Pathogenesis of Polycystic ovary syndrome due to genetic factors

S.Sadrzadeh[1,2], J. M. Vink[3], R. Homburg[1], C.B. Lambalk[1] , D.I. Boomsma[3]
[1] Division of Reproductive Medicine, Department of Obstetrics & Gynaecology, VU University medical centre, Amsterdam, The Netherlands. [2]Department of Clinical Genetics and Human Genetics, VU University Medical Center, Amsterdam, The Netherlands. [3]Department of Biological Psychology, Vrije Universiteit Amsterdam, The Netherlands
Tel + 31 20 44 40070; Fax + 31 20 44 40045; E-mail s.sadrzadeh.vumc.nl

VU medisch centrum

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age. PCOS is associated with infertility, obesity and insulin resistance. Familial clustering suggest a genetic component, but up to now the genetic influence on the pathogenesis of PCOS (heritability) has not been quantified.

Table1. Diagnostic criteria of polycystic ovary syndrome (PCOS)

2 out of 3

- Oligo- or anovulation
- Clinical and/or biochemical signs of androgen excess
- Polycystic ovaries on ultrasound (fig 1)

2003 Rotterdam PCOS consensus,Fertil Sterill

AIM

To estimate the heritability of PCOS.

METHOD

Twins and their siblings registered with the Netherlands Twin Register (NTR) receive mailed surveys every 2-3 years. In 2000 the survey contained items on number of natural menstrual cycles in a year, hirsutism and acne. PCOS was defined as less than 10 menstrual cycles a year with hirsutism and/or acne (see Table 2). The influences of additive genetic factors (A), common environment (C), and unique environment (E) on the pathogenesis of PCOS were estimated using model-fitting techniques. Estimates are based on data from monozygotic (MZ) twins who are genetically identical, and dizygotic (DZ) twins and sisters who share 50% of their segregating genes.

Table 2. Characteristics of female twins and their sisters

	Monozygotic n= 1619	Dizygotic n= 842	Opposite sex n= 594	Female sibs n=1146
Age [1]	31	30	28	31
Age at menarche[1]	13	13	13	13
BMI[2]	22,46	22,86	22,73	23,48

[1] Age in years
[2] BMI defined as [weight/ (height in cm) [2]]

RESULTS

The polychoric correlations for PCOS were .71 for MZ twins, .36 for DZ twins and .44 for sisters, suggesting substantial genetic influences. In the full model, genetic factors account for 58%, common environment factors for 12% and unique environmental factors account for 29% of the variances in the pathogenesis of PCOS. The full model could be reduced to a model including genetic factors (A = 71%) and unique environmental factors (E = 29%). However, the power of our analysis did not allow distinguishing between the later model and a model only accounting for common (C = 57%) - and unique environmental (E =43%) factors (table 3).

Table 3.

Model	-2LL[a]	df[b]	Δdf	Δchi[2]	p	A[c]	C[c]	E[c]
ACE	713.799	2881				0.5889	0.1186	0.2925
AE	713.911	2882	1	0.112	0.738	0.7190	0	0.2810
CE	715.985	2882	1	2.186	0.139	0	0.5669	0.4331
E	2058.945	2883	2	24.647	0.000	0	0	1

[a/] A represents additive genetic influences (heritability), C represents shared environmental influences, E represents unique environmental influences

CONCLUSION

Our study may point to a strong contribution of genetic factors to the pathogenesis of PCOS.