Effect of CYP19 Gene on Polycystic Ovary Syndrome Phenotype in Iraqi Women

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Abstract

Background
Ovarian androgen overproduction is the key physiopathologic feature of polycystic ovary syndrome and the bulk of evidence points to the ovary being the source of excess androgens, which appears to result from an abnormal regulation (dysregulation) of steroidogenesis. Aromatase is an enzyme complex responsible for a key step in the biosynthesis of estrogen. It is encoded by CYP19.

Objective
To examine whether the rs2414096 of CYP19 gene contributes to genetic susceptibility to the polycystic ovary syndrome hyperandrogenism in Iraqi women.

Methods
A Case control study was conducted in the High Institute of Infertility Diagnosis and Assisted Reproductive Technologies, Al-Nahrain University and Al-Nahrain Forensic DNA Unit, Baghdad, Iraq for the period from February 2012 to February 2013. Sixty-five healthy women serves as the control group and eighty-four infertile women with polycystic ovary syndrome, divided into two subgroups depending on the body mass index (< and ≥30 kg/m\textsuperscript{2}) were studied. Restriction fragment length polymorphism analysis was performed to determine the genotypes of rs2414096 of CYP19. Clinical, anthropometric, hormonal and biochemical parameters were also estimated.

Results
Genotypic distribution of rs2414096 of CYP19 was significantly different in polycystic ovary syndrome patients from that of control women. The frequency of GG genotype was higher in the patients, while AA genotype was higher in control women. Those with GG genotype have lower estradiol, estradiol/testosterone and higher testosterone, luteinizing hormone, follicular stimulating hormone than those with AA genotype.

Conclusion
The present data suggests that single-nucleotide polymorphisms rs2414096 in the CYP19 gene is associated with susceptibility to polycystic ovary syndrome hyperandrogenism in Iraqi women.

Keywords
Polycystic ovary syndrome, CYP19 gene, reproductive hormones, Iraqi women.

List of Abbreviation: PCOS = polycystic ovary syndrome, FSH = follicle stimulating hormone, Kb = kilobase, SNP = single nucleotide polymorphism, BMI = body mass index, LH = lutinizing hormone, E\textsubscript{2} = estradiol, FBS = fasting blood sugar, LDL = low density lipoprotein, HDL = high density lipoprotein, VLDL = very low density lipoprotein, GnRH = Gonadotropin releasing hormone.

Introduction
The etiology of polycystic ovary syndrome (PCOS) is still unknown; there is increasing evidence to support a major genetic basis, since the syndrome is strongly familial \cite{1}. It is clear, however, that more than one gene (and probably several) contributes to the heterogeneous phenotype \cite{2,3}.

Ovarian androgen overproduction is the key physiopathologic feature of PCOS and the bulk of evidence points to the ovary being the source of excess androgens, which appears to result from dysregulation of steroidogenesis \cite{4}. Genetic variation at androgen receptor \cite{5}, suggesting that hyperandrogenism in PCO may be partly genetically determined.