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Evaluation of Pentraxin 3 in Poly Cystic Ovarian syndrome

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Abstract :

Objective. The aim of the current study was to assess the role of pentraxin 3 (PTX3) levels and thyroid hormone in Polycystic ovary syndrome (PCOS) women.

Materials and methods: Biochemical measurements of thyroid hormones levels by Minivans, while PTX3 measured by kit is based on sandwich enzyme-linked immune-sorbent assay technology.

Results: There was a highly significant decrease ($p<0.0001$) in the serum levels of PTX3 in the PCOS group when compared with control group. Also, there was no significant difference ($P>0.05$) between A1 and A2 in control group and the PCOS group, and a highly significant decrease ($p<0.0001$) in the serum levels of PTX3 in A1 PCOS group when compared with A1 control group, and in serum levels of PTX3 in A2 PCOS group when compared with the A2 control group. The optimal criterion value for PTX3 in groups was estimated depending on ROC curves, according to results, the test is positive if the test ≤ threshold (criterion values). Results indicated that the PTX3 is closely related to PCOS. T3 and T4 levels were decreased significantly ($p<0.05$), while TSH level was a significantly increased ($p<0.001$) in patients group when compared with control group.

Conclusion: PTX3 level was found to be low in newly diagnosed PCOS patients.

Keywords: Pentraxin, PTX3, PCOS, thyroid hormones.

تقييم البنتراكسين 3 في متلازمة المبيض المتعدد الكيسات

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مستخلص:

كان الهدف من الدراسة الحالية هو تقييم دور مستويات البنتراكسين 3 (PTX3) وهرمون الغدة الدرقية في النساء المصابات بمتلازمة المبيض المتعدد الكيسات (PCOS).

المواد والطرق: القياسات البيوكيميائية لمستويات هرمونات الغدة الدرقية بواسطة الشاحنات الصغيرة، في حين أن قياس PTX3 بواسطة مجموعة يعتمد على تقنية مقايسة الامتصاص المناعي المرتبط بالإنزيم. النتائج: كان هناك انخفاض معنوي كبير ($P<0.0001$) في مستويات PTX3 في مجموعة متلازمة تكيس المبايض بالمقارنة مع مجموعة السيطرة. كما لم يكن هناك فرق معنوي ($P>0.05$) بين A1 و A2 في مجموعة السيطرة ومجموعة PCOS، كما حدث انخفاض معنوي كبير ($P<0.0001$) في مستويات PTX3 في مصل الدم في مجموعة A1 PCOS بالمقارنة مع مجموعة السيطرة A1. ، وفي مستويات مصل PTX3 في مجموعة A2 PCOS بالمقارنة مع مجموعة التحكم A. تم تقدير قيمة المعيار الأمثل لـ PTX3 في المجموعات اعتمادًا على منحنيات ROC، ووفقًا للنتائج، يكون الاختبار إيجابيًا إذا كان الاختبار ≤ العتبة (قيم المعيار). أشارت النتائج إلى أن PTX3 يرتبط ارتباطًا وثيقًا بمتلازمة تكيس المبايض. انخفض مستوى T3 و T4 بشكل معنوي ($P<0.05$)، في حين ارتفع مستوى TSH بشكل معنوي ($P<0.001$) في مجموعة المرضى بالمقارنة مع مجموعة السيطرة.

الاستنتاج: وجد أن مستوى PTX3 منخفض لدى مرضى متلازمة تكيس المبايض الذين تم تشخيصهم حديثا.

الكلمات المفتاحية: البنتراكسين، PTX3، متلازمة تكيس المبايض، هرمونات الغدة الدرقية.

1. Introduction

Many women worldwide who are of reproductive age are affected by the diverse endocrine condition known as polycystic ovary syndrome (PCOS). This condition is frequently linked to enlarged and dysfunctional ovaries, high levels of androgen, insulin resistance, etc. According to estimates, one in ten women battle with PCOS and associated problems before menopause [1]. Menstrual abnormalities, recurrent anovulation, hirsutism, hair loss or androgenic alopecia, and acne are the hallmarks of PCOS, a diverse illness. Patients may appear at the time of diagnosis with a range of symptoms, depending on the phenotype of the illness, the patient's age, and lifestyle. The majority of individuals, however, seek medical care as a result of the clinical manifestations of the PCOS, which include: irregular menstruation, hyperandrogenism and infertility [2]. Although the highest ratio of luteinizing hormone (LH) to follicle-stimulating hormone (FSH) and Increasing gonadotropin-releasing hormone (GnRH) frequency is one of the known root causes of the PCOS [3], the exact etiology and pathophysiology have not been comprehensively understood or well-known [4]. Evidence points to the involvement of several internal and external variables, including as genetics, epigenetics, elevated testosterone levels (HA), insulin resistance (IR), and environmental variables. It's also important to note that the PCOS raises the chance of other issues including cardiovascular illnesses [5], type 2 diabetes mellitus(T2DM), metabolic syndrome [6], depression, and anxiety [7]. The raised in body-mass index (BMI) is an established risk factor for heart disease, stroke, and type 2 diabetes. Overweight and obese women are more exposed to reproductive issues such irregular menstruation and infertility. The PCOS, which affects 6-12% of women of reproductive age, and obesity are closely related [8].

Pentraxins are multi-functional protein families that include long pentraxins like pentraxin 3 (PTX3) and short pentraxins like serum amyloid P and C-reactive protein (CRP). Pentraxins are inflammatory indicators. A member of the pentraxin superfamily, PTX3 has a role in both acute and chronic inflammation as well as innate immunity. The

degree of the immune-inflammatory activity affects by how much PTX3 is present in the body [9,10]. PTX3 is a crucial element of humoral innate immunity that is secreted in response to microbial agents, tumor necrosis factor, and interleukin (IL)-1[11]. While the short pentraxin prototype CRP must be generated by the liver in response to interleukin IL-6 during the acute-phase reaction, PTX3 may be promptly released by both tissue cells and circulate leucocytes. PTX3 can be viewed as an early and "close-to-the-action" inflammatory sign as a result. In fact, long pentraxin 3 has a role in the control of inflammation, including activation of complement, and resistance to certain infections [12].

The thyroid hormone is widely recognized for regulating development, metabolism, and several other body processes. The hypothalamic-pituitary-thyroid axis is a self-regulatory circuit made up of the thyroid gland, anterior pituitary gland, and the hypothalamus. The main hormones that produced by the thyroid gland are thyroxine / tetraiodothyronine (T4) and triiodothyronine (T3). Thyrotropin-releasing hormone (TRH) from the hypothalamus, thyroid-stimulating hormone (TSH) from the anterior pituitary gland, and T4 work in synchronous harmony to maintain proper feedback mechanism and homeostasis [13]. Almost every organ system in the body is impacted by thyroid hormone, including the heart, autonomic nervous system, CNS, bone, and metabolism. Thyroid hormone typically activates the genes for elevating metabolic rate and thermogenesis when it attaches to its intranuclear receptor. An increase in metabolic rate results in more energy and oxygen being used. [14,15]. The thyroid hormone controls adult metabolism as well as metabolic processes necessary for healthy growth and development. It is generally known that body weight and the energy consumption are correlated with thyroid hormone levels [16].

2. Materials and methods

The study conducted in tikrit City, from 12/8/2022 to 1/2/2023. Blood samples were obtained from 60 PCOS women, and 30 from healthy (control), and age ranged between 17 to 49 years. Biochemical measurements of thyroid hormones levels by Minividas, while

PTX3 measured by kit is based on sandwich enzyme-linked immune-sorbent assay technology (ELISA) from Sun Long Biotech - China. Statistical Analysis: Data were analyzed by used XLSTATE software. Distribution was determined by used Student's t-test. The probability P were < 0.001=highly significant, P < 0.05 = significant, P > 0.05 = non-significant. Also, ROC (Receiveroperating characteristics) curves was Also measured.

3. Results & Discussion

A- PTX3

The mean (±SD) of PTX3 concentration in serum of control group and PCOS Patients groups are illustrated in table (1) and figure (1) and (2). There was a significant decrease (p<0.0001) in the serum levels of PTX3 in PCOS group when compared with control group. Also, there was no significant difference (P>0.05) between A1 and A2 in control group and in PCOS group, and a highly significant decrease (p<0.0001) in the serum levels of PTX3 in A1 PCOS group when compared with A1 control group, and in serum levels of PTX3 in A2 PCOS group when compared with A2 control group.

Table (1): The Mean ± SD of PTX3 (ng/ml) levels for Patients and Control Groups according to BMI

Groups	Mean ± SD of PTX3 (ng/ml)	
	Control	PCOS
Total	1947.83 ±187.42	1716.16 ±149.61
A1 (BMI =24-26)	1975.75± 188.00	1711.33± 155.59
A2 (BMI=29-32)	1892.00 ±182.66	1727.66± 155.28

P value				
Control/ PCOS	A1 Control /A2 Control	A1 PCOS / A2 PCOS	A1 Control / A1 PCOS	A2 Control / A2 PCOS
P < 0.0001	P > 0.05	P > 0.05	P < 0.0001	P = 0.0085

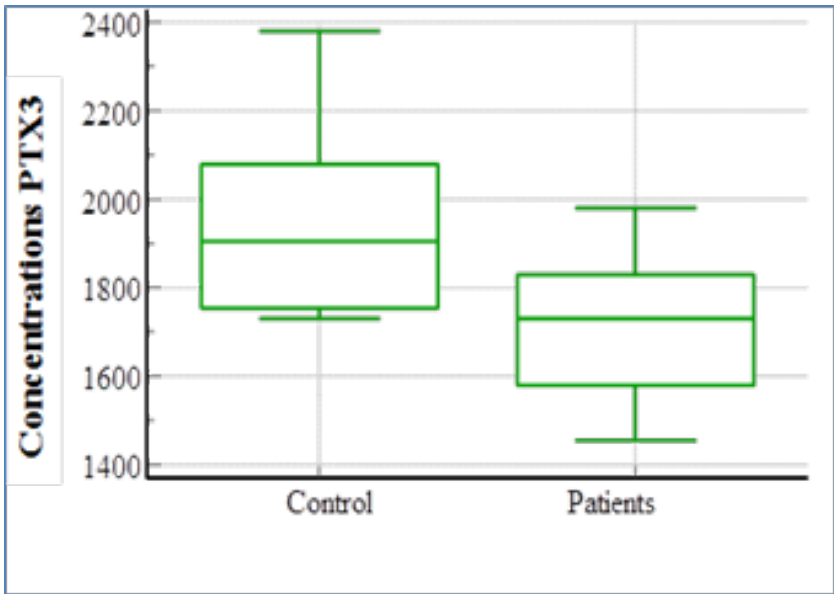

Figure (1): The Mean ± SD of PTX3 (ng/ml) levels for Patients and Control

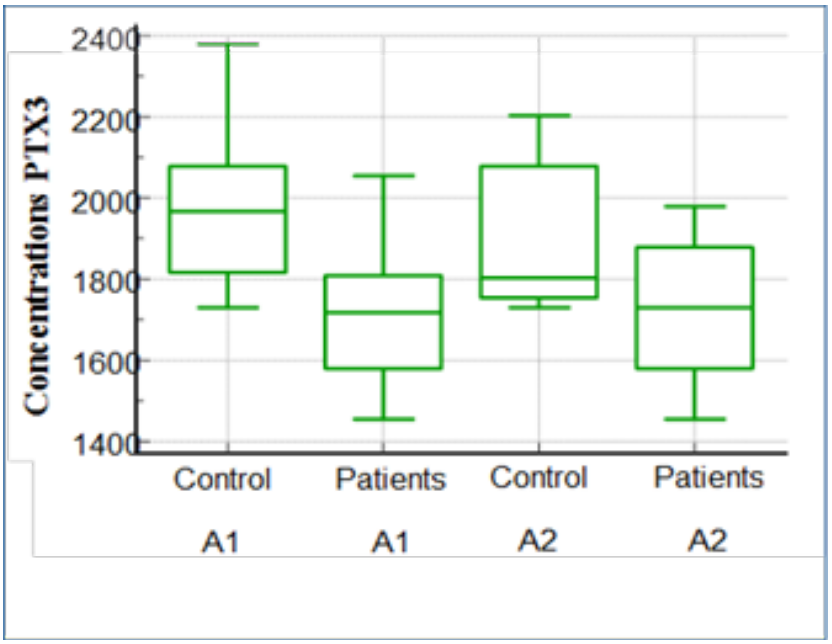

Figure (2): The Mean ± SD of PTX3 (ng/ml) levels for Groups according to BMI

The ROC curve were used to estimate the performance of PTX3 as a marker for diagnostic test, and to determine the appropriate criterion values. Area under the curve (AUC), Sensitivity% and specificity% which used as a measure of accuracy were shown in table (2) and figure (3). The opti-

mal criterion value for PTX3 in groups was estimated by depending on ROC curves, according to results, the test is positive if the test ≤ ≤1729.5 (criterion values). Results indicated that the PTX3 is closely related to PCOS.

Table (2): Predictive values of serum PTX3

Groups	Sensitivity	Specificity	Criterion	AUC
Control/ PCOS	**55.00%**	**93.33%**	**≤1729.5**	**0.822**

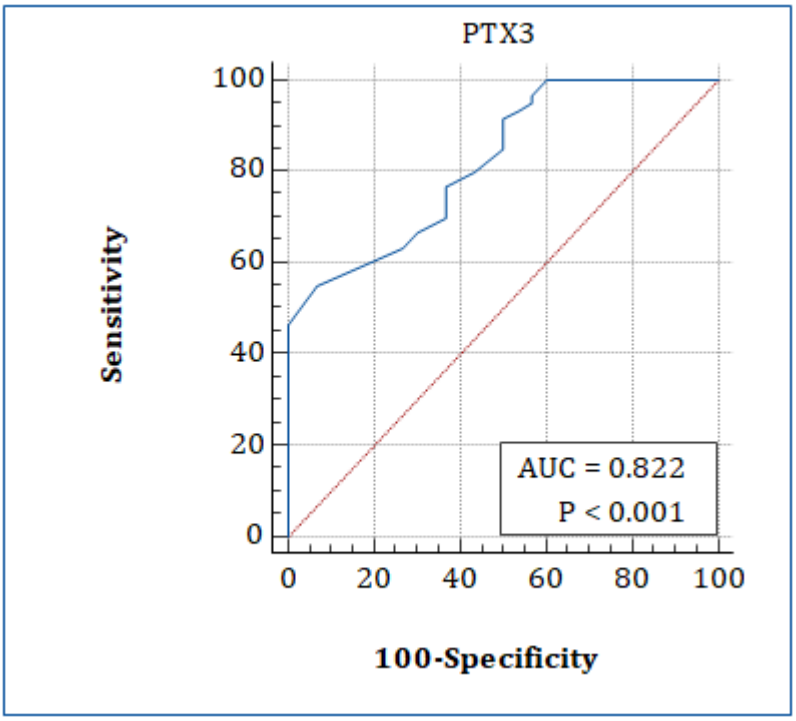

Figure (3): ROC curve of PTX3 in PCOS / Control

The findings of PTX3 levels in PCOS women are in agreement to Sahin's. et al. [17] and to Tosi et al. [18], that found lower PTX3 levels in PCOS cases than in that in control group, and the finding of Sari et al. [19] indicated no difference existed between women who had PCOS and those who did not, while they disagreement with the findings provided by Aydogdu et al. [20]. These differences understood and partially may be a result by used ELISA kits, produced from different manufactures [21]. A small number of research

have previously looked at the PTX3 levels of PCOS patients. PTX3 level was also discovered to be curiously greater, lower, or equal to the healthy controls [22].

Similar to data, Numerous studies have found that obese people and those with PCOS had lower PTX3 levels [23]. It has been found that: the adiponectin level is lowered secondary due to increased oxidative stress in adipose tissue. Probably, raised reactive oxygen species cause suppressed to PTX3 which leading to lowering level of PTX3 [24]. Low levels of PTX3, which block the classical complement pathway, may cause chronic inflammation in obese people [25]. Also, PTX3 has been found to be in low level in early hours of exposure to myocardial infarction. Low levels of PTX3 enhance thrombocyte aggregation because it suppresses the release of p-selectin from neutrophils, which may lead to atherosclerotic disease [26]. It was found not statistically significant in PTX3 level of female non-obese PCOS was lower than the obese females. As is well known, oxidative stress plays a significant role in PCOS. According to findings, elevated oxidative stress in female PCOS can reduce PTX3 levels. These results indicate that PTX3 levels are low, especially in the early stages of PCOS. New researches are required in this area because it is unclear if PTX3 levels are lower in PCOS, particularly in individuals who are obese [27]. A protein called PTX3 guards against metabolic syndrome. Obesity has been linked to its low level [29].

B- Thyroid hormones

The mean (±SD) of thyroid hormones Levels in serum of control group and PCOS patients are illustrated in table (3). The results revealed that T3 and T4 levels were decreased significantly ($p<0.05$) in patients group when compared with control group. While TSH level was a highly significantly increased ($p<0.001$) in patients group when compared with control group.

Table (3): The Mean ± SD of thyroid hormones

Groups / parameters	Mean ± SD		
	T3	T4	TSH
Control (n=30)	1.685±0.147	9.538±1.671	0.677±0.156
Patients (n=60)	1.151±0.194	9.046±1.370	1.831±0.137
P Value	<0.05	<0.05	<0.001

Numerous studies have already shown connections and associations of factors: hormonal, metabolic, genetic, and immunologic that may be a potential caused to the increased risk of thyroiditis in patients PCOS [30].

Insulin resistance, dyslipidemia and obesity are examples of metabolic abnormalities types that PCOS patients may have [4]. It has also been demonstrated that hypothyroidism decreases the generation and consumption of glucose, resulting in insulin resistance. Increased androstenedione /testosterone conversion, hyperlipidemia, reduced sex hormone-binding globulin (SHBG) levels, and weight gain are other symptoms of thyroid hormone deficiency [31]. Additionally, hypothyroidism may impact the functioning of the ovaries, resulting in anovulatory cycles [32]. Due to the strong association between insulin residence and disorder of reproductive with both hypothyroidism and suffering from PCOS, patients diagnosed with overt hypothyroidism are excluded to being diagnosed with PCOS. Therefore, thyroid dysfunction and PCOS may they have similar symptoms, such as irregular menstruation, ovulation issues, infertility, endometrial thickening, and the development of polycystic ovaries [33]. Therefore, it is imperative to rule out overt hypothyroidism prior to making the PCOS diagnosis since PCOS symptoms might be explained by thyroid malfunction rather than having both PCOS and hypothyroidism simultaneously [34,35].

The potential autoimmune pathophysiology of both illnesses may possibly contribute to the link between PCOS and thyroid dysfunction [36]. Similar to how estrogen and progesterone may not be in balance, autoimmunity also contributes to the pathophys-

iology of PCOS. Progesterone and estrogen work together to stimulate the immune system. Low progesterone levels are caused by anovulatory periods in people with PCOS. Additionally, it raises the estrogen to progesterone ratio, which may weaken the immune system and increase the risk of autoimmunity [37].

Conclusions

PTX3 level was found to be low in newly diagnosed PCOS patients. PTX3 is a protein that guards against metabolic syndrome. Obesity and coronary artery disease have been linked to its low level, according to reports. Low PTX3 levels are likely to contribute to PCOS. It was necessary to test the novel biomolecule PTX3 on PCOS patients.

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