

Journal of Education for Pure Science

Vol.15, No.3 (2025)
DOI: https://doi.org/10.32792/jeps.v15i3.702



Website: <u>iceps.utq.edu.iq</u>

Email: iceps@eps.utq.edu.iq

Investigation The Effect of Polycystic Ovary Syndrome on The Level of Adrenal Hormones

Randa T. Naser1, Hazar S. Saleh 2, Rozzana M.Said3 and Amir Muhriz Abdul Latiff4

¹ Biology Department, Collage of Education for Pure Sciences, University of Thi- Qar, Iraq.

Department of Basic Sciences, Faculty of Health Sciences, Universiti Teknologi MARA Selangor Branch, ³ Puncak Alam Campus, Selangor, Malaysia.

⁴Department of Pathology, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh Campus, Malaysia

randtalib.bio@utq.edu.iq, hazarsaleh@utq.edu.iq,rozan480@uitm.edu.my

Received 28/04/2025, Accepted 22/6/2025, Published 1/9/2025



This work is licensed under a <u>Creative Commons Attribution 4.0 International License.</u>

Abstract:

Polycystic ovary syndrome (PCOS), is characterized by an imbalance in the hormonal balance that may lead to other health problems unless followed up or treated appropriately. Research shows that PCOS does not directly affect Epinephrine Aldosterone or Cortisol levels together with adrenal function in female laboratory rats yet analyzes this PCOS impact in stabilizing physiological conditions of the adrenal gland. This study aims to investigate the effect of Polycystic Ovary Syndrome (PCOS) on the secretion and function of adrenal gland hormones, including cortisol, aldosterone, and epinephrine, in order to understand the hormonal alterations associated with the syndrome and to assess the potential link between ovarian and adrenal gland dysfunctions. The research study separated rats into two groups with eight rats present in each section. The control group contained normal rats that received no drug administration yet the second group received letrozole at 0.2 mg per kg through oral delivery. Research personnel collected blood samples which enabled evaluation of Epinephrine, Aldosterone, Cortisol, Estrogen and Testosterone hormone. The attained findings showed the steady rise in the Epinephrine, Estrogen as well as Testosterone levels and a decrease in the Aldosterone and Cortisol levels was also observed. Wrapping up the results of this study, it can be stated that the adrenal hormones are impaired in PCOS, thus causing pathophysiological alterations in the adrenal gland, and it was ascertained that the adrenals' activity is diminished.

² Biology Department, Collage of Education for Pure Sciences, University of Thi- Qar, Iraq.

Keywords: Adrenal gland, Aldosterone, Cortisol, Epinephrine, Letrozole and Polycystic ovary syndrome (PCOS)

1-Introduction:

Currently polycystic ovary syndrome (PCOS) is ranked one of the main glandular pathology affecting women of the childbearing age, with the main symptoms being hormonal, ovulation, disorders and increase in androgen levels. However, studying the given pathological condition, it has been found that the adrenal gland also has a significant role in the formation of the pathological condition, though the ovary is considered to be the target organ [1]. Adrenal gland is a small triangular endocrine gland that is connected to the kidney and it is involved in the biosynthesis of steroids and regulation of stress levels in the body. The adrenal gland has cortex that produces fatty substances including cortisol, aldosterone and androgens while the pulp produces adrenaline and noradrenaline substances[2]. Exactly, this gland is known to be regulated by the hypothalamic-pituitary adrenal axis and is therefore susceptible to various physiological and pathological impact factors. Furthermore, gland change in histological and functional level may happen due to systemic diseases such as tumors, or due to other hormonal disorders like PCOS and it has been postulated that hyperandrogens could be attributed to partly hyperstimulation of the retinal region of adrenal gland[3]. In the view of this, this particular study sought to assess the impact that PCOS has on the three adrenal hormones: Epinephrine, Cortisol and Aldosterone.

2-Research Gap:

Although several studies have explored the endocrine effects of PCOS, the effect of PCOS on the functions of the adrenal is still under investigation, particularly in animal models such as rats. The relationship between PCOS and disorders in the adrenal gland has not been thoroughly examined. This gap in the current literature limits the development of a clear concept of how PCOS affects adrenal function, necessitating further research to clarify these effects.

3- Methods:

3.1 Animals Husbandry

All experimental procedures in the described study were conducted based on the general guidelines for the use of the laboratory at the College of Education for Pure Sciences / University of Thi-Qar. Thi-Qar ethical committee for animal research gave their approval to this research (Issue7/ 52/ 1727). Sixteen female rats aged 3-4 months with an average weight of 170-230 grams were used. The animals were maintained in a plastic cage at the College of Education for Pure Sciences, University of Thi-Qar, under standard condition of temperature (22± 25) ° C and light illumination (12:12 hours light and dark frash for two weeks before

and during the experimental period). During the experiment the rats were offered ad-libitum access to feed and water at all given times. For this purpose, the rats were divided into two groups, group I (normal control group) and group II Letrozole doses of 0.2 mg per kg were administered orally for 28 days to have PCOS.

3.2 Biochemical Analysis

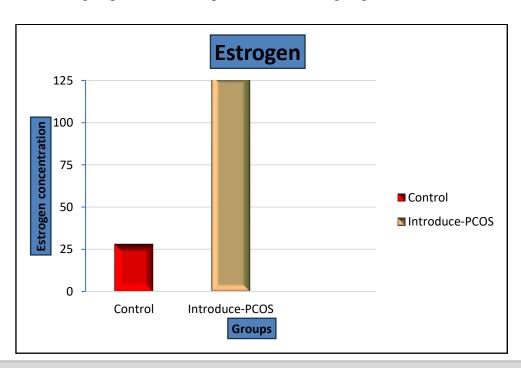
Serum Aldosterone (Ald), Cortisol (Cor), Epinephrine (Epi), Estrogen and Testosterone were determined using commercial kits (Elisa, BT LAB, China). After the end of the experimental period, blood was collected directly from the heart by cardiac puncture using medical syringes with a capacity of (5) ml. The blood was placed in tubes containing gel tubes evacuated from the air and left for an hour at room temperature until it clotted. Then the serum was separated by centrifugation for 5-3 minutes at 3500 rpm. The serum was kept in small plastic tubes at a temperature of (-20°C) until the test was conducted.

3.3 Statistical analysis:

The data were statistically analyzed according to the Completely Randomized Design (One Way ANOVA) with ten replicates, and the means were compared using the Tukey test at a probability level (P < 0.05) using the Statistical Package for the Social Sciences (SPSS), Version 21. The standard deviation (Means \pm SD) was used to analyze the results and demonstrate their significance.

4- Results:

The research findings in this study revealed increased values for Estrogen and Testosterone in the induction group of PCOS as depicted in Figure 1 and Figure 2, while a decrease for aldosterone and cortisol as presented in Figure 3 and Figure 4. The hormonal Epinephrine also shown in Figure 5 significantly enhanced in the induced group of PCOS compared with control group.



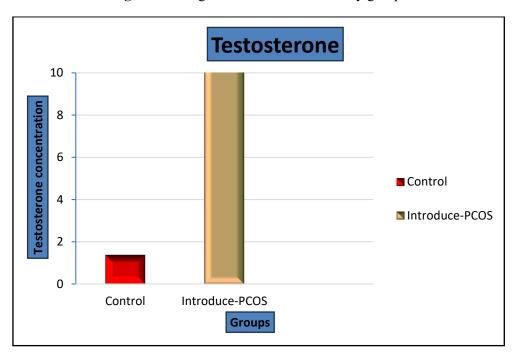
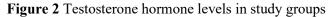


Figure 1 Estrogen hormone levels in study groups



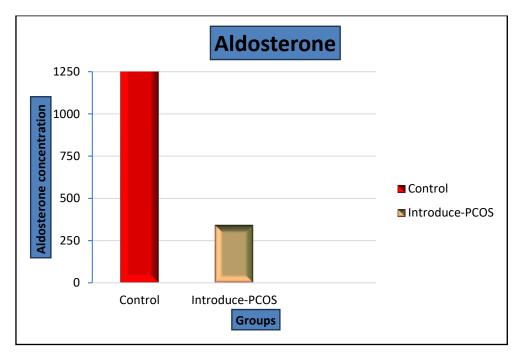


Figure 3 Aldosterone levels in study groups

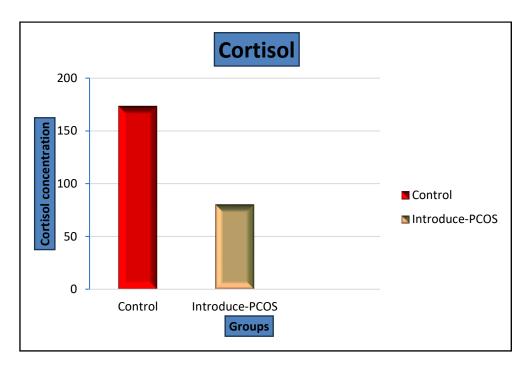


Figure 4 Cortisol levels in study groups

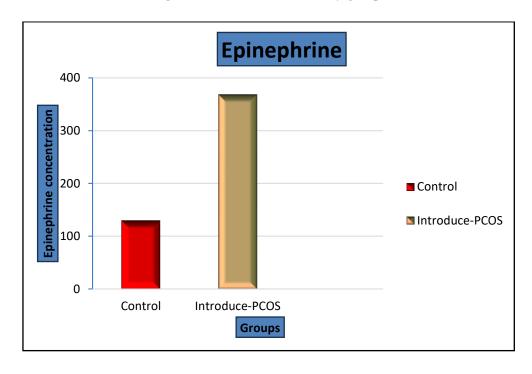


Figure 5 Epinephrine hormone levels in study groups

5- Discussion:

The purpose of this study was to establish the impact of PCOS on gland hormones including Epinephrine, Aldosterone and Corttisol. In the present study conducted on the PCOS induced group, there were significant changes in estrogen level. It has been evidenced from previous research that rats with PCOS used in the study displayed changes in several hormones, mainly increased estrogen levels. This is partly due to increased efficiency of tissue aromatase that contributes to the conversion of androgen into

estrogen [4]. Moreover, due to over-secretion of androgens in PCOS ovaries these hormones get stored and further metabolically converted into estrogens[5]. The incapacitation of the meanly negative feedback loop here depicted as the hypothalamic-pituitary-ovarian axis also affects the continuous stimulation of the follicles without ovulation leading to unending secretion of estrogen with no regulation by progesterone[6]. This hormonal pattern is usually reflected when using animal models caused by, for instance, letrozole injection or long-term exposure to testosterone[7]. This is in line with the findings of the studied research as it points out that. The outcome of the present study revealed a rise in the levels of testosterone and this could be because of changes in the HPO axis thus provoking increased stimulation to the ovaries and therefore androgen development [8]. This is as well in concordance with the results of the current study.

In the same group above, the following findings were recorded: lower hormone of aldosterone, decrease in aldosterone has been applauded to the dysfunction of renin–angiotensin–aldosterone system (RAAS). According to the literature, chronic stress and sympathetic hyperactivity linked to PCOS may prevent normal renal response and lead to low renin output and therefore low aldosterone production[9]. Also, insulin resistance characteristic of PCOS may affect angiotensin II receptor availability in the adrenal cortex and decrease the common sensibility of cells, which are responsible for aldosterone production [10]. The present findings are in line with the given hypothesis and null hypothesis of this study.

Regarding the decline of the hormone cortisol is related on diminished central activation of the adrenal glands because of the regulatory hormones like, CRH (corticotropin-releasing hormone) and ACTH (adrenocorticotropic hormone) where in PCOS models these hormones are changed[11]. Moreover, abnormal levels of androgens, which are apparent in PCOS, have been said to cause alteration of the HPA axis inclusive of impaired cortisol production from the adrenal gland[12]. The same observation is valid for the current study as well.

For several reasons, there are positive correlations with the increase in epinephrine including; hyperactivation of sympathetic nervous system accounts for most of these results. Thereby, the essential finding of this present study is the increased sympathetic pre-ganglionic nerve fibres to the ovary in PCOSinduced rats through further stimulating catecholamine secretion comprising epinephrine [13]. This increase activity also occurs with higher levels of norepinephrine in the peripheral nerve tissue stimulating secretion Furthermore, the oxidative stress in PCOS may play a role in the of epinephrine by the adrenal glands[14]. activation of the hypothalamic-pituitary-adrenal (HPA) axis and thereby increases the levels of stress hormones such as epinephrine[15]. Another supporting evidence of sympathetic nervous system overactivity in PCOS is that insulin resistance, which is characteristic of this condition, has been found to be positively related to both increased sympathetic nervous activity and elevated epinephrine levels[16]. This is consistent results with the of our current study.

6- Conclusion:

We conclude from the current study that letrozole-induced polycystic ovary syndrome (PCOS) in female laboratory mice significantly affects the secretion of adrenal hormones, resulting in increased levels of estrogen, testosterone, and epinephrine, along with a decrease in both aldosterone and cortisol levels, thus

impacting the functional aspect of the adrenal gland.

Conflicts Of Interest

The authors should pledge that they don't have any conflict of interest in regards of their research. If there are no conflict of interest then authors can declare the following "The authors declare no conflicts of interest".

Acknowledgment

I would like to express my sincere gratitude to the University of Thi-Qar, College of Education for Pure Sciences, Department of Biology, for their valuable support and guidance throughout the course of this study. Their academic environment and continuous encouragement greatly contributed to the success of this work.

Reference

- [1] Azziz, R., et al. (2004). The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril, 91(2), 456–488. https://www.fertstert.org/article/S0015-0282(08)01392-7/pdf
- [2] Bornstein, S. R., Engeland, W. C., Ehrhart-Bornstein, M., & Herman, J. P. (2004). Dissociation of ACTH and glucocorticoids. Trends in Endocrinology & Metabolism, 15(5), 175–180. https://doi.org/10.1016/j.tem.2004.03.007
- [3] Nieman, L. K. (2015). Cushing's syndrome: Update on signs, symptoms and biochemical screening. European Journal of Endocrinology, 173(4), M33–M38. https://doi.org/10.1530/EJE-15-0461
- [4] Wang, Y., Ma, X., Zhou, L., Liu, Y., Ma, Z., & Wang, Y. (2016). Aromatase expression in adipose tissues and its role in hyperestrogenism in PCOS rat model. Endocrine Journal, 63(2), 123–130. https://doi.org/10.1507/endocrj.EJ15-0423
- [5] Zhao, X., Xu, F., Qi, L., Zhang, D., & Wu, X. (2018). Endocrine and metabolic characteristics of a PCOS rat model induced by DHEA. Journal of Ovarian Research, 11(1), 45. https://doi.org/10.1186/s13048-018-0415-4

- [6] Kafali, H., Iriadam, M., Ozardali, I., & Demir, N. (2004). Letrozole-induced polycystic ovaries in the rat: a new model for cystic ovarian disease. Archives of Medical Research, 35(2), 103–108. https://doi.org/10.1016/j.arcmed.2003.11.005
- [7] Stener-Victorin, E., Padmanabhan, V., Walters, K. A., & Campbell, R. E. (2010). Animal models for the study of PCOS: a critical assessment. Molecular and Cellular Endocrinology, 373(1–2), 76–86. https://doi.org/10.1016/j.mce.2012.10.005
- [8] Wang, N., Zhang, Y., Wang, Y., Ma, X., & Zhang, J. (2019). Hormonal regulation of steroidogenesis in polycystic ovary syndrome. Reproductive Biology and Endocrinology, 17(1), 1-10. https://doi.org/10.1186/s12958-019-0505-2
- [9] Duleba, A. J., & Dokras, A. (2012). Is PCOS an inflammatory process? Fertility and Sterility, 97(1), 7–12. https://doi.org/10.1016/j.fertnstert.2011.11.023
- [10] Rashid, N., Moulana, M., Abid, S., & Hussain, T. (2013). Angiotensin II type 1 receptor expression is altered in PCOS rat model. Journal of Endocrinological Investigation, 36(10), 796–802. https://doi.org/10.3275/8992
- [11] Kauffman, A. S., Thackray, V. G., Ryan, G. E., Tolson, K. P., Glidewell-Kenney, C. A., Semaan, S. J., ... & Mellon, P. L. (2015). Polycystic ovary syndrome: a neuroendocrine perspective. Frontiers in Neuroendocrinology, 39, 1–15. https://doi.org/10.1016/j.yfrne.2015.08.002
- [12] Elsenbruch, S., Hahn, S., Kowalsky, D., Henschel, F., Möhler, H., Janssen, O. E., & Mann, K. (2003). Altered responses of the hypothalamus–pituitary–adrenal axis and the sympathetic nervous system to stress in women with polycystic ovary syndrome. Journal of Clinical Endocrinology & Metabolism, 88(12), 6296–6302. https://doi.org/10.1210/jc.2003-030346
- [13] Lara, H. E., Ferruz, J. L., Luza, S., Bustamante, D. A., Borges, Y., & Ojeda, S. R. (2000). Evidence for a local effect of noradrenaline on ovarian steroidogenesis in polycystic ovary syndrome. Endocrine, 12(3), 267–274. https://doi.org/10.1385/ENDO:12:3:267
- [14] Elenkov, I. J., Wilder, R. L., Chrousos, G. P., & Vizi, E. S. (2000). Stress, catecholamines, and immune response. Neuroimmunomodulation, 7(3), 161–179. https://doi.org/10.1159/000026484
- [15] González, F., Rote, N. S., Minium, J., & Kirwan, J. P. (2012). Inflammation in polycystic ovary syndrome: underpinning of insulin resistance and ovarian dysfunction. Steroids, 77(4), 300–305. https://doi.org/10.1016/j.steroids.2011.12.003

[16] Carter, J. R., Panerai, R. B., & Robinson, T. G. (2012). Sympathetic neural responses to stress in women with polycystic ovary syndrome. Clinical Autonomic Research, 22(1), 39–45. https://doi.org/10.1007/s10286-011-0133-0