



## Evaluation of serum Neuregulin4 level in Polycystic ovary syndrome patients

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ABSTRACT

**Subject :** Polycystic ovary syndrome (PCOS) is most common female disease characterized by characterized by ovarian cyst formation that lead to irregular menstrual cycle and hormones secretion .Neuregulin 4 (NRG4) is one of adipokines members that it synthesis and secretion from adipose tissues ,it act to active the epidermal growth factor receptor (EGFR) .

**Objective of the Study:** Assessment of serum NRG4 level in PCOS patients .

**Materials and Methods:** This study was done on 30 patients with PCOS and 30 control, the all subjects age within this study were more than 18 years of females .After obtained serum , immediatly used quantity method for measured level of serum NRG4 concentration . Also the all individuals were measured the body mass index (BMI

**Results:** This study shows elevation of serum NRG4 level and BMI in PCOS group compare with control group .

**Conclusion:** This study confirms that serum NRG4 concentration level can act as compensate mechanism at PCOS disease .

**Keywords:**

PCOS ,NRG4 and BMI

### Introduction

Polycystic ovary syndrome (PCOS) is exist small fluid-filled sacs develop along the outer ovary edge , known as cysts. The cysts contain immature eggs, known as follicles. The follicles impair to regularly release of eggs . PCOS coupled with problem with hormones that happens during the reproductive years , and may not have periods very often (1) . The exact cause of PCOS is unknown , but there are some commonly causes of PCOS such as obesity , diabetes type 2 , inherited and others Important PCOS signs and symptoms included period irregularation , gain of weight , acne , hirsutism , androgen hormones increase and other(2) .

Body Mass Index (BMI) is indicator refer to assessment of body weight

related to body height , and give suggestion to fat body containing . BMI measured via divided weight (Kg) on height square (m<sup>2</sup>) of body (3) . BMI classify the body into :-

Body Mass Index (BMI)	Weight Status
Below 18.5	Underweight
18.5 - 24.9	Normal
25.0 - 29.9	Overweight
30.0 plus	Obese

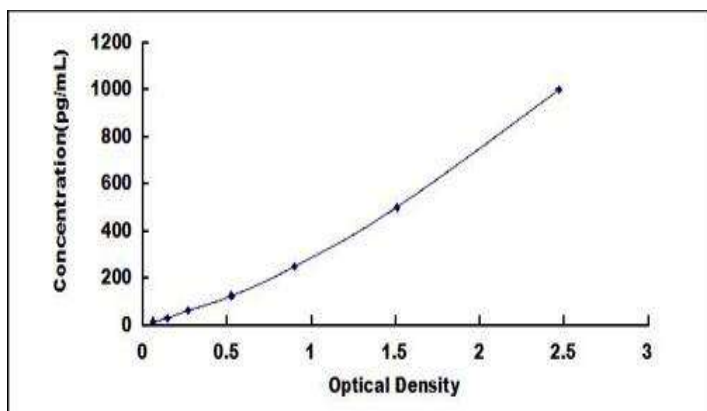
Neuregulin 4 (NRG4) is protein encoded by NRG4 gene that mostly present at brown adipose tissue cells , classify as one of neuregulin family member (4) . NRG4 important for erb-b2 receptor tyrosine kinase 4

(ERBB4) activation that begin cytosolic tyrosine phosphorylation to formation signaling between cells , specially in , endocrine and paracrine signal systems . Also , the NRG4 has other functions in human body such as inflammation and apoptosis inhibition (5).

This study aim to evaluation of serum level of NRG4 in PCOS patients due to the one of important causes the PCOS is obesity .

**Material and method**

The current study was included 60 women's divided into 2 groups, group 1 of 30 women with PCOS ( patients ) and group 2 of 30 healthy women (controls) . All group's individuals diagnosed as control or PCOS by depended on the clinical examination and laboratory investigations . Individual ages of the all groups were more than 18 years of females . 5 ml of blood was withdraw from all groups then immediately separation by centrifuge to obtain serum sample to use for the quantity measurements via immunoassay method ( technique called Sandwich ELISA Catalog Number. CSB -EL016080HU - CUSABIO company - USA ) for assessment the serum NRG4 level , also BMI measured for all study individuals .The present study was done in Al-yarmouk technical hospital – Baghdad from (.....) 2022 to (.....) 2022 after agree the (.....) . See figure 1



**Figure 1: Standard curve of serum NRG4 level**

Statistic analysis

The current study enrolled comparison of PCOS group with control group depending on serum NRG4 level and BMI by use method of T-test (mean ± standard deviation (SD)) and p-value (significant value < 0.05)

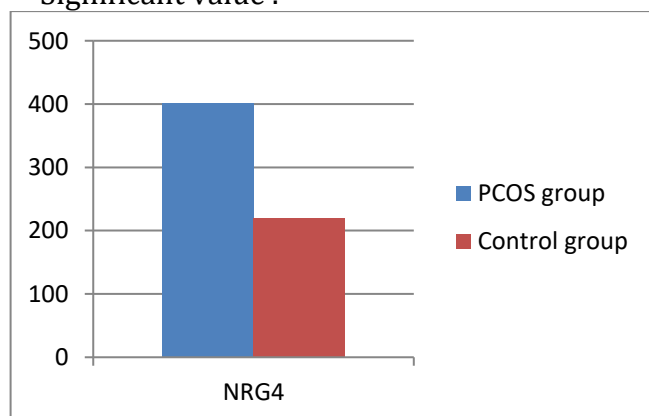
**Results**

This study results confirm some statistic significant values of biomarkers after comparison between PCOS and control groups . According to serum NRG4 level ,show significant increase in PCOS group (402.4±18.7 ) compared with control group (220.3±17.8) . On the other hand , According to BMI ,show significant increase in PCOS group (28.9 ± 1.8 ) compared with control group (20.3 ± 2.1) . See table 1 and figure 2 and 3.

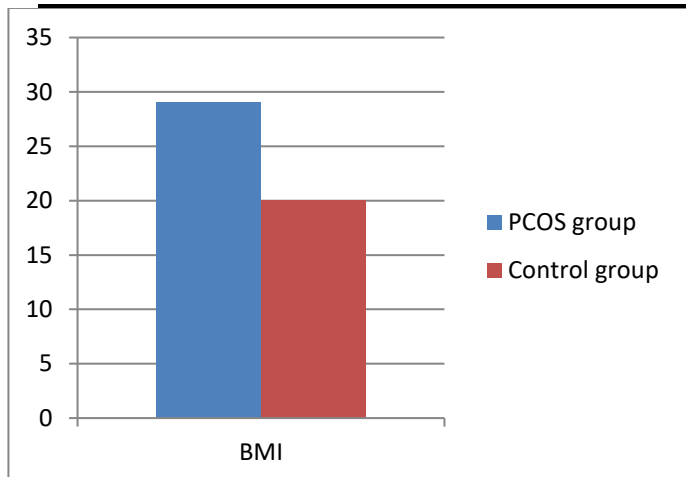
**Table 1 : Comparison depend on serum NRG4 level and BMI by T test statistical method between PCOS group and control group**

Parameter	PCOS group No. 30 (mean±SD)	Control group No. 30 (mean±SD)	P-value
Serum NRG4 level (pg/ml)	402.4±18.7	220.3±17.8	<0.001*
BMI (Kg/m <sup>2</sup> )	28.9 ± 1.8	20.3 ± 2.1	<0.001*

\*\*Significant value .



**Figure 2 : Comparison depend on serum NRG4 level by T test statistical method between PCOS group and control group**



**Figure 3 : Comparison depend on BMI by T test statistical method between PCOS group and control group**

### Discussion

PCOS is consider common females disorders characterized by ovarian cyst formation that lead to irregular menstrual cycle and hormones secretion (6) . PCOS have various causes but the main cause is obesity ( increase of BMI ) (7) . This study result demonstrate elevation of BMI level at PCOS group compared with control group , this finding explain role of obesity on PCOS via relation it with metabolic syndrome that lead to alteration of hypothalamic pituitary ovarian (HPO ) axis function

Obesity consider as common cause to increase of insulin level and production of ovarian androgen , also the obesity coupled with elevation of adipose tissues that cause androgens aromatization to estrogen that act negative feedback on the HPO axis and lead to disturbance gonadotropin production . On other hand , elevation of adipose tissues can result to hyperinsulinemia with insulin resistance . These all condition can impaired ovulation and cause abnormal menstrual cycle (8) .

The present of elevation of BMI at PCOS group give indicator to exist the high of adipose tissues , these adipose tissues act as gland to secretion various biomarkers like adipokines.

NRG4 is one of adipokines members that it synthesis and secretion from

adipose tissues ,it act to active the epidermal growth factor receptor (EGFR) (9) . The EGFR have important role in the healthy luteinizing hormone-releasing hormone (LHRH) function that it responsible for female normal pubertal development because any deficiency in EGFR can cause failed LHRH secretion . Also , PCOS is consider as a low-grade chronic inflammatory disease and at this type of disease the NRG4 levels become high as compensation mechanism during disease (10) . This study results agree with KRUSZEWSKA, Jagoda and et al 2022 that also confirm elevation NRG4 level in PCOS patients that have BMI elevation (11)

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