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A BIOCHEMICAL AND MOLECULAR STUDY OF TUMOR NECROSIS FACTOR-α IN FEMALE WITH POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT : Polycystic ovary syndrome (PCOS) is one of the most common endocrine dysfunctions in women of reproductive age .it isrefers to a heterogeneous group of gynecologic disorders with variable degrees of ovarian and adrenal hyperandrogenism. Tumor necrosis factor-á are related with gynecological pathologies including preeclampsia, endometriosis and PCOS. Insulin resistance and TNF-á was measured from fasting glucose, TNF-á gene polymorphisim estimation using PRC-RFLPin a group of 50 PCOS females and 50 age compare with healthy controls. The age in both study groups no significant difference for patients (22.44 ± 3.20) and controls (23.34 ± 2.95). All the PCOS had elevated body mass index (27.70 ± 5.07), waist to hip ratio (0.85 ± 0.04), fasting insulin (10.76 ± 2.86), homeostatic model assessment (HOMA) score (3.18 ± 1.14) and serum TNF-á (23.19 ± 3.95), when compared with controls. There was a significant (r=0.244, P=0.01), (r=0.293, P=0.003) positive correlation of IR with BMI and waist to hip ratio, respectively. Also, a significantly (r=0.543, P<0.001) positivecorrelation were found between TNF-á and insulin resistance. Genotype distribution for the C-850T polymorphism was observed with the frequency of the variant T allele being 16% in the PCOS group and 6% in the control group (p>0.11). In conclusion, present examinations suggested that the TNF-á might contribute to the pathogenesis of PCOS, being the basis of increase body weight which lead to development of insulin resistance. While the incidence of PCOS independent of a polymorphism of the TNF-á C850T (rs 1799724) in population studied.

Key words : Polycystic ovary syndrome, Tumor Necrosis Factor Alpha, Insulin resistance, Polymorphism of TNF-á C850T (rs1799724).

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine dysfunctions in women of reproductive age with a prevalence of approximately 5%–10% worldwide (Conway *et al*, 2014). A diagnosis of PCOS is based at least 2 of the following 3 criteria: oligo-ovulation or anovulation, clinical or biochemical evidence of hyperandrogenism, and polycystic ovaries on ultrasound assessment (>12 small natural follicles in an ovary) , with the exclusion of medical conditions such as congenital adrenal hyperplasia, androgen-secreting tumors or Cushing's syndrome (Conway *et al*, 2014). Although, all women with PCOS have evidence of insulin resistance it is more pronounced in those with chronic an ovulation (Yousouf *et al*, 2012; Escobar-Morreale *et al*, 2011). Patients with PCOS have central obesity, increased deposition of fat around waist. The obesity is android in type with increased waist to hip ratio andandfat in anterior abdominal wall and mesentery (Esser *et al*, 2014). Hyper expression of TNF-á in muscle and adipose tissues is implicated in the development of IR in humans, by decreasing the tyrosine kinase activity of the insulin receptor (Daniele *et al*, 2014). TNF-á promotes IR, causes Hyperandrogenism, and is involved in follicular development and, hence, it has been implicated in the pathophysiology of PCOS. The TNF-á gene is located on 6p21.3, spans approximately 3 kb and has four exons G308A and -C850T polymorphisms in the promoter region of TNF-á have been associated with chronic inflammatory diseases such as ulcerative colitis , rheumatoid arthritis, and Crohn's disease (Chatrchyan *et al*, 2011). Although, the results were not consistent among different ethnic populations, the meta-analysis revealed that TNF-á is a potential susceptibility factors for PCOS (Wu *et al*, 2015).

SUBJECTS AND METHODS

Present study includes 100 females, divided in two groups, the first group includes 50 females with PCOS and the second group includes 50 apparently healthy females. The samples were taken from patients attended to Infertility center in Maternity and Children Hospital in Babylon province in Hilla city, medical staff and relatives