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ANTI-MULLERIAN HORMONE GENE POLYMORPHISM (RS10407022) AND ITS ASSOCIATION WITH THE INCIDENCE OF POLYCYSTIC OVARY SYNDROME IN IRAQI WOMEN

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ABSTRACT : Polycystic ovary syndrome (PCOS) affects 5 - 10% of reproductive age women and is the leading cause of ovulatory dysfunction. Anti-Müllerian hormone (AMH) is an important regulator offolliculogenesis in the ovaries. AMH inhibitory action on FSH-induced aromatase production likely contributes to hyper and rogenism in PCOS, which further enhances insulin resistance. The objective of the present study was to investigate the association of the AMH Ser49Ile (rs10407022) polymorphism with PCOS susceptibility in Iraqi women.

Genetic and hormonal studies were performed on 50 PCOS patients and 50 apparently healthy controls. AMH gene was genotyped using TaqMan genotyping kit by RT-PCR. Serum concentrations of LH, FSH, TSH and prolactin were determined. Comparisons of studied parameters were achieved by statistical analysis system (SAS).

Serum FSH hormone concentrations were significantly ($p<0.05$) lower in PCOS patients compared with controls (4.87 versus 10.63 IU/L, respectively). Serum FSH concentrations were increased in GT genotype carriers compared with those of GG and TT genotypes. Also, there was a G allele-related decrease in serum prolactin concentrations. *In silico* study revealed that the prediction of the Provean tool for the effect of rs10407022 SNP of AMH gene was neutral. This variant was predicted to be possibly damaging using PolyPhen-2 tool. Also, this variant was predicted to be probably benign using Panther classification system. The predicted protein stability of this variant was decreased. As related with GG (wild) genotype, the frequency was in patients with PCOS significantly ($p<0.05$) higher than in apparently healthy controls (14 versus 2%, respectively; $X^2 = 5.133$; OR = 0.806). The frequency of combined (heterozygous + homozygous) genotypes was significantly ($p<0.05$) higher in controls when compared with PCOS patients (98 versus 86%, respectively; $X^2 = 4.039$; OR = 0.692).

It can be concluded that no association between both heterozygous and homozygous mutants at rs10407022 with the incidence of PCOS in Iraqi women.

Key words : PCOS, AMH gene, polymorphism, hormones.

INTRODUCTION

Polycystic ovary syndrome is a complicated multisystem endocrinopathy occur ineach 7–17 reproductive age females worldwide. PCOS is heterogeneous in clinical features and the diagnostic standard still staydialectical. At present time, the pathogenesis of PCOS stayambiguous. There are fundamentally three groups of diagnostic criteria (AzzizandAdashi, 2016) include: polycystic ovarian morphology, ovulatory dysfunction and hyperandrogenism and its symptoms such as hirsutism, acne and/or alopecia, menstrual irregularity (Azziz *et al*, 2009; Walters *et al*, 2012). Genetic and environmental agents that organize female reproductive function. PCOS is related with numerous another morbidity/ diseases – associated agents like overweight and another cardiovascular disease (CVD) risk factors.

Anti-Müllerian hormone (AMH), a 140 KDa glycoprotein, is considered to be an important candidate gene for PCOS, well known for its function through male sexual differentiation (Burns, 1977). AMH needs to be cleaved to be energetic and it does its influence by linking to a particular type II receptor (AMHR2). In women, AMH is secreted by granulosa cells (GCs) at a low level