal coronary artery disease.[6]

Consistent with previous reports,[7] in the present study cohort BMI was strongly associated with the severity of some symptoms, particularly hirsutism, as well as with most of the adverse metabolic factors noted above. Obesity is a particular problem in many native Pacific Island cultures and is often exacerbated by exposure to western lifestyles.[15] Obesity and the consequent worsening of the primary hyperinsulinism associated with PCOS exacerbate androgen excess symptoms, metabolic indices and infertility in PCOS, as well as being independent risk factors for cardiac disease. The success of a culturally appropriate program in achieving weight loss, reducing hypertension and lowering cholesterol has been demonstrated in Hawaiians.[16] The present data suggest that within New Zealand prevention and control of obesity should be an important priority for these susceptible ethnic groups, and that PCOS may be an important marker of increased risk within such populations.

In conclusion, the prevalence and presentation of PCOS is influenced by ethnicity. PCOS was most common in Indian women. Although Maori and Pacific Island women with PCOS were seen in proportion to the general population, they were the most likely to present with obesity and risk factors for future cardiovascular disease. The presence of polycystic ovaries in this ethnic group should prompt a search for adverse metabolic factors and consideration of therapeutic strategies to control obesity and insulin resistance.

ACKNOWLEDGEMENTS

We are most grateful to Associate Professor Cindy Farquhar and Dr Kalpana Singh for assistance with patient recruitment, Mr Michael Backhurst for statistical advice and to Mrs Vivienne Topping for assistance with the manuscript.

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