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The Role Beclin 1 on Autophagy in Polycystic Ovary Syndrome

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Abstract

This research was made to evaluate the plasma beclin-1 level in the pathogenesis of polycystic ovary syndrome in females and to find relationship between autophagy and polycystic ovary syndrome through determination of the biochemical parameters and marker test. The level LH, FSH, testosterone, progesterone, were determined and analysed using analysis of variance software at P-Value of P<0.05, which showed significance difference between pcos women and healthy women. Beclin 1 levels determined and analysed in this study and showed insignificance difference between PCOS women and healthy women. The results demonstrated that there is no significance difference between PCOS women and healthy women in Beclin 1 levels

Keywords: *PCOS, Beclin 1, autophagy*

1. Introduction

A prevalent reproductive endocrine condition called polycystic ovarian syndrome (PCOS) affects at least 10% of women of reproductive age(Coutinho & Kauffman, 2019). Symptoms of (PCOS) involve menstrual cycles irregular, increase hair growth, infertility, and difficulties getting pregnant have all been related to PCOS (Louwers & Laven, 2020). In accordance with the ESHRE/ASRM-approved criteria, Rotterdam's criteria for diagnosing PCOS include the presence of the(Acne, hirsutism, and androgenetic alopecia are symptoms of these diseases, as are polycystic ovarian morphology (PCOM), which is identified by an ovary with at least 20 follicles and a diameter of 2 to 9 mm or a volume of at least 0.5 mL(Szeliga et al., 2022). Within the ovary, appropriate active autophagy is necessary for all stages of oocyte formation, follicle growth, and degeneration. It is necessary to maintain appropriate conditions for follicular atresia, follicular development and differentiation, oocyte production, and the reproductive cycle., follicular cells must participate in autophagy (Kumariya et al., 2021). Beclin1 is crucial autophagy regulator and is essential for the autophagic initiation process, which includes the development of the phagophore and the nucleation of the autophagic vesicle (Sahni et al., 2014).

2. Materials And Methods

A case control study with 100 women was conducted from October 2022 to April 2023. The University of Kerbala's College of Applied Medical Sciences and Karbala Health Directorate gave their permission for the study's ethical conduct. The administration of the gynecological and obstetric teaching hospital and every patient granted their agreement after being informed of the study's objectives.

(A) Blood collection

For blood collection, Needles and syringes 5ml were disposable.

In day two of the cycle, vein punctures were used to collect blood samples from PCOS patients and co ntrol groups. at room temperature the samples of blood were allowed to coagulate for 10–15 minutes.

After dividing the blood into four equal pieces, we centrifuged it at 2000 x g for 10 to 15 minutes to separate the serum. The samples were stored in a deep freezer at a temperature of -80 degrees ºC.

(B) Statistical analysis

ANOVA table with least significant difference for data measurement were used in statistical assessment using SPSS (Statistical Package for the Social Sciences which is version twenty-four)The information is shown as a mean accompanied by a standard deviation (SD).Statistical significance was assumed to exist at the (p0.05) level.

3. Results and Discussion

Table 1: showed the LH, and FSH, Progesterone, Free testosterone, Beclin 1of both the PCOS patients and the control groups

Samples	LH (m.IU/mL)	FSH (m.IU/mL)	Progesterone	Free testosterone pg/mL)	Beclin 1
Patient group N=70 Mean	9.82±5.87	5.13±1.29	3.16±4.18	2.55±1.17	(1310.28± 1018.08)
Control group N=30 Mean	4.8 ±1.66	6.421± 1.98	10.34±4.46	1.52±0.72	(1216.35 ±467.85

Luteinizing hormone stimulates the generation of androgens by acting predominantly on ovarian theca cells that have LH receptors(Ashraf et al., 2019) . FSH actions on the ovarian granulosa cells and alters the androgens produced in the theca cells into estrogens, primarily estradiol, which is essential to the formation of follicles(Liu et al., 2021) .

Patients with PCOS demonstrate an Luteinizing hormone levels are higher, which encourages ovarian theca cells to secrete androgens(Szeliga et al., 2022) .

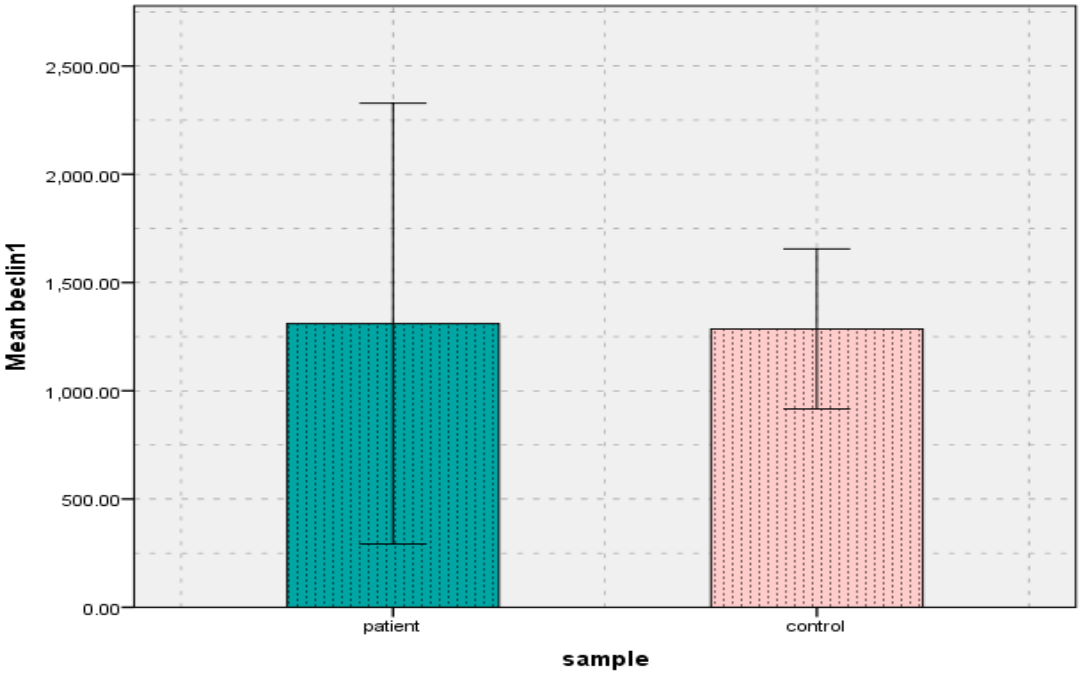
An imbalance in gonadotropin-releasing hormone (GnRH) secretion causes a greater proportion luteinizing hormone to follicle-stimulating hormone (FSH). The aberrant feedback process that led to an increase in LH release was triggered on by ovarian estrogen(Saadia, 2020) .In a normal ovarian cycle, the dominant follicle is the only one that responds to the peak surge of luteinizing hormone. Early terminal differentiation was seen in tiny follicles that are antral from a set of female with PCOS-related anovulation in response to increased LH levels (Szeliga et al., 2022). Ovarian theca cells expand (hyperplasia) as a consequence of elevated amounts of the luteinizing hormone (LH). As a result of this process, a string of pearl-like cystic structures called follicles forms along the border of the ovary. The theca cells in the ovaries are responsible for this condition, which occurs naturally(Ashraf et al., 2019). The levels of FSH could be increased, decrease lower than their typical levels, or stay stable in patients of condition (PCOS)(Mohammed & Qasim, 2021).An imbalance along the hypothalamic-pituitary-ovarian (HPO) pathway is thought to be able to arise, according to the beliefs of several experts because of neuroendocrine system instability(Walters et al., 2018). Recurrent, cyclical lowering of LH (GnRH) pulsatility is brought on by cyclic (luteal) rises in progesterone in ovulatory women(Billhaq & Lee, 2023). PCOS is characterized by the presence of persistent oligoovulation or anovulation cycles. women who have PCOS almost never experience the post-ovulatory surge in progesterone which is typical of women who have regular menstrual (Blank et al., 2006). In fact, the steadily increasing GnRH pulse rate, which is a hallmark of PCOS in adult women may be caused by decreased levels of progesterone that are related with anovulation. In line with previous results, elevated LH levels also suppressed progesterone levels in our investigation(Malini & George, 2017).

Women with PCOS frequently present with an irregular menstrual cycle and anovulation, which leads to reduced or absent P4 levels production, as shown by the thicker endometrium when comparing PCOS patients to non-PCOS controls (X. Li et al., 2014). Free Testosterone is a type of androgen that is biologically active. It is a chemical that is secreted, and its origins may be linked to both the ovary and

the adrenal zona fasciculate (Y. Sun et al., 2021).Only 1% unbound amounts of testosterone are present, with most of it was connected to albumin and sex hormone-binding globulin (about 33% and 66%, respectively)(Njoroge et al., 2022). It is interesting to note testosterone that is unbound is the only type of the hormone with biological activity, while testosterone bound to proteins is inactive form(Zamir et al., 2021) **.**PCOS patients who have elevated the amount of free testosterone as well as the free androgen index (FAI) been diagnosed with the condition known as hyperandrogenism (Maksym et al., 2019) .

Through the process of autophagy, cells recycle nutrients from damaged organelles and proteins to preserve cellular homeostasis, often referred to as macro autophagy, a lysosomal breakdown catabolic process that has been conserved over evolutionary time. There are several functions for which autophagy has been demonstrated. Autophagy, for instance, is physiologically distinct from apoptosis and necrosis in terms of programmed cell death. A former is a proactive process of cell killing that is carried out through blebbing of the plasma membrane without changes to the organelles found within the cytoplasm, whereas the latter involves a ruptured plasma membrane ,the loss of intracellular content, and ultimately death of cells (Zhou et al., 2019). The each of the three unique kind of autophagy—chaperone-mediated autophagy, microautophagy, and macroautophagy—is a process(Hubert et al., 2022). The macroautophagy process is the one that has garnered the most interest among the many autophagy processes. as well as is broken down into two successive stages: The first stage representation of the formation structure consisting of two membranes that is known as the phagophore, that's engulfs cargo and develops into ultimately reaching the form an enclosed vesicle with two membranes that is known as an autophagosome.

The next step is lysosomes and autophagosomes joining together to create autolysosomes, which are in charge of digesting and recycling contained(Peters et al., 2019) . The start of the autophagy process with the development of the autophagosome, afterwards, the autophagosomal membrane initiates nucleation, elongation, sealing, and closure (Chen et al., 2021) .Beclin -1 performs a crucial Impact on the beginning stages of autophagy., which involves the phagophore's creation and the nucleation of the autophagic vesicle (Kaur & Changotra, 2020) .



We found no statistically significant differences between the study groups.in which the beclin 1 in pcos female (1216.35 ±467.85)

in compared to control group. Beclin-1 has been shown to take crucial part of the development of autophagosomes(Xing et al., 2017). Within the framework of autophagy and the sorting of proteins, Beclin 1 has an important role. It serves as a scaffold for the formation of a multi protein assembly during the initial stages of autophagy(Kaur & Changotra, 2020). The ovary needs adequate, effective

autophagy for the development of follicles, the origin of oocytes, and their degradation. the progress that has been made in understanding the significance of autophagy in relation to PCOS-related metabolic diseases. The process of Autophagy is essential part of the regulation of the activation of inflammasomes as a result of metabolic stress(D. Li et al., 2017).

4. Conclusion

Autophagy helps keep the human ovary healthy and works in the process of luteal decline. It also affects the ability of granulosa cells to live. And regulated indirect by sestrins . According to the current findings, PCOS may have started as a result of beclin 1 irregularities in the serum of PCOS patients.

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