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Hormonal Disturbances in Women with Premature Ovarian Insufficiency

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Abstract— Background: 3.7% of women before the age of 40 have premature ovarian insufficiency (POI), which is characterized by the loss of ovarian activity and is still a common cause of infertility in women [1]. Objective: Measuring Body Mass Index (BMI) and concentrations of some parameters (Anti Mullerian Hormone (AMH), Follicular Stimulating Hormone (FSH), Luteinizing Hormone (LH), testosterone, and Estradiol (E2) in serum of POI patients. Materials and Procedures: A case-control study involving 100 women (50 POI patients and 50 healthy control). BMI, AMH, Follicular Stimulating Hormone (FSH), Luteinizing Hormone (LH), testosterone, and Estradiol (E2) were measured using an enzyme-linked immunosorbent assay and chemiluminescent automated immunoassay system (ECL) (Cobas e 411). Results: The study's findings demonstrated There were statistically significant differences in the mean BMI values between the POI patients and the control group, The results also showed a significant increase in levels of FSH and LH, and significant decrease in levels of AMH, testosterone, and Estradiol (E2) in POI women in comparison with healthy women. Conclusion: The BMI group between (25-29.5 kg/m^2) is the most category predispose to have Premature Ovarian Insufficiency (POI) among the BMI groups in the study. Increase in levels of FSH and LH, and decrease in levels of AMH, testosterone, and Estradiol (E2) can act as an indicators in POI-affected women.

***Index Terms*— Premature Ovarian Insufficiency (POI), Estradiol E2, Anti Mullerian Hormone (AMH).**

Abbreviation

BMI: Body Max Index
POI: Premature Ovarian Insufficiency
FSH: Follicular Stimulating Hormone
AMH: Anti Mullerian Hormone
E2: Estradiol
LH: Luteinizing Hormone

1. Introduction

Deficient ovarian sex hormones and a diminished ovarian reserve are two characteristics of premature ovarian insufficiency (POI), which together cause an early start of menopause and a rapid reduction in ovarian function [2]. It is possible that moderate clinical signs and a relative lack of awareness contributed to the delayed diagnosis of POI. The majority of POI diagnoses come after menarche; if it manifests prior to menarche, it must be differentiated from gonadal dysgenesis, which results in ovaries that differ in both morphology and histology [3]. The projected incidence rate ratio changes with age: 1:100 cases by the time a person is 40 years old, 1:250 cases when they are 35 years old, 1:1000 instances by the time a person is 30 years old, and 1:10,000 cases when they are 18 to 25 years old. The occurrence of POI is also influenced by ethnicity, according to epidemiological research [4], [5]. Other common symptoms, such as hot flashes, dyspareunia, night sweats, dry eyes, and decreased desire for sexual activity, are similar to those of menopause or estrogen deficiency. Nevertheless, hypoestrogenism symptoms might never appear in women with primary amenorrhea. Turner syndrome symptoms, including small height, webbed neck, short fourth and fifth metacarpal bones, shield-like chest, wide carrying angle elbow, low set ears, and low hairline, can occasionally be seen in women with POI. The most prevalent genetic cause of POI is Turner syndrome, which typically manifests clinically prior to menarche [6]. Between 4 and 30 percent of POI cases are caused by autoimmunity [7], [8]. Follic dynamics are negatively impacted by systemic pro-inflammatory circumstances, which changes ovarian homeostasis [9]. Autoimmunity mostly attacks the steroid-producing cells in the corpora lutea and pre-ovulatory follicles, although it can also occasionally cause fibrosis, follicular depletion, and aberrant activation of epithelial cells [10], [11].

2. Material and Methods

From October 2023 to April 2024, 100 women (50 control and 50 patients) ranging age between 18 and 40 were participated in a case control study. The ethical conduct of the study was approved by the Karbala Health Directorate and the University of Kerbala College of Applied Medical Sciences. After learning the objectives of the study, all patients as well as the management of the gynecological and obstetric teaching hospital gave their consent. Each subject underwent a physical examination, person's height and weight were recorded by using kg/m^2, the body mass index (BMI) was computed. A sample of venous blood, about 5 mL, was taken. Gel tubes were filled with the blood. After letting each blood sample clot, it was spun for ten minutes to extract the sera and conduct chemical tests for AMH using an enzyme-linked

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immunosorbent assay while a chemiluminescent automated immunoassay system (ECL) (Cobas e 411, Roche Diagnostic, Germany) was used to test other hormones.

A. Statistic Evaluation

This examination is best described as a case-control study. SPSS (Statistical Package for the Social Sciences, version 24) was utilized for statistical assessment, and an ANOVA table with the variation in data measurement that is least substantial was employed. The data is displayed as mean with standard deviation (SD) attached. At the (p0.05) threshold, statistical significance was considered to exist. The comparison between the groups yielded the P value, or the least significant difference.

3. Results

A. BMI Comparison Between the Patients and Controls

The relationship between patients and control according to their BMI was estimated by examining the serum of 50 POI women and 50 healthy women working as a control group. Corresponding to the outcomes displayed in figure 1 and table 1. The BMI mean values varied statistically significantly between the control group (25.87±2.56) and the patients' groups of POI (27.88±4.52).

Table 1
The body mass index mean and standard deviation for girls with and without POI

	Sample	Mean	Std. Deviation	P Value
BMI Kg/m²	Controls	25.87	2.56	0.007
	Patients	27.88	4.52	

The information displayed as mean ± SD

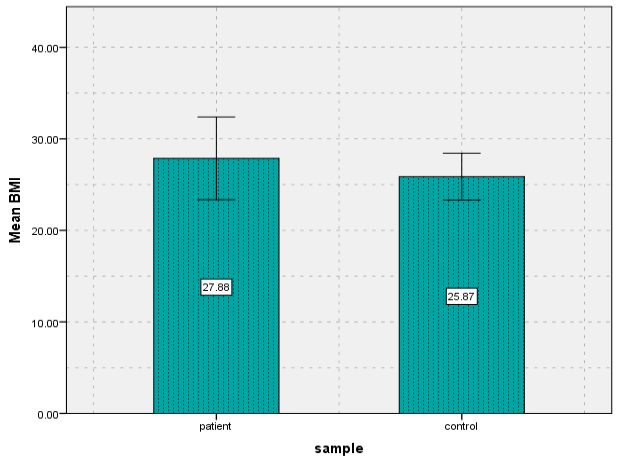

Fig. 1. Mean of level BMI in POI and control groups

B. Measuring of LH and FSH in Study Groups

Table 2, figure 2 and figure 3 provided the results, which indicated a significant increase in FSH levels. (23.56±25.79) in women with POI compared with healthy women (5.39±3.84), as well as significant increase levels of LH in POI women (12.95±11.46) in comparison with healthy women (8.54±8.92).

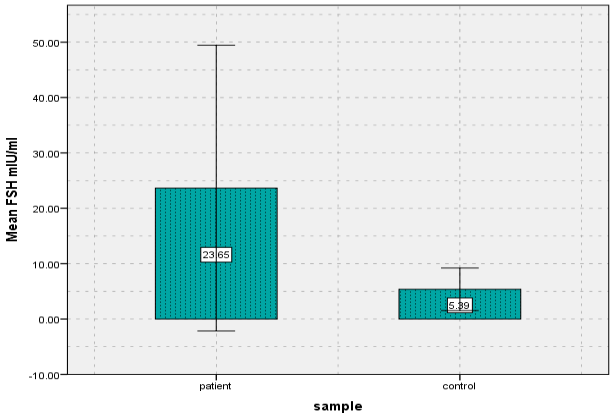

Fig. 2. The average FSH level in the control and POI groups

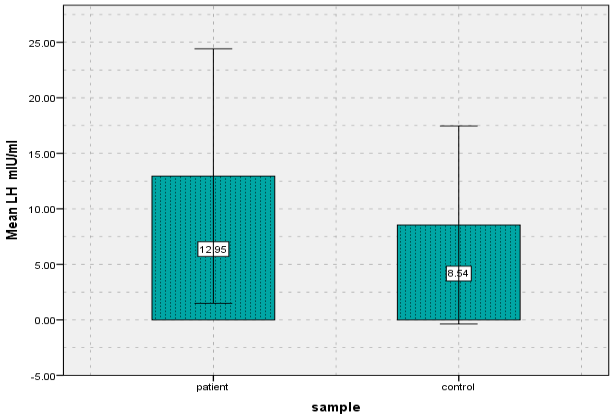

Fig. 3. The average LH level in the control and POI groups

C. Estradiol and Free Testosterone in Individuals with POI and a Control Group

The offered records presented in the table 3 and appearing significantly decreased in Estradiol concentrations of POI group (20.49±16.54) in contrast to control group (87.59±66.61) as in figure 4, as well as there was significantly decrease in the levels of free testosterone of POI groups (0.15±0.15) than healthy groups (0.24±0.20) as presented in figure 5.

Table 2
Displayed the LH and FSH concentrations of the POI patients as well as the controls group

Parameters	Control group, N=50, Mean	SD	Patient group, N=50, Mean	SD	P value
LH (m.IU/mL)	8.54	8.92	12.95	11.46	0.034
FSH (m.IU/mL)	5.39	3.84	23.65	25.79	0.000

The information displayed as mean ± SD

Table 3
Estradiol and Free testosterone in control and POI groups

Parameters	Control group, N=50, Mean	SD	Patient group, N=50, Mean	SD	P value
Estradiol (pg/mL)	87.59	66.61	20.49	16.54	0.000
Free testosterone (ng/mL)	0.24	0.20	0.15	0.15	0.012

The data represented as mean ± SD

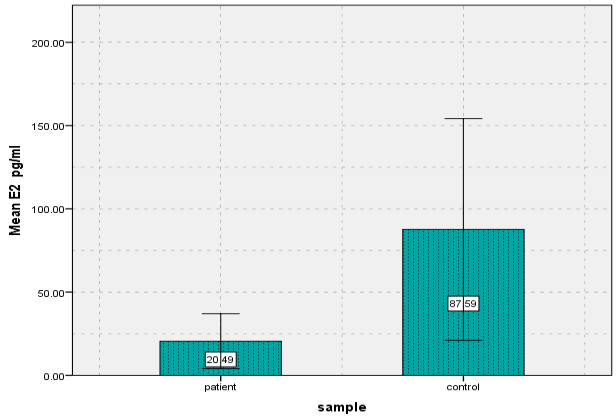

Fig. 4. Mean of level Estradiol in control and POI groups

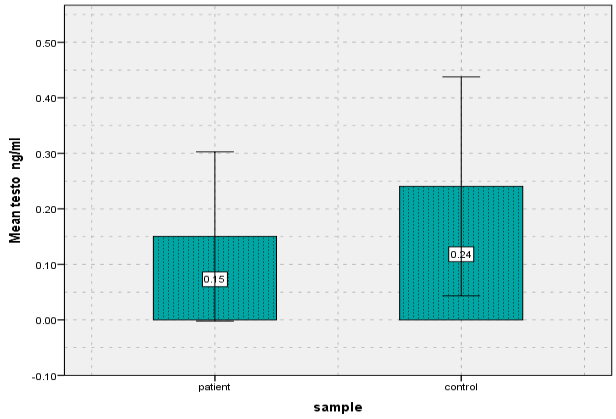

Fig. 5. Mean of free testosterone in control and POI groups

4. Discussion

The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) define overweight, obese, and severely obese as having a body mass index (BMI) of more than 25 kg/m^2, 30 kg/m^2, and 40 kg/m^2, respectively [12]. Women with a high BMI are more prone than those of normal weight to have irregular menstrual periods, ovulatory dysfunction, and disruptions in the hypothalamic-pituitary-ovarian axis, which can result in greater rates of infertility. Additionally, research has demonstrated that a woman's high BMI is a significant risk factor for unfavorable pregnancy outcomes [13]. Numerous studies have demonstrated the effects of obesity on the oocyte. Oocyte competence and maturation may be affected by changes in a variety of hormones, including those that initiate oocyte maturation, in individuals who are obese. Adipose tissue is overproduced in obesity because it is an essential location for the synthesis of steroid hormones and metabolism [14]. The pulsatile release of gonadotropin-releasing hormone by the hypothalamus typically stimulates the pituitary gland to release gonadotropins, such as LH and FSH. Luteinizing hormone acts primarily on ovarian theca cells that have LH receptors, which enhances the production of androgens [15]. The granulosa cells of ovary are impacted by FSH, which converts androgens made in the theca cells into estrogens, mainly estradiol, which is necessary for the development of follicles [16]. In comparison to healthy control women, women with POI exhibited significantly higher levels of FSH, luteinizing hormone (LH), and BMI (J Wu, 2021).

Patients with POI presented with significantly higher FSH and decreased AMH levels [17]. An increased FSH level is one of the diagnostic criteria for POI. One would anticipate hypogonadotrophic hypogonadism if FSH and LH levels were low. Measuring estradiol levels when POI is suspected is a helpful adjunct to confirm that it is low, validating the POI diagnosis [18]. Many physiological processes are negatively impacted by low estrogen, including moisture, wrinkles, atrophy of the skin, poor wound healing and barrier function, a decrease in the perception of one's own beauty, and even psychological health. Women experiencing changes in their skin due to menopause look for medical and cosmetic procedures that will improve their self-image and prevent their skin from aging, especially on exposed areas like the hands, neck, and face [19].

The majority of osteoporotic postmenopausal women suffer bone loss associated with low estrogen levels. An imbalance between bone production and resumption and an increase in bone turnover lead to the rapid loss of bone mass. Excessive use of glucocorticoids can also cause osteoporosis by demineralizing bone and altering its microscale spatial heterogeneities, which increases the risk of fracture [20]. Recent studies have revealed alterations in osteocytes during estrogen deprivation, which may be crucial in the development of the illness. Advanced knowledge of these alterations is necessary to determine the effectiveness of osteocyte-targeted therapeutics in preventing restart and secondary mineralization, which would shift the paradigm for osteoporosis treatment [21].

Androgens include compounds that can be turned to testosterone, dihydrotestosterone, and testosterone itself. The production of circulating testosterone comes from peripheral conversion of adrenal androgens (50%) and the ovaries (25%) as well as the adrenal cortex (25%). Furthermore, the intracellular synthesis of testosterone in target tissues plays a major role in the female androgen action.5. Reduced testosterone production after menopause has been connected to sexual issues [22].

5. Conclusion

Within the current study, The BMI group between (25-29.5 kg/m2) is the most category predispose to have Premature Ovarian Insufficiency (POI) among the BMI groups in the study. Increase in levels of FSH and LH, and decrease in levels of AMH, testosterone, and Estradiol (E2) can act as an indicators in POI-affected women.

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References

[1] Hanni Ke, Shuyan Tang, Ting Guo, Dong Hou, Xue Jiao, Shan Li, Wei Luo, Bingying Xu, Shidou Zhao, Guangyu Li, Xiaoxi Zhang, Shuhua Xu, Lingbo Wang, Yanhua Wu, Jiucun Wang, Feng Zhang, Yingying Qin, Li

Jin & Zi-Jiang Chen (2023), Landscape of pathogenic mutations in premature ovarian insufficiency, Nature Medicine 29, 483–492.
[2] Wesevich, V., Kellen, A. N., and Pal, L. (2020). Recent advances in understanding primary ovarian insufficiency. F1000Res 9:1101.
[3] Taylor, H. S., Pal, L., and Sell, E. (2019). Speroff's Clinical Gynecologic Endocrinology and Infertility. Philadelphia, PA: Lippincott Williams & Wilkins.
[4] Rebar, R. W. (2009). Premature ovarian failure. Obstet. Gynecol. 113, 1355–1363.
[5] Rudnicka, E., Kruszewska, J., Klicka, K., Kowalczyk, J., Grymowicz, M., Skorska, J., et al. (2018). Premature ovarian insufficiency – aetiopathology, epidemiology, and diagnostic evaluation. Prz Menopauzalny, 17, 105–108.
[6] Torrealday, S., Kodaman, P., and Pal, L. (2017). Premature ovarian insufficiency - an update on recent advances in understanding and management. F1000Res, 6:2069.
[7] Silva, C. A., Yamakami, L. Y., Aikawa, N. E., Araujo, D. B., Carvalho, J. F., and Bonfá, E. (2014). Autoimmune primary ovarian insufficiency. Autoimmun. Rev. 13, 427–430.
[8] Ebrahimi, M., and Akbari Asbagh, F. (2011). Pathogenesis and causes of premature ovarian failure: an update. Int. J. Fertil. Steril. 5, 54–65.
[9] Kirshenbaum, M., and Orvieto, R. (2019). Premature ovarian insufficiency (POI) and autoimmunity-an update appraisal. J. Assist. Reprod. Genet. 36, 2207–2215.
[10] Warren, B. D., Kinsey, W. K., McGinnis, L. K., Christenson, L. K., Jasti, S., Stevens, A. M., et al. (2014). Ovarian autoimmune disease: clinical concepts and animal models. Cell. Mol. Immunol. 11, 510–521.
[11] Sullivan, S. D., Sarrel, P. M., and Nelson, L. M. (2016). Hormone replacement therapy in young women with primary ovarian insufficiency and early menopause. Fertil. Steril. 106, 1588–1599.
[12] Chooi YC, Ding C, Magkos F. The epidemiology of obesity Metabolism. 2019;92:6–10.
[13] Larissa M. Ribeiro, Lizandra M.P. Sasaki, Adelino A. Silva, Elivan S. Souza, Amanda Oliveira Lyrio, Ana C.M.G. Figueiredo, Leila B.D. Gottems, (2022), Overweight, obesity and assisted reproduction: A systematic review and meta-analysis.
[14] Al-yasiry, Rabab Zahir; Jwad, Mufeda Ali1; Hasan, Muhjah Falah2; Alsayigh, Haythem Ali (2022), How Obesity Affects Female Fertility, Medical Journal of Babylon 19(2), pp. 111-114, Apr–Jun 2022.
[15] Ashraf S, Mudasar Nabi, Shayaq ul Abeer Rasool, Fouzia Rashid & Shajrul Amin, (2019), Hyperandrogenism in polycystic ovarian syndrome and role of CYP gene variants: a review Volume 20, article number 25.
[16] Liu, K., Guo, C., Lao, Y., Yang, J., Chen, F., Zhao, Y., & Yang, Y. (2020). A fine-tuning mechanism underlying self-control for autophagy: deSUMOylation of BECN1 by SENP3. Autophagy, 16(6), 975–990.
[17] Peihao Liu, Xiruo Zhang, Jingmei Hu, Linlin Cui, Shidou Zhao, Xue Jiao, Yingying Qin, (2020), Dysregulated cytokine profile associated with biochemical premature ovarian insufficiency.
[18] Waduge Dhanushi Fernando Amanda Vincent Karen Magraith (2023), Premature ovarian insufficiency and infertility.
[19] Edwin D. Lephart & Frederick Naftolin (2021), Menopause and the Skin: Old Favorites and New Innovations in Cosmeceuticals for Estrogen-Deficient Skin, Review, 11, 53–69.
[20] Chu-Han Cheng, Li-Ru Chen, and Kuo-Hu Chen, Osteoporosis Due to Hormone Imbalance: An Overview of the Effects of Estrogen Deficiency and Glucocorticoid Overuse on Bone Turnover, Int. J. Mol. Sci. 2022, 23(3), 1376.
[21] Laoise M. McNamara, Current Osteoporosis Reports, Osteocytes and Estrogen Deficiency, 19, 592–603.
[22] Nora Johansen, Angelica Linden Hirschberg, Mette H. Moen, 2020, The role of testosterone in menopausal hormone treatment. What is the evidence?, Journal of Obstetrics and Gynaecology Research.