

## **Circular Pentraxin-3 and Betatrophin as Novel Predictors and Promising Biomarkers in Polycystic Ovary Syndrome with or without Type 2 Diabetes Mellitus**

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### **KEYWORDS**

PTX3, Betatrophin, Insulin Resistance, Diabetes Mellitus; Polycystic Ovary Syndrome

### **ABSTRACT**

Background: Two recently discovered circulating proteins, pentraxin 3 (PTX3) and betatrophin, have a strong correlation with a number of illnesses, obesity, and the metabolic syndrome. Objective: This study was made to investigate whether pentraxin-3 (PTX3) and betatrophin levels are sensitive markers associated with PCOS in women with or without diabetes. Materials and methods: We conducted a case-control clinical study. Samples were collected from "infertility center" at Basra hospital for Obstetrics and children in Basra province-Iraq during the period from August 2023 till end of February 2024. Results: Levels of Ts, PRL, HOMAIR, PTX3, betatrophin, and MDA were elevated ( $p < 0.01$ ), LH and insulin were increased ( $p < 0.05$ ) and ( $p < 0.01$ ), E2 and TAC decreased ( $p < 0.01$ ), while BMI and FSH levels showed non-significant changes ( $p > 0.05$ ) in PCOS women with or without diabetes (both 1<sup>o</sup>PCOS and 2<sup>o</sup>PCOS), respectively, as compared to the healthy control. Glucose was increased ( $p < 0.01$ ) in PCOS women with diabetes (both 1<sup>o</sup>PCOS and 2<sup>o</sup>PCOS), and AMH had increased ( $p < 0.05$ ) in PCOS women without diabetes. The area under the curve (AUC) indicate that PTX3 (AUC= 0.95, 0.90, 0.88, 0.85) and betatrophin (AUC= 0.89, 0.87, 0.86, 0.85) could potentially be used as greater predictive biomarkers in PCOS women (both 1<sup>o</sup>PCOS and 2<sup>o</sup>PCOS) with or without diabetes. Conclusion: Dysregulation of PTX3 and betatrophin may be associated with the metabolic consequences of PCOS. Therefore, we suggest that PTX3 and betatrophin may potentially serve as an independent predictor for the prognosis and development of PCOS in at-risk women, especially those with insulin resistance.

### **1. Introduction**

Polycystic ovary syndrome (PCOS) is an endocrine disorder associated with women infertility due to anovulation. PCOS is characterized by chronic anovulation and hyperandrogenism, either in the form of biochemical androgen excess or clinically as hirsutism, acne, and/or male pattern alopecia. Moreover, PCOS has been linked to obesity, type 2 diabetes mellitus (T2DM), dyslipidemia, hypertension, and heart disease (1). Although PCOS was described more than 50 years ago, the underlying cause of the disorder is still unclear. Recently, many studies have documented the presence of insulin resistance (IR) in both obese and lean PCOS patients, and some investigators consider IR to be an important risk factor for the development of metabolic syndrome in women with PCOS (2).

Accumulating evidence suggests that PCOS is a chronic inflammatory disease. The ovaries of women with PCOS exhibit inflammation and fibrosis; the peripheral blood of women with PCOS have reduced numbers of anti-inflammatory regulatory T cells and elevated serum levels of autoantibodies, and a recent study also indicated the pathogenic role of CD19+ B cells in the development of PCOS (3). Humoral innate immune molecule pentraxin 3 (PTX3), which belongs to the same superfamily of acute reactants as C-reactive protein (CRP), is a member of the long pentraxin family and has multifunctional properties for its capacity to interact with different types of ligands. In particular, PTX3 plays a non-redundant role in innate immunity by opsonizing selected pathogens and in female fertility. Recent research has demonstrated that PTX3 in circulation is associated with PCOS, but its role in PCOS is so far inconclusive. Unlike short pentraxin, PTX3 is produced at the local site of the inflammation, including follicle cells, and it is essential for the organization of the cumulus oophorus extracellular matrix and in vivo fertilization (4).

Betatrophin, also known as angiopoietin-like protein (ANGPTL8), is highly conserved in all mammalian species and is a newly identified circulating protein predominantly produced in the liver and adipose tissue. This protein regulates glucose homeostasis and lipid metabolism. It is induced as