Estimation the level of Neudesin in Polycystic ovarian syndrome patients

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Abstract. Polycystic ovary syndrome (PCOS) is a common hormonal condition that affects women of reproductive age. The aim of the current study were to detect the analytic estimation of serum Neudesin as well as studying the relation between this biomarker and Body Mass Index (BMI), age, waist /hip ratio and type of infertility in Polycystic ovarian syndrome patients. Methods: The current study was conducted on 90 women (60 patients with polycystic ovary syndrome and 30 healthy control) ranging in their ages from 15-39 years in period from March to June, 2023. Blood samples were collected from women and serum samples prepare to estimate the serum levels of Neudesin. Results: The results indicated that there was a significant decrease (P-Value< 0.05) in Neudesin levels in patients group when compare with control group. Also, after dividing the group of patients into three groups according to ages, we notice a significant decrease (P-Value< 0.05) in Neudesin levels in age less than 20 years when compare with age 20-29 years and age 30-39 years, and a significant decrease (P-Value< 0.05) in Neudesin levels in age 20-29 years when compare with age 30-39 years. On the other hand, When dividing the group of patients according to body mass index we notice a significant increase (P-Value< 0.05) in Neudesin level in overweight group when compare with obese group and significant increase(P-Value< 0.05) in Neudesin level in moderate W/H ratio group than high W/H ratio group and no significant difference found between primary and secondary infertility. Conclusion: The current study concluded that a Neudesin is a prognostic marker and early detection of polycystic ovarian syndrome.

1 Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder characterized by chronic ovulation dysfunction and overabundance of androgens; it affects 6–20% of women of reproductive age [1]. PCOS involves various pathophysiological factors, and affected women usually have significant insulin resistance [2], which is a major cause of PCOS [3]. IR and compensatory hyperinsulinaemia have differing pathogeneses in various tissues, and IR varies among different PCOS phenotypes [1]. Recent studies have suggested that genetics, epigenetic changes, environmental factors, oxidative stress, chronic low-grade inflammation, mitochondrial dysfunction, and metabolic disorders are involved in PCOS, thus damaging normal ovarian function [4, 5, 6, 7, 8].

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Neudesin (also known as NENF (neuron-derived neurotrophic factor) is a 172 amino acid secreted protein that belongs to the cytochrome b5 family and MAPR subfamily. Neudesin possesses neurotrophic activity, which is enhanced by binding to heme, and may contribute to neuronal differentiation and neural cell proliferation [9]. The distribution pattern of Neudesin gene expression is very similar to the progesterone receptor in the rat forebrain, especially regions including anteroventral, periventricular, arcuate and ventromedial nuclei. Therefore, it has been suggested that neudesin might be involved in regulation of neuroendocrine functions via progesterone receptors [10]. And neuroendocrine abnormalities contribute to the pathogenesis of PCOS [11].

2 Methods

2.1 Subject population

Ninety subject's women were concluded in this study, 60 as patient group with polycystic ovarian syndrome and 30 as control group which are apparently healthy women with ages range from (15 – 39) years. The Patient females were collected from private clinic for obstetrics and gynecology in AL-Hilla city were the patients are diagnosed by using of sonograph technique and clinical feature according to 2003 Rotterdam criteria [12] from March to June 2023. Patients group were divided into subgroups according to age, body mass index, waist /hip ratio and type of infertility.

2.2 Exclusion criteria

Women with chronic diseases such as kidney or liver disease, hyperprolactinemia, diabetes, high blood pressure, or Cushing's syndrome, as well as women taking thyroid hormones or antithyroid medications, were excluded from the study. In addition, women who received hormonal therapy, including oral contraceptive pills, were also excluded.

2.3 Collection of blood samples

Blood samples were drawn from vein by using 5 ml disposable syringe. The samples were emptied in gel tube without of anticoagulant for preparing of serum. Blood was left at room temperature for 10 minutes for clotting then it will be Centrifuge (at 2000-3000 RPM) for 20 minutes, and then serum was separated and freezing at -80 °C until time for performed the laboratory analysis for study.

2.4 Body Mass Index (BMI)

The computation of BMI is performed by electronic balance and height device for calculating the weight and height. The most commonly used definitions, established by the World Health Organization [13] in 1995 and published in 2000, with some modification done in 2004, the equation is: BMI = weight (kg)/height (m2)

2.5 Waist /Hip ratio

The Waist Hip Ratio is calculated by dividing the waist measurement (just above the upper hip bone) by the hip measurement (widest part) by using measuring tape, The formula is: WHR= waist circumference / hip circumference. Ideally, women should have a waist-to-hip ratio of 0.8 or less, whereas men should have a waist-to-hip ratio of 0.95 or less [14].

2.6 Estimation of serum Neudesin concentration

The assessment of serum Neudesin concentration is performed by (Shanghai YL Biont/China) sandwich immunoassay technique (enzyme linked immunosorbent assay – automated microtiter plate), ELIZA reader (Bio kit YLA3718HU).

2.7 Statistical analysis

For statistical analysis, IBM-SPSS statistics 24 was used. T-test , one way ANOVA and Standard Error were applied to test the variability and the statistical significance of this experiment. In addition, effects are considered statistical significant at P value < 0.05 [15, 16].

3 Results

The result in figure (1) showed a significant decrease (P value <0.05) in Neudesin concentration of PCOs group (0 .75 ±0.05) ng/ml in comparison with that of control group (2.86 ±0.06) ng/ml.

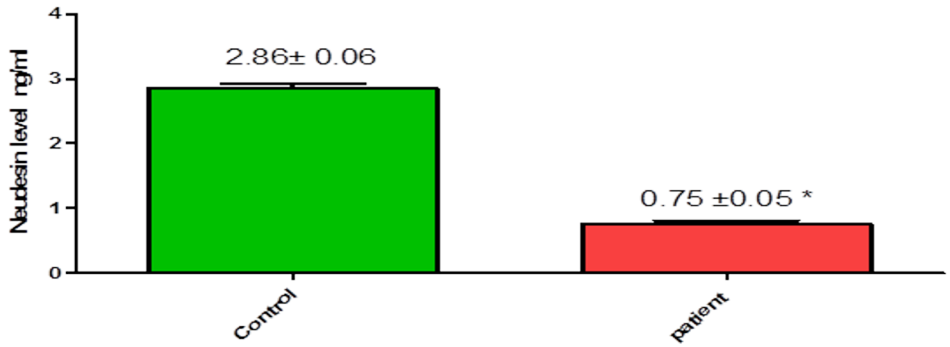

Fig. 1. Neudesin level (ng/ml) in patients group compare with control group. * refer to significant differences (P- Value <0.05) Patients n=60, Control n=30.

The level of Neudesin in three groups of patients as shown in figure (2). The results indicate the presence of a significant decrease (P< 0.05) in serum Neudesin in age less than 20 (0.24 ±0.019) ng/ml in comparison with age 20-29 and age 30-39 groups (0.658±0.042) ng/ml and (1.25±0.028) ng/ml respectively. Also there is a significant decrease (P< 0.05) in age 20-29 (0.658±0.042) ng/ml when compare with 30-39 group (1.25±0.028) ng/ml.

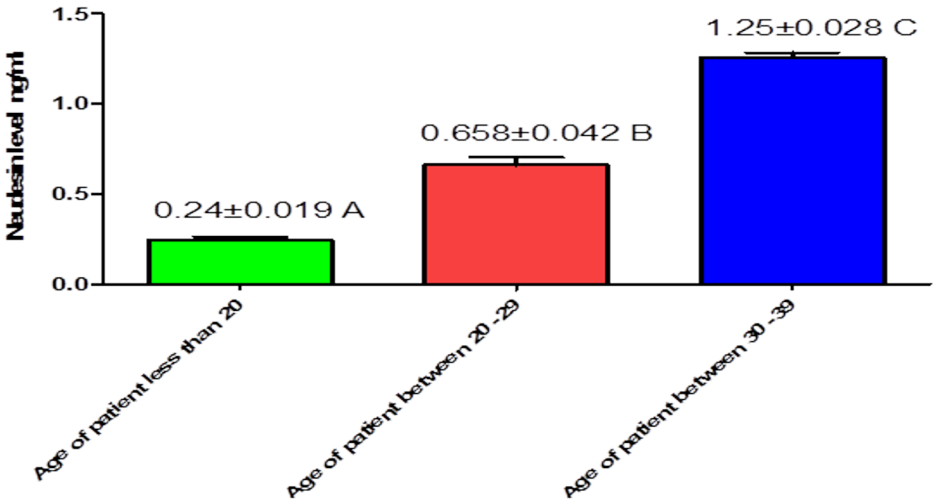

Fig. 2. Level of Neudesin (ng/ml) in age less than 20, 20-29, 30-39 group of patients with poly cystic ovary syndrome. Different letter refer to significant differences (P- Value <0.05). Age less than 20 n=15, 20-29 n=25, 30-39 n=20.

Figure (3) show to presence of significant decrease ($p<0.05$) in neudesin level in obese group (0.43±0.04) ng/ml as compared to overweight group (1.2±0.03) ng/ml of poly cystic ovary syndrome patients.

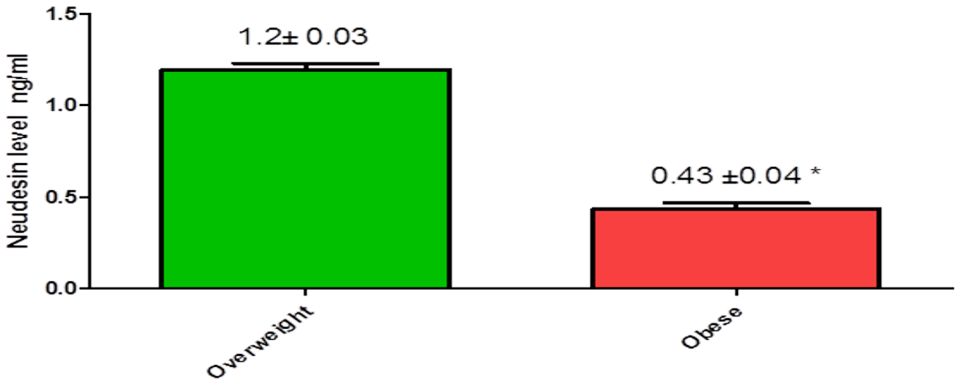

Fig. 3. Neudesin level (ng/ml) in obese group compare with overweight group of poly cystic ovary syndrome patients. * refer to significant differences (P- Value <0.05) obese n=35, overweight n=25.

Figure (4) show to presence of significant decrease ($p<0.05$) in Neudesin level in high waist/hip ratio group (0.5±0.04) ng/ml as compared to moderate waist/hip ratio group (1.25±0.03) ng/ml of poly cystic ovary syndrome patients.

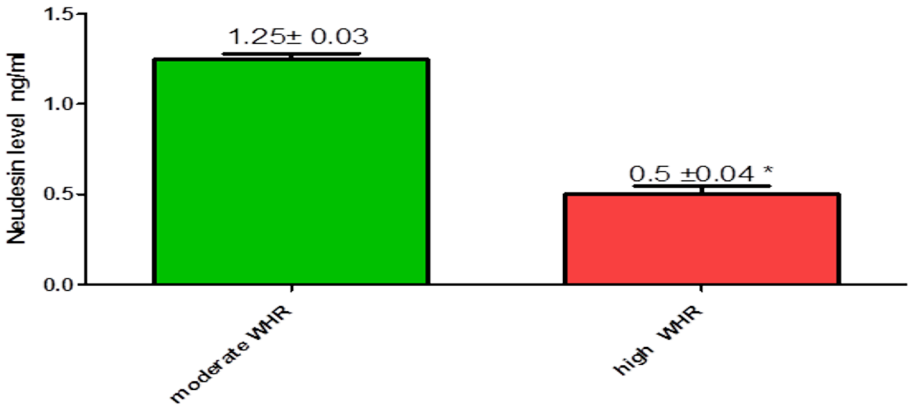

Fig. 4. Neudesin level (ng/ml) in high WHR compare with moderate WHR group of poly cystic ovary syndrome patients. * refer to significant differences (P- Value <0.05) moderate WHR n=20, high WHR n=40.

Figure (5) show no significant difference in Neudesin level in primary infertility group (0.75±0.08) ng/ml as compared to secondary infertility group (0.74±0.08) ng/ml of poly cystic ovary syndrome patients.

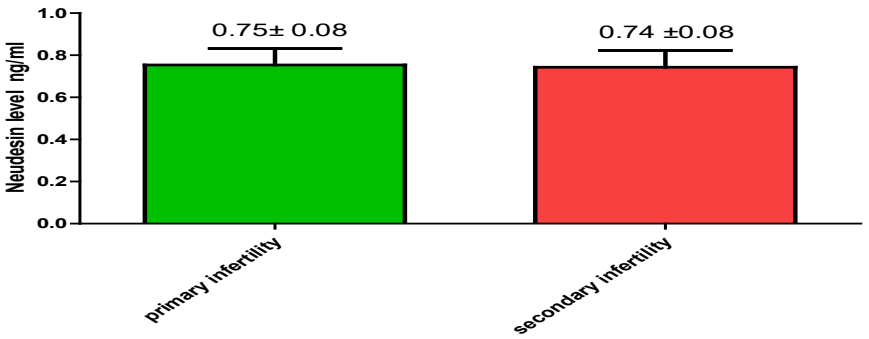

Fig. 5. Neudesin level (ng/ml) in primary infertility compare with secondary infertility group of poly cystic ovary syndrome patients. Primary infertility n=30, secondary infertility n=30.

4 Discussion

The current study in figure (1) indicates a significant decrease in Neudesin level in PCOs women in compare with control group. The present results agree with recent studies has been postulated a several mechanisms for this decrement with Neudesin, one of these explanation may depended on association or binding of a group of protein like heme-binding domain related to cytochrome p450 monooxygenase system called progesterone receptor membrane protein component 1(PGRMC1) has a diverse effect on cholesterol/ steroid biosynthesis by interact with cytochrome 450 and one of these protein is a Neudesin, therefor low level of neudesin with low level of progesterone contribute to suppress a negative feed on pituitary gland effect on GnRh and inhibition of GnRh but release of LH [10,17].

Another mechanism for neudesin low level may lead to immortalized GnRh neurons (GT1-7cells) and calcium level in GnRh has been inhibited leading to FSH level decrement and LH release [18].

The activation of cytochrome p450 may be associated by neudesin decrement level and lead to high level of androgen biosynthesis due to high LH level and effect on theca cells to convert of cholesterol in a series in theca cells to form pregnenolone then dihydropandrostendione and androstendione to form testosterone and dihydrotestosterone [19, 20].

The explanation of low Neudesin level in PCOs may be discussed in present study because hydroandrogenism in PCOs associated with high level of LH and FSH decrement [21] so that decrement of Neudesin may be related with high LH level because it's a binding protein to progesterone receptor lead to release of progesterone so low level of neudesin with low level of progesterone then lead to suppress of feedback of progesterone on LH and high pulsatile of LH level in pituitary gland act on theca cell to high production of androgen by activation of cytochrome 450 17C.

The figure (2) show a highly significant decrease in neudesin level in age less than 20 years than others, no previous study has been studied the neudesin level in ages different group according to age therefor the explanation of current results may be discussed due to the roles of Neudesin as neurotropic hormone regulate energy homeostasis and food intake and decrease in physical activity and increase food intake, also low expression of neudesin to paraventricular nuclei and aracuate nuclei which are consider as an important area for regulation of appetite in hypothalamus and mechanism of activation to melanocortin signaling by melanocortin-4 receptor (MC4R) lead to increase food intake in these ages less than 20 in compare with other ages. Only one study Celikkol et al (2022) has been proved that neudisn level was low in adolescents subject than others [21]. Also Byerly et al (2013) has been postulated that administration of neudesin increase proopiomelanocortin (POMC) lead to decrease food intake in adolescents [22].

The present study revealed a significantly decrease level of neudesin in obese polycystic ovary women in compare with overweight as in figure (3). Many previous studies has been showed a lower neudesin level in obese subject and negative correlation between neudesin and BMI in adults and animal models [23].

Other studies agree with current results and has been postulated that a potential role in development of obesity and food intake and regulation of appetite [24, 25]. In study of Bozkaya et al (2020) has been proposed that lower level of Neudesin in obese and overweight polycystic ovarian patients as compare with control (healthy group) [26, 27]. Also a study of Byerly et al (2013) has been studied experimentally administration of neudesin and showed decrease in food intake by increasing POMC and MC4P/mRNA expression [21].

Former studies has been investigated a level of Neudesin in subcutaneous and visceral adipose tissue with and without diabetes type 2 and found do not differs between obese and lean subjects, but another study showed a significant correlation between Neudesin and BMI in children [28, 29].

The physiological role mechanism have been examined in mice feed on high fat diet or normal chow food and indicate low level of Neudesin in knockout mice of Neudesin with increase food intake but mice wild type and Neudesin knockout mice fed a high fat diet showed a resistance to diet induced obesity [22].

The negative correlation between Neudesin level and BMI are proved in present study in obese subject than overweight give that a Neudesin is a good prognostic markers in PCOs associated with obesity or higher BMI.

The results of figure (4) showed a significant decrease in Neudesin level in high waist /hip ratio than moderate ratio, no previous study deals with the relation between W/H ratio and Neudesin level.

The discussion on this results depend on body mass index because the women patients that suffer from high BMI at the same has a high W/H ratio therefor the higher ratio may also consider as one of the obesity indicator and related negatively with Neudesin. Also may be related with adiposity and fat deposition and central obesity, in addition W/H ratio is a risk factor of obesity and may be related also with food intake [30, 31].

Current results as in figure (5) indicate no significant differences between primary and secondary fertility in PCOs women patient. No previous studies deals with a polycystic ovarian syndrome and infertility types therefor a non-differences between primary and secondary infertility may be discuss as Neudesin is a neurotropic hormone which effect on hypothalamus-pituitary axis, on theca cells, also on progesterone level at the same mechanism in both types of infertility.

5 Conclusion

The current study concluded that Neudesin can be considering as a prognostic marker for detection of polycystic ovarian syndrome.

References

1. H. Zhao, J. Zhang, X. Cheng, X. Nie, B. He, Journal of Ovarian Research, **16(1),** 9 (2023).
2. S.H. Alwaid, A. Noori-Aldujaili, AIP Conference Proceedings, **2386(1)** (AIP Publishing, 2022).
3. A.N.G. Al-Dujaili, W.R.H. Al-Kraity, Research Journal of Pharmacy and Technology, **11(1),** 317-320 (2018).
4. B. Yilmaz, P. Vellanki, B. Ata, B. Yildiz, Fertil Steril., **110(3),** 523-33 (2018).
5. Q. Liu, Y. Xie, L. Qu, M. Zhang, Z. Mo, Taiwan J Obstet Gynecol., **58(4),** 447–53 (2019).
6. D. Armanini, M. Boscaro, L. Bordin, C. Sabbadin, Int J Mol Sci., **23(8),** 4110 (2022).
7. M. Malamouli, I. Levinger, A. McAinch, A. Trewin, R. Rodgers, A. Moreno-Asso, J Mol Endocrinol., **68(3),** 11–23 (2022).
8. H. Sadeghi, I. Adeli, D. Calina, A. Docea, T. Mousavi, M. Daniali, et al., Int J Mol Sci., **23(2),** 583 (2022).
9. A.N.G. Al-Dujaili, W.R.H. Al-Kraity, Research Journal of Pharmacy and Technology, **11(1),** 317-320 (2018).
10. S.L. Petersen, K.A. Intlekofer, Moura-Conlon PJ, et al., Front Neurosci., **7,** 164 (2013). doi: 10.3389/fnins.2013.00164.
11. A. Szeliga, E. Rudnicka, M. Maciejewska-Jeske, M. Kucharski, A. Kostrzak, M. Hajbos, B. Meczekalski, International journal of environmental research and public health, **19(5),** 3089 (2022).
12. European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine ESHRE/ASRM. Consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Human Reproduction,* **19,** 41–47 (2004).

13. WHO, Expert consultation, Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies, *The Lancet,* 157-163 (2004).
14. WHO Waist circumference and waist–hip ratio: report of a WHO expert consultation, (Geneva, 2008)
15. R.S. Toma, S.K. Al-Hadraawy, A.A.J. Aljanaby, AIP Conf. Proc., **2977,** 040093 (2023).
16. R.S. Toma, A.A.J. Aljanaby, S.K. Al-Hadraawy, AIP Conf. Proc., **2977,** 040127 (2023).
17. W.R.H. Al-Kraity, A.N.G. Al-Dujaili, Research Journal of Pharmacy and Technology, **10(6),** 1657. (2017).
18. C.J. Krebs, E.D. Jarvis, J. Chan, et al., Proc Natl Acad Sci U S A., **97(23),** 12816–12821 (2000). doi: 10.1073/pnas.97.23.12816.
19. H.J. Hammod, A.N. Al-Dujaili, M. NooriAl-Dujaili, Res J Pharm Biol Chem Sci., **7(3),** 804-8 (2016).
20. R.L. Rosenfield, D.A. Ehrmann, Endocr Rev., **37(5),** 467–520 (2016). doi: 10.1210/er.2015- 1104.
21. S. Salam, A.N. Al-Dujaili, AIP Conference Proceedings, **2547(1)** (AIP Publishing, 2022).
22. Aliye Çelikkol, Çiğdem Binay, Özge Ayçiçek, Savaş Güzel, J Clin Res Pediatr Endocrinol., **14(1),** 69-75 (2022).
23. M.S. Byerly, R.D. Swanson, N.N. Semsarzadeh, P.S. McCulloh, K. Kwon, S. Aja, T.H. Moran, G.W. Wong, S. Blackshaw, Am J Physiol Regul Integr Comp Physiol., **304,** 1085- 1095 (2013).
24. H. Ohta, M. Konishi, Y. Kobayashi, A. Kashio, T. Mochiyama, S. Matsumura, K. Inoue, T. Fushiki, K. Nakao, I. Kimura, N. Itoh, Sci Rep., **5,** 10049 (2015).
25. H. Ohta, J Phys Fitness Sports Med, **5,** 229-233 (2016).
26. H.J. Hammod, A.N. Al-Dujaili, M.N. Al-Dujaili, Research journal of pharmaceutical biological and chemical sciences, **7(3),** 809-814 (2016).
27. G. Bozkaya, O. Fenercioglu, İ. Demir, A. Guler, B. Aslanipour, M. Calan, Gynecol Endocrinol., **36,** 849-853 (2020).
28. H. Kratochvilova, Z. Lacinova, J. Klouckova, P. Kavalkova, A. Cinkajzlova, P. Trachta, J. Krizova, M. Benes, K. Dolezalova, M. Fried, Z. Vlasakova, T. Pelikanova, J. Spicak, M. Mraz, M. Haluzik, Diabetes Metab Syndr Obes., **12,** 423-430 (2019).
29. A. Polkowska, I.E. Pasierowska, M. Pasławska, E. Pawluczuk, A. Bossowski, *Biomed* Res Int., **2019,** 6128410 (2019).
30. W.R.H. Al-Kraity, A.N.G. Al-Dujaili, Research Journal of Pharmacy and Technology, **10(6),** 1675-1678 (2017).
31. D.A. Kadhim, A.N. Al-Dujaili, AIP Conference Proceedings, **2290(1)** (AIP Publishing, 2020).