

Assessment of Neuregulin4 function in patients with polycystic ovary syndrome disorder

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Abstract

Subject: Polycystic ovary syndrome (PCOS) is female disorder caused by cysts formation in ovarian that results disorder of hormones secretion and menstrual cycle. Neuregulin 4 (NRG4) is one of adipokines family members synthesis and release via adipose tissues, it acts as activator the epidermal growth factor receptor (EGFR).

Objective of the Study: Assessment role of NRG4 in PCOS patients.

Materials and Methods: Present study included 30 PCOS patients with 30 controls, the age individuals of tow group at study were 18 years and above of females. At this study measured serum NRG4 level by quantity method for all study individuals, the body mass index (BMI) also measured for all study individuals.

Results: Present study explain increase of NRG4 level in serum samples and BMI in PCOS patients group compared with control group.

Conclusion: Current study demonstrate role of NRG4 level that act as compensate mechanism in PCOS disorder.

Keywords: BMI, NRG4 and PCOS.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is present small sacs that fluid-filled at outer ovary edge, called cysts that have immature eggs, called follicles. The follicles cannot release of eggs by regular time. PCOS lead to hormones secretion disorders, this condition mostly occurs through reproductive time, and may absent the menstrual cycle (1). The main PCOS cause is unknown to yet, but the commonly PCOS causes are inherited, diabetes type 2, obesity and others. Addition, the important symptoms and signs of PCOS included hirsutism, gain of weight, acne, period irregularity, androgen hormones elevation and others (2).

Body Mass Index (BMI) is parameter refer to evaluation the weight and height of body that related together, and give indication to fat body index.

BMI measurement method is included divided weight (by Kg) on height square (by m²) of body (3). According to BMI can classify the body in to:

Less than 18.5 (Underweight)-

Between 18.5-24.9 (Normal)-

Between 25-29.9 (Overweight)-

More than 30 (Obese)-

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How to cite this article: Lara Balasim Al-Dahy, Yasir Khaleel Almusawi, Arwa Fadil Haqi Ballur, Assessment of Neuregulin4 function in patients with polycystic ovary syndrome disorder, J PHARM NEGATIVE RESULTS 2022;13: 676-678.

Access this article online

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DOI:
10.47750/pnr.2022.13.04.090

Neuregulin 4 (NRG4) is protein factor encoded via NRG4 gene that mostly exist in brown adipose tissue, attend to neuregulin family as one of members it (4). NRG4 function is important activator for erb-b2 receptor tyrosine kinase 4 (ERBB4) that start tyrosine phosphorylation in cytoplasm to formation cell signaling, especially at paracrine and endocrine signal systems. Also, there are other functions for NRG4 in human body for example apoptosis and inflammation inhibition (5).

This study aims to explain of the NRG4 role in females with PCOS because the obesity considers as one of the causes PCOS disorder.

Material and Methods

This study was enrolled 60 females classify into 2 groups, first group of 30 PCOS females (patients) and second group of 30 healthy females (controls). All study's individuals were diagnosed as PCOS and control depended on the clinical and laboratory examinations. The ages of the all-groups individuals were 18 years and above of females. Blood samples (5 ml) was obtained from all individuals then separated by centrifuge to obtain serum sample; this serum samples use to quantity measurements by immunoassay method for serum NRG4 level measurement. BMI also measured for all groups individuals. The current study done in Al-Yarmouk technical hospital – Baghdad -Iraq. See Figure 1.

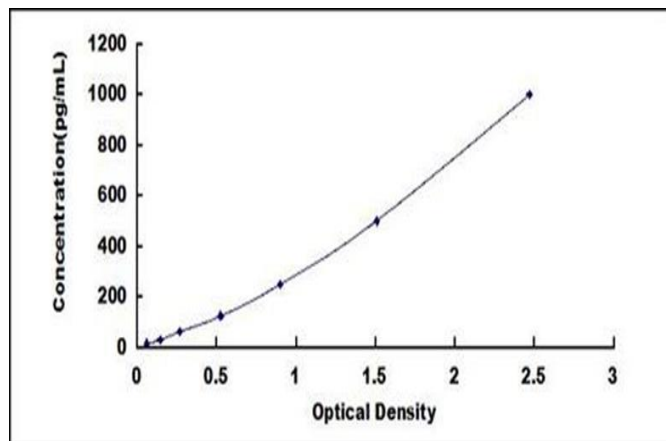


Figure 1: Standard curve of NRG4

*Technique called Sandwich ELISA Catalog Number. CSB -EL016080HU - CUSABIO company – USA

Statistical analysis:

This comparison study included comparison of PCOS with control groups according to NRG4 level in serum and BMI via used T-test statistic method (mean + standard deviation (SD)) and p-value (less than 0.05 consider as significant value).

Results

The present study results confirm significant values for biomarkers after done comparison between groups with PCOS and control groups. Depending on NRG4 level in serum samples, explained the significant high level in group with PCOS (412.3+17.7) compared with control (230.1+16.8). In addition, BMI show significant elevation in group with PCOS (29.9 + 1.9) compared with control (21.2 + 2.4). See table 1 and figure 2 and 3.

Table 1: Comparison depend on serum NRG4 level and BMI by T test statistical method between PCOS group and control group

Parameter	PCOS group (No. 30) (mean±SD)	Control group (No. 30) (mean±SD)	P-value
Serum NRG4 level (pg/ml)	412.3±17.7	230.1±16.8	<0.001**
BMI (Kg/m ²)	29.9 ± 1.9	21.2 ± 2.4	<0.001**

**Significant value

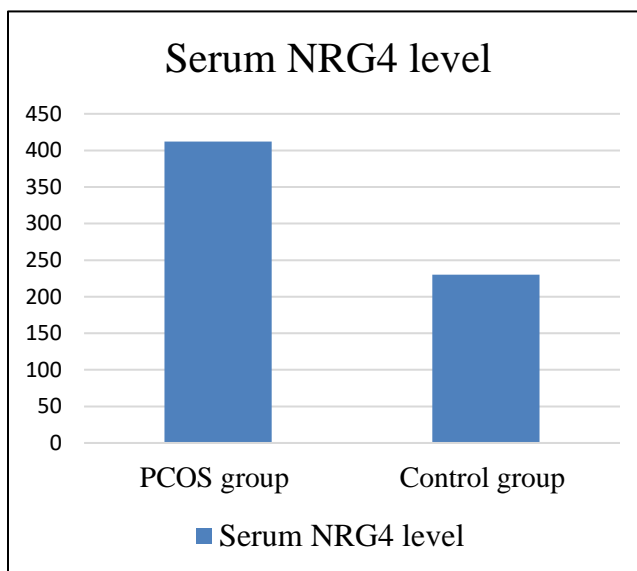


Figure 2: Comparison between PCOS and control groups according to NRG4 via T test method.

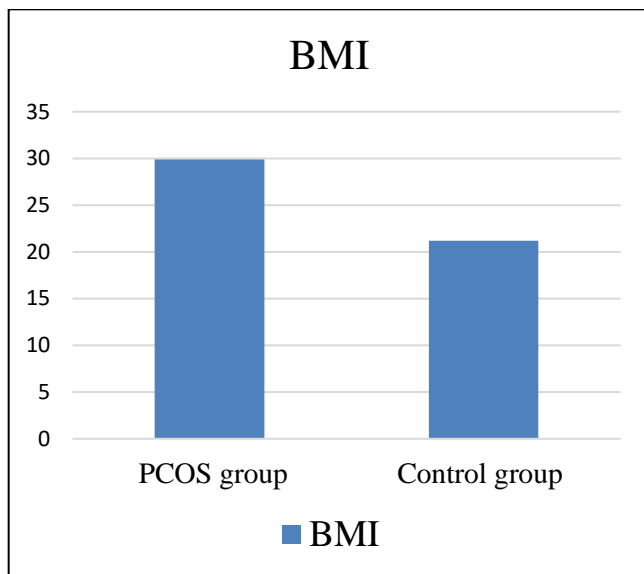


Figure 3: Comparison between PCOS and control groups according to BMI via T test method

Discussion:

PCOS is most common disorders of females caused by cyst formation in ovarian that results defect at hormones secretion and menstrual cycle (6). PCOS causes are various but the mainly cause is increase of BMI (obesity) (7). The current study results confirm BMI level elevation at group with PCOS compared with control group, these results show obesity role on PCOS by relation it with the metabolic syndrome that led to function alteration of hypothalamic pituitary ovarian (HPO) axis.

Obesity is most cause to high level of insulin and ovarian androgen production, also the obesity already coupled with adipose tissues elevation that cause androgens aromatization to estrogen that can act negative feedback for HPO axis and results disturbance gonadotropin secretion. In addition, the adipose tissues elevation can lead to hyperinsulinemia with generation the insulin resistance. These all condition can failure ovulation and cause dysregulation of menstrual cycle (8). At present study results the BMI elevation at PCOS patients group consider as indicator to present the elevation of adipose tissues, the adipose tissues can act as gland to synthesis and secretion many of biomarkers such as adipokines.

NRG4 is consider as one of adipokines synthesis in adipose tissue then secreted into blood stream and secretion, it functions as activator the epidermal growth factor receptor (EGFR) (9). This receptor (EGFR) has important function in the healthy luteinizing hormone-releasing hormone (LHRH) function that it responsible for female normal pubertal development because the deficiency of EGFR can cause impaired LHRH secretion. Also, PCOS is classified as a low-class chronic inflammatory disease for this disease type the NRG4 become elevated as compensation mechanism

through disease (10).

The present results of study agree with KRUSZEWSKA, Jagoda and et al 2022 that also demonstrated increase NRG4 level in PCOS females that have elevation BMI (11).

Acknowledgment: Non

Ethical Approval: This study was conducted with the permission of the participants and the relevant centers .

Funding: This research received no external funding

Authorship Contributions: All authors have read and agreed to the published version of the manuscript.

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