# CORRELATION BETWEEN BMI AND GONADOTROPIN HORMONES IN THE FEMALE GENDER

# Adelina ELEZI<sup>1</sup>, Sheqibe BEADINI<sup>2\*</sup>, Irena KOSTOVSKA<sup>3</sup>, Egzona ZIBERI<sup>4</sup>

<sup>1</sup> Department of Pathology, Faculty of Medical Sciences, University of Tetova, Republic of North Macedonia

<sup>2</sup>Department of Biochemistry, Faculty of Medical Sciences, University of Tetova, Republic of North Macedonia

<sup>3</sup> Institute of Biochemistry, Faculty of Medical Sciences, St. Cyril and Methodius University, Skopje, Republic of North Macedonia

<sup>4</sup> Albimedika Laboratory, Tetova, Republic of North Macedonia

\*Corresponding author e-mail: sheqibe.beadini@unite.edu.mk

#### **Abstract**

**Introduction:** The pituitary gland affects growth and development. Its main function is in the activity of sexual/reproductive hormones and in the functioning of the glands (thyroid gland, adrenal glands and gonads). Gonadotropin hormones (gonadostimulins) are so named because they stimulate the function of the gonads - male and female sex glands (testicles and ovaries) in which sex cells - sperm and egg cells are created.

Overweight is a state of metabolic disorders where excess body fat accumulates to the extent that it can negatively affect human health.

Obesity as a BMI factor is related to the functioning of the thyroid gland with its hormones and the pituitary gland with gonadotropin hormones.

**Purpose of the study:** This paper aims to present the correlation between BMI and gonadotropin hormones in reproductive and postmenopausal women.

The aim of the paper will also consist in the status of gonadotropin hormones and the functional state of these hormones by comparing them with metabolic disorders such as BMI, obesity and the synthesis of follicle stimulating hormone and gonadotropin hormone.

**Material and method:** A total of 20 patients will be included in the research, divided according to age group into two categories. The first group will include patients aged 10-40 years, the second group patients over 41 years old. Blood (serum) samples will be taken from patients for analyzing gonadotropin hormones: FSH, LH, PRL and thyroid hormones: TSH, FT<sub>4</sub>, FT<sub>3</sub>.

They will be analyzed with the modern automatic fluorescent enzyme immunoassay method (Vidas-Biomerie). The BMI of the body will be measured with a metric formula where the weight of the patient (in kg) divided by the height of the patient (in m²) set to the square power will give us the measure of body index-BMI (%).

SPSS – Software package version 20.0

Numerical series were analyzed using central tendency measures (average, median, minimum values, maximum values), as well as distribution measures (standard deviation);

To determine the regularity of the frequency distribution of the examined variables, the Shapiro-Wilk W Test was used:

Non-parametric tests for two independent parameters were used to test the significance and difference between some numerical parameters with irregular frequency distribution (Mann Whitney U test);

To determine statistical significance, a two-way analysis was used with a significance level (means) of p<0.05.

**Results:** The results of the research will give a real insight into the data of gonadotropic hormones FSH, LH, PRL and thyroid hormones TSH, FT<sub>4</sub>, FT<sub>3</sub> of the female sex in the Tetova region. The results of the research will also provide information about the correlation of BMI and gonadotropin and thyroid hormones.

Conclusion: From the analyzes performed on patients of different age groups we come to the conclusion that:

- Gonadotropin hormonal disorders can lead to the phenomenon of metabolic diseases such as BMI.
- These disorders can have consequences such as: polycystic ovary diseases in women, Hashimoto's genetic syndrome, Graves, infertility in women, etc.

Keywords: gonadotropin hormones, pituitary gland, thyroid hormone, BMI, metabolic syndrome, infertility.

### 1. Introduction

Body mass index (BMI), a measurement based on a person's height and weight, allows the classification of individuals into categories such as obese or overweight. With these classifications, we can assess risk for hypertension, diabetes, cancer, hypercholesterolemia, and other chronic diseases (Khanna D, et al 2022).

The rising prevalence of obesity has had a profound impact on female reproductive health. Increased body mass index (BMI) is associated with ovulatory subfertility and anovulatory infertility. Overweight and obese women have poorer outcomes following fertility treatment. They respond poorly to clomiphene induction of ovulation and require higher doses of gonadotrophins for ovulation induction and superovulation. Ovarian stimulation for assisted reproduction produces fewer follicles resulting in the harvest of fewer oocytes. Fertilization rates are poorer and the embryo quality is impaired in younger women who are obese. Pregnancy rate in some studies is lower and there is an increased risk of early pregnancy loss. Weight loss regularizes menstrual cycles and increases the chance of spontaneous ovulation and conception in anovulatory (Shilpi Pandey, et al 2010).

The ovary is made up of two cellular components that are separately activated by LH and FSH to produce ovarian steroids (Wright KL, et al 2003).

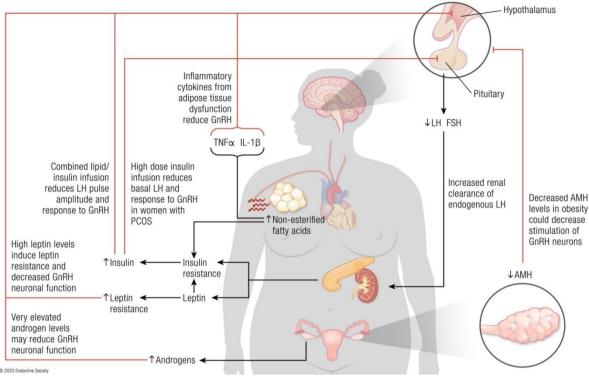
FSH is in responsible of follicular development and estrogen production. Estradiol, the main estrogen in humans, augments FSH's effects in the later stages of follicular development (Poppe K, et al 2007).

Despite the fact that follicle growth can be induced by FSH even in the absence of LH, there is evidence that the follicles may have developmental abnormalities, such as abnormally low estradiol synthesis and a lack of luteinization and rupture upon hCG stimulation (Rijal B, et al 2011).

The most frequent cause of female infertility is anovulatory infertility, which is frequently characterised by irregular menstruation, amenorrhea, or oligomenorrhoea. In order to release and maintain a normal amount of estrogen and progesterone during a menstrual cycle, thyroid hormone works synergistically with FSH and LH on the ovary. Thyroid disease has been linked to anovulatory cycles with lower fecundity and, as a result, infertility (Kumkum A, et al 2006).

Increased prolactin may have an adverse effect on reproduction by inhibiting the hypothalamus GnRH neurons and/or the pituitary gland's ability to secrete the gonadotropins luteinizing hormone (LH) and follicle stimulating hormone (FSH), which reduces the amplitude and frequency of LH pulses (Kokay IC, et al 2011).

As there is little information on the effects of various endocrine hormones, including TSH, FSH, LH, estrogen, progesterone, and prolactin, on female fertility, this study aims to evaluate and determine the correlation between the same in the diagnostic and management aspects of women who are presenting to gynaecological clinics with primary or secondary infertility, so that management can be planned accordingly (Siddharth Sharma et al., 2023).



**Figure 1.** Corelation between obesity and gonadotrop hormon in women. (https://doi.org/10.1210/endrev/bnad027)

## 2. Purpose of the paper

This paper aims to present the correlation between BMI and gonadotropin hormones in reproductive and postmenopausal women.

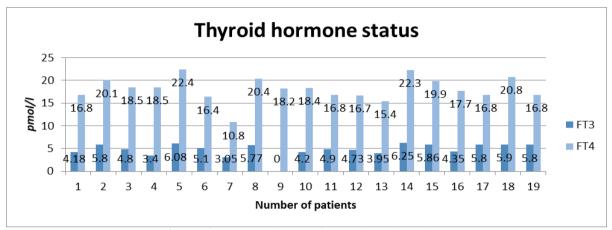
The purpose of the paper will also consist in the status of gonadotropin hormones and the functional state of these hormones by comparing them with metabolic disorders such as BMI, obesity and the synthesis of follicle stimulating hormone and gonadotropin hormone. The analyzed patients were also studied for the pathologies and function of the thyroid gland in correlation with the index of body mass and gonadotropin hormones.

#### 3. Material and method

A total of 20 patients will be included in the research, divided according to age group into two categories. The first group will include patients aged 10-40 years, the second group patients over 41 years old. Blood (serum) samples will be taken from patients for gonadotropin hormones: FSH, LH, PRL and thyroid hormones: TSH, FT<sub>4</sub>, FT<sub>3</sub>. They will be analyzed with the modern automatic fluorescent enzyme immunoassay method (Vidas-Biomerie). The BMI of the body will be measured with a metric formula where the weight of the patient (kg) divided by the height of the patient (m<sup>2</sup>) set to the square power will give us the measure of body mass index-BMI (%).

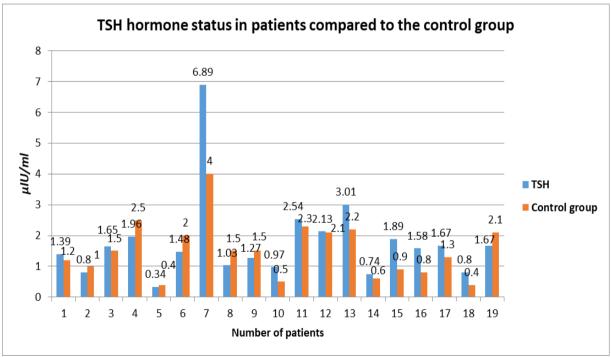
## 4. Results

The analyzed female patients for metabolic syndrome, infertility, obesity and correlation with the thyroid gland are presented in the graphics above.



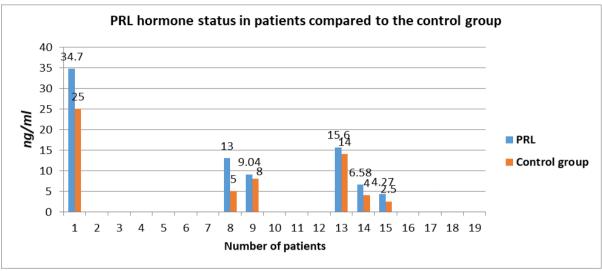
**Graph.1:** Hormonal status of FT<sub>4</sub> and FT<sub>3</sub> in patients.

In the graphic above we see a status of  $FT_4$  and  $FT_3$  in patients where the correlation between them is observed so that when the value of  $FT_3$  increases, so does the value of  $FT_4$ , which expresses a significant relationship with thyroid gland disorders and the presence in correlation with obesity.



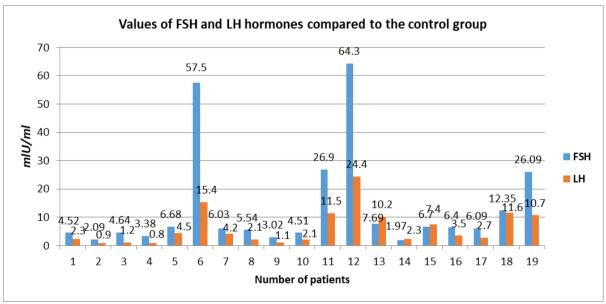
**Graph.2:** TSH levels in patients compared to the control group.

The prevalence of TSH hormone status in patients with overweight imbalance by 20 patients analyzed for the thyroid gland, we see a disorder or hypothyroidism in patients with high TSH values and significant overweight, which indicates a metabolic syndrome and reduced metabolism.



**Graph.3:** Prolactin levels in patients compared to the control group.

Prolactin levels in women with overweight and FSH & LH disordered synthesis from the analyzed patients presents a significant correlation between prolactin and gonadotropin hormones.



**Graph.4:** FSH and LH levels in women patients

The graphic clearly shows us the levels of FSH hormone increases compared to the LH hormone level as the BMI levels increase too. Gonadotropin hormones are correlated with thyroid gland hormones and express an increase in prolactin in patients with hypothyroidism.

### 5. Discussion

The prevalence of obesity is increasing at an alarming rate in many countries. An unhealthy diet and a sedentary lifestyle are the main risk factors for obesity (Arthur Pate de Souza et al., 2019).

Also, the weight excess has a well-known negative impact on female fertility, mainly related to ovulation disorders (Chavarro JE et al., 2007).

In conclusion, the present study shows that overweight women have lower gonadotropin, estradiol, and inhibin B levels and suggests a direct inhibitory effect of body mass on FSH, LH, and estradiol production. However, it shows that these alterations are not sufficient to reduce the number of follicles and fertility in women with simple obesity and normal menstrual cycles (Giovanni De Pergola et al., 2006).

Seddigheh Esmaeilzadeh et al. (2015) described that the overweight/obese women with PCOS are at an increased risk for sonographic view of polycystic ovaries. It has proved that age  $\geq$ 35 years, BMI  $\geq$ 25 kg/m² and acne are as significant predictors of metabolic disorder in PCOS women. Therefore, it is suggested that successful weight loss is the most effective method of restoring ovulation and menstruation that should be used as major advice in obese PCOS patients (Seddigheh Esmaeilzadeh et al., 2015).

Reduced gonadotropin production or action may cause clinically significant LH and FSH deficiency associated with reduced gametogenesis and steroidogenesis. This may explain why some women treated with MAR have an 'unexpected' hypo-response to standard OS with r-hFSH alone, notwithstanding their normal gonadotropin levels and normal ovarian reserve, and may contribute to a reduced ovarian response in women of AMA.

It may also pave the way to precision medicine solutions for fertility patients (Mol et al., 2018), and thus improve reproductive outcomes, particularly in AMA and hypo-responder patients who may benefit from OS with r-hFSH and r-hLH (E.Bosch et al., 2021).

Charlotte Berglund et al., (2015)stated that today. IVF/ICSI (in vitro fertilizatio/intracytoplasmic sperm injection) is a valuable procedure for people suffering from infertility. Controlled ovarian hyperstimulation, whose purpose is to stimulate production of mature oocytes for fertilization, is one of the crucial parts. BMI's (body mass index) impact on the number of received oocytes is disputed and suspicion towards reduced number of oocytes in women with higher BMI has been suggested. She also described in their study that they found that obese women received fewer oocytes in COH (Controlled Ovarian Hyperstimulation), even if they received significantly higher total doses of FSH, compared to the women with normal BMI. There were, however, some limitations in this study making the results uncertain, regarding whether or not overweight and obesity are obstacles in COH (Charlotte Berglund et al., 2015).

#### 6. Conclusion

Metabolic syndrome is one of the major human health problems and is always increasing in both men and women.

Hypothyroidism represents one of the major concerns related to gonadotropic hormones such as follicle-stimulating and luteinizing hormone and metabolic syndrome and overweight or obesity.

From the obtained results, we see that patients with problems with the thyroid gland have a relationship with gonadotropin hormones and a significant relationship with overweight patients.

Hypothyroidism is closely related to hyperprolactinemia in overweight patients with metabolic syndrome.

Hyperprolactinemia and hypothyroidism are the main causes of female infertility and are also closely related to overweight and obesity.

The main factor is the way of eating and physical activity, which maintains and regulates the human metabolism and at the same time the body mass index.

Our results show us that women with overweight and obesity and with thyroid gland problems have lower values of follicle-stimulating gonadotropin hormones and luteinizing hormone.

Women with hypothyroidism have a prevalence of overweight and obesity and at the same time they also have problems with primary and secondary infertility.

According to the obtained results, it is very important for women of different age groups, adults, premenopause and menopause to be careful in terms of healthy nutrition, organic foods, the use of prebiotics and regular physical activity.

#### References

- [1] Bosch E, Alviggi C, Lispi M, Conforti A, Hanyaloglu AC, Chuderland D, Simoni M, Raine-Fenning N, Crépieux P, Kol S, Rochira V, D'Hooghe T, Humaidan P. Reduced FSH and LH action: implications for medically assisted reproduction. Hum Reprod. 2021 May 17;36(6):1469-1480. doi: 10.1093/humrep/deab065. PMID: 33792685; PMCID: PMC8129594.
- [2] Charlotte Berglund, Mikael Lood, MD, Karin Franzén MD, PhD, Örebro, Sweden. The impact of BMI on response to controlled ovarian hyperstimulation in in vitro fertilization/intracytoplasmic sperm injection cycles, a retrospective cohort study. May 2015
- [3] Chavarro JE, Rich-Edwards JW, Rosner BA, Willett WC. Diet and lifestyle in the prevention of ovulatory disorder infertility. Obstet Gynecol. 2007 Nov;110(5):1050-8. doi: 10.1097/01.AOG.0000287293.25465.e1. PMID: 17978119.
- [4] De Pergola G, Maldera S, Tartagni M, Pannacciulli N, Loverro G, Giorgino R. Inhibitory effect of obesity on gonadotropin, estradiol, and inhibin B levels in fertile women. Obesity (Silver Spring). 2006 Nov;14(11):1954-60. doi: 10.1038/oby.2006.228. PMID: 17135611.
- [5] Esmaeilzadeh S, Andarieh MG, Ghadimi R, Delavar MA. Body mass index and gonadotropin hormones (LH & FSH) associate with clinical symptoms among women with polycystic ovary syndrome. Glob J Health Sci. 2014 Sep 28;7(2):101-6. doi: 10.5539/gjhs.v7n2p101. PMID: 25716399; PMCID: PMC4796454.
- [6] Ferreira APS, Szwarcwald CL, Damacena GN. Prevalence of obesity and associated factors in the Brazilian population: a study of data from the 2013 National Health Survey. Rev Bras Epidemiol. 2019 Apr 1;22:e190024. Portuguese, English. doi: 10.1590/1980-549720190024. PMID: 30942330.
- [7] Khanna D, Peltzer C, Kahar P, Parmar MS. Body Mass Index (BMI): A Screening Tool Analysis. Cureus. 2022 Feb 11;14(2):e22119. doi: 10.7759/cureus.22119. PMID: 35308730; PMCID: PMC8920809.
- [8] Kokay IC, Petersen SL, Grattan DR. Identification of prolactin-sensitive GABA and kisspeptin neurons in regions of the rat hypothalamus involved in the control of fertility. Endocrinology. 2011 Feb;152(2):526-35. doi: 10.1210/en.2010-0668. Epub 2010 Dec 22. PMID: 21177834.
- [9] Kumkum A, Jasmine K, Shweta G, Pal Ajeshwar N. Hyperprolactinema and its coorelation with hypothyroidism in infertile women. J Obstet Gynecol India. 2006;56(1):68-71.
- [10] Mol BW, Bossuyt PM, Sunkara SK, Garcia Velasco JA, Venetis C, Sakkas D, Lundin K, Simón C, Taylor HS, Wan R, Longobardi S, Cottell E, D'Hooghe T. Personalized ovarian stimulation for assisted reproductive technology: study design considerations to move from hype to added value for patients. Fertil Steril. 2018 Jun;109(6):968-979. doi: 10.1016/j.fertnstert.2018.04.037. PMID: 29935655.
- [11] Pandey S, Pandey S, Maheshwari A, Bhattacharya S. The impact of female obesity on the outcome of fertility treatment. J Hum Reprod Sci. 2010 May;3(2):62-7. doi: 10.4103/0974-1208.69332. PMID: 21209748; PMCID: PMC2970793.
- [12] Poppe K, Velkeniers B, Glinoer D. Thyroid disease and female reproduction. Clin Endocrinol (Oxf). 2007 Mar;66(3):309-21. doi: 10.1111/j.1365-2265.2007.02752.x. PMID: 17302862.
- [13] Rijal B, Shrestha R, Jha B. Association of thyroid dysfunction among infertile women visiting infertility center of Om Hospital, Kathmandu, Nepal. Nepal Med Coll J. 2011 Dec;13(4):247-9. PMID: 23016472.

- [14] Sharma, Siddharth & Meena, Kusum & Tabiyad, Aditi & Bhardwaj, Manish & Jaiswal, Aditi & Mehta, Mili. (2023). Correlation between prolactin, thyroid, LH, FSH, estradiol and progesterone in the infertile women. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 12. 1017-1022. 10.18203/2320-1770.ijrcog20230805.
- [15] Wright, Kerry L. "Defining infertility: what infertility means for clinicians and clients." *Network*, December 22, 2003, 4. *Gale OneFile: Health and Medicine* (accessed June 6, 2024). https://link.gale.com/apps/doc/A119740879/HRCA?u=anon~ba25e18e&sid=googleScholar&xid=7e9ebf88.