Clinical and endocrine profiles of 62 Malaysian women with polycystic ovary syndrome

T.T. Tan, MCRP (UK)
Lecturer

S.K. Lui, BSc (Hons)
Research Assistant

*N. Satgunasingam, PhD
Head, Department of Radiochemistry

B.A.K. Khalid, FRACP, PhD
Associate Professor and Deputy Dean

*Department of Medicine, Universiti Kebangsaan Malaysia and *Institute for Medical Research, Kuala Lumpur.*

Summary

62 cases of polycystic ovary syndrome (PCO) were reviewed with regards to their clinical and endocrine features. The subgroup of patients with acanthosis nigricans (AN) was further studied in detail. The prevalence of the syndrome was significantly higher in the Indian (35.5% of cases). Obesity, AN, hirsuitism, non-insulin dependent diabetes mellitus (NIDDM) and raised level of serum testosterone were present in 77.1%, 74%, 79%, 21% and 48% of the cases respectively. Patients with AN was associated with higher body mass index, serum testosterone level, and prevalence of hirsuitism and NIDDM than patients without AN. These observations are in keeping with the hypothesis that hyperinsulinemia may be of importance in the pathogenesis of a sub-group of PCO associated with insulin resistant states.

Key words: Polycystic ovary syndrome, Malaysian women, acanthosis nigricans, hyperinsulinemia.

Introduction

The clinical syndrome of amenorrhoea, hirsutism and obesity in association with bilateral sclerocystic ovaries was first described by Stein and Levanthal in 1935.[1] Subsequent publications indicated that the syndrome is characterised by a much more varied clinical and endocrine manifestations.[2-5] Polycystic ovary syndrome (PCO), the prefered generic term, encompasses all the heterogenous presentations of this disorder. The syndrome has been observed in association with a variety of endocrine disorders like Cushing's syndrome, congenital adrenal hyperplasia, hypothyroidism and hyperprolactinemia.[3] In addition, strong familial clustering has been noted in this disorder.[6,7] The pathogenesis is unclear and remains the most controversial subject in the field of reproductive endocrinology.[8,9] It is currently believed that the syndrome arises from heterogenous disorders.[9]

In this report we described the clinical and endocrine profiles of 62 Malaysian women with the syndrome seen over the period 1982–88. The high prevalence of acanthosis nigricans noted in this population of PCO leads to further characteristisation of this subgroup of PCO.

Materials and Methods

62 consecutive cases of PCO attending the Endocrine Clinic of Universiti Kebangsaan Malaysia (UKM) were reviewed with regards to their clinical and endocrine features. The diagnosis of PCO

was based on the presence of oligomenorrhoea (cycle interval longer than 2 months) or amennorrhoea and an inappropriately elevated serum luteinising hormone (LH) level in the presence of a normal or low follicular stimulating hormone (FSH) level and follicular phase levels of progesterone.[3] Endocrine disorders known to be associated with PCO were excluded from analysis. The clinical and biochemical data at initial presentation were used for the study. The hormones studied, their normal values, the methods employed and characteristics of their assays are shown in Table 1.

Table 1
Summary of reagents, variability and normal values of hormone assays

		Antisera	Standards	Methods	Interassay CV (%)	Normal Values
LH	(IU/L)	F87/2 (Butt)	IRP68/40	RIA[a]	10.1	2.4–14.0 (F)
FSH	(IU/L)	M93/2 (Butt)	IRP78/549	RIA[a]	10.2	1.1–5.7 (F)
E2	(pmol/L)	K158320*	*	RIA[b]	11.2	59–327 (EF)
T	(nmol/L)	K888510*	*	RIA[b]	11.2	0.9–2.8
P	(mU/L)	G/R/51–5ABC (Guildhay)	IRP75/504	RIA[a]	7.4	117–468

E2 = Estradiol, T = Testosterone (bound and free), P = Prolactin. * = Supplied by World Health Organisation Matched Reagent Programme. IRP = International Reference Preparation. RIA = Radioimmunoassay. a = Double Antibody. b = Extraction, charcoal separation. F = Follicular Phase. EF = Early Follicular Phase. CV = Coefficient of variation.

Statistical Analysis

Unpaired Student's T tests and chi-square tests were used for statistical analysis of continuous and discrete data respectively.

Results

Of the total of 62 cases studied, 30 (48.4%) were Malay (M), 10 (16.1%) were Chinese (C) and 22 (35.5%) were Indian (I). Using the 1987 UKM Polyclinic attendances (M:C:I = 51.2 : 30.3 : 17.3) as a basis for comparison, the prevalence of PCO in Indian is significantly higher than the other races ($P < 0.001$). The mean age and body mass index (BMI) at presentation were 24.7 years (range 14–38) and 29.5 kg/m^2 (95% C.I = 28.1–30.9) respectively. 77.1% of the cases had BMI greater than 25 kg/m^2. Hirsuitism (HIR), acanthosis nigricans (AN) and non-insulin dependent diabetes mellitus (NIDDM) were present in 79%, 74% and 21% respectively. The endocrine profiles of the patients are summarised in Table 2. Hyperprolactinemia (> 468 mU/L) and raised serum testosterone (> 2.8 nmol/L) were noted in 15% and 48% of the cases respectively.

Table 2
Endocrine profiles of the 62 patients with PCO

LH (IU/L)	FSH (IU/L)	E2 (pmol/L)	T (nmol/L)	P (mU/L)
		$\bar{x}$ (Range)		
13.1	3.6	184	3.0	292
(4.6–31.8)	(1.0–5.7)	(16–665)	(1.4–6.7)	(85–1000)

The clinical and endocrine features of those with and without AN are shown in Table 3 and 4 respectively. Patients with AN had significantly higher BMI and lower LH values than those without. The proportions of patients with NIDDM, HIR and higher serum testosterone level were also greater in those with AN. These, however, did not reach statistical significance. In the group of patients with NIDDM, the serum testosterone level was significantly higher (P = 0.04) than those who were not NIDDM [3.7nmol/L (27.–4.7) vs 2.8nmol/L (2.6–3.0); $\bar{x}$ (95% C.I)].

Table 3.
Clinical characteristics of patients with and without AN

	Race (M:C:I)	Age (yr)	BMI (kg/m^2)	NIDDM	HIR
		$\bar{x}$ (95% C.I)		n (%)	n (%)
With AN (n = 46)	23:4:19	24.2 (22.6–25.8)	30.9 (29.3–32.5)	12 (26)	39 (85)
	ns	ns	P < 0.0001	P = 0.2	P < 0.02
Without AN (n = 16)	7:6:3	26.2 (23.4–29.0)	25.7 (23.7–27.7)	1 (6)	10 (6%)

Table 4.
Endocrine profiles of patients with and without AN

	LH (IU/L)	FSH (IU/L)	E2 (pmol/L)	T (nmol/L)
		$\bar{x}$ (95% C.I)		
With AN (n = 46)	12.3 (10.7–13.9)	3.5 (2.9–4.1)	200 (153–247)	3.2 (2.8–3.6)
	P = 0.04	ns	ns	P = 0.1
Without AN (n = 16)	15.9 (12.3–19.5)	4.0 (3.2–0.8)	148 (94–202)	2.6 (2.1–3.1)

Discussion

A precise defination of PCO that could be agreed upon by all interested parties is still elusive. The main problem lies in the fact that a significant proportion of normal subjects have PCO on ultrasonography but without any clinical or biochemical features of PCO and vice versa.[4,9] We have therefore used the functional or biochemical definition of PCO in this study and have not attempted any analysis of the morphological component of the disorder.

The preponderence of the condition in Indians in this study is interesting. This could be explained by a genetic predisposition to this disorder.[6,7] The prevalence of hyperprolactinemia in this series is similar to that reported by Frank and Conway.[4,5] However, the prevalence of obesity and AN in our series is much higher than theirs. They reported 35% incidence of obesity in both their series and the incidence of AN were only 1% and 2% respectively. The high number of PCO with obesity in our series could perhaps be due to the likelihood that our endocrine clinic received a disproportionately higher number of PCO with obesity as the major presenting problem. The association of AN with gross obesity has been described.[10] The high prevalence of AN in this study could be related to the greater prevalence of obesity.

Growth factors like insulin and insulin-like growth factor 1 (IGF 1) are known to modulate the ovarian response to gonadotropins.[11–12] Ovarian stroma cells from patients with PCO when incubated in the presence of insulin in the culture medium secrete more androgen.[13] Both obesity and AN are associated with insulin resistant states and resulting hyperinsulinemia.[14,15] By mediating the hyperandrogenism in PCO, hyperinsulinemia may play a role in the pathogenesis of this sub-group of PCO with insulin resistant state. Our observation of significant association between obesity and AN with NIDDM, HIR and hypertestosteronemia is in keeping with this hypothesis.

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