

HORMONAL IMBALANCES AS DETERMINANT OF INFERTILITY

Medina LATIFI*, Mergime ABDULI, Sheval F. MEMISHI

Department of Biology, Faculty of Natural Sciences and Mathematics, University of Tetova, RNM
Corresponding author: m.latifi319042@unite.edu.mk

Abstract

Infertility represents a major reproductive health concern affecting both women and men worldwide, with hormonal imbalances being among the most significant underlying determinants. The endocrine system plays a crucial role in regulating ovulation, spermatogenesis, implantation, and overall reproductive function through hormones such as follicle-stimulating hormone (FSH), luteinizing hormone (LH), estrogen, progesterone, testosterone, prolactin, and thyroid hormones. Disruptions in these hormonal pathways may lead to anovulation, menstrual irregularities, impaired follicular development, reduced sperm quality, and altered endometrial receptivity. Common clinical conditions associated with hormonal infertility include polycystic ovary syndrome (PCOS), thyroid dysfunction, hyperprolactinemia, hypogonadism, and insulin resistance. This paper aims to analyze the relationship between hormonal dysregulation and infertility by examining the main hormonal factors involved, their physiological impact on reproductive processes, and the diagnostic approaches used in clinical practice. Furthermore, it highlights evidence-based strategies for management, including lifestyle modifications, pharmacological interventions, and assisted reproductive technologies. A deeper understanding of hormonal imbalances and their reproductive consequences is essential for early diagnosis, personalized treatment, and improved fertility outcomes.

Keywords: Infertility, hormonal imbalance, endocrine disorders, PCOS, thyroid dysfunction, prolactin, reproductive health.

1. Introduction

This topic is of particular importance for understanding the complexity of hormonal interactions and their impact on an individual's ability to achieve conception. The influence of reproductive hormones is an indispensable part of the functioning of the reproductive system and includes FSH (follicle-stimulating hormone), LH (luteinizing hormone), and estrogen (Melmed et al., 2020). This topic will examine in depth how these hormones influence the processes of ovulation in females and sperm production in males. The reproductive system includes the reproductive organs and the production of hormones; any problem with the reproductive organs or with the regulating hormones can cause infertility (Endocrine Society, 2022). The hypothalamus produces GnRH, which stimulates the pituitary gland to release FSH and LH. These hormones control ovulation in females and sperm production in males. The main reproductive hormones are estrogen, testosterone, and progesterone, which are essential for sexuality and fertility. They are responsible for pregnancy, puberty, menstruation, menopause, sexual desire, sperm production, and many other functions (Melmed et al., 2020). The pituitary gland produces, stores, and stimulates other reproductive hormones such as: human chorionic gonadotropin (hCG), prolactin, luteinizing hormone (LH), follicle-stimulating hormone (FSH), anti-Müllerian hormone (AMH), androgens, estrogens, estradiol, progesterone, relaxin, and testosterone (Endocrine Society, 2022). Anti-Müllerian hormone (AMH) indicates ovarian reserve and plays a role in the development of the reproductive system (Dewailly et al., 2014). Androgens (Testosterone & DHT) in males are essential for sexual development and sperm production. Low levels in men lead to decreased

sexual desire and reduced sperm production, while in females, high levels can cause hormonal disorders (Clavijo & Hsiao, 2018). Estrogens (Estradiol) are the main hormones in females. They regulate the menstrual cycle, ovulation, and the health of the reproductive organs. Progesterone prepares the uterus for pregnancy and helps maintain pregnancy during the early weeks. Relaxin helps with implantation and prevents uterine contractions in the early stages of pregnancy. Testosterone is the primary male hormone; it regulates sexual development and reproductive function (Endocrine Society, 2022). The female reproductive system includes the ovaries, fallopian tubes, uterus, and vagina. The ovaries produce eggs and the main hormones, estrogen and progesterone, which regulate the menstrual cycle and female sexual development (Reed & Carr, 2018). Ovulation is the process during which a mature egg is released from the ovary, usually occurring in the middle of the menstrual cycle. FSH and LH increase, causing the egg to be released from the ovary and travel toward the fallopian tube for the possibility of fertilization. The menstrual cycle is controlled by FSH and LH and is divided into two phases: the follicular phase and the luteal phase (Reed & Carr, 2018). Initially, FSH stimulates the development of ovarian follicles. Granulosa and theca cells produce estrogen, which gradually increases and inhibits FSH through negative feedback. When estrogen levels become very high, they trigger a sudden surge in LH (positive feedback), leading to ovulation. After ovulation, the luteal phase begins: follicular cells transform into the corpus luteum, which produces progesterone. If fertilization does not occur, the corpus luteum degenerates, progesterone levels fall, and menstruation occurs (Reed & Carr, 2018). The male reproductive system includes the testes, epididymis, vas deferens, prostate gland, and penis. The testes produce sperm cells and the hormone testosterone, which controls male development and sperm production (Clavijo & Hsiao, 2018). Leydig cells in the testes produce testosterone under stimulation from LH. Cholesterol is converted into testosterone through several biochemical steps within the cell. Testosterone binds to receptors inside cells, activates DNA, and causes changes related to male development, sperm production, and sexual functions (Clavijo & Hsiao, 2018). Fertility is the natural ability of an individual or a couple to conceive and maintain a pregnancy. Infertility refers to the inability to conceive after a prolonged period (usually one year) without using contraceptive methods, causing significant mental and physical strain (ASRM, 2021). Obesity disrupts hormonal balance and reduces pregnancy chances in both sexes. In females, obesity increases insulin and androgen levels, causing anovulation, while in males, it reduces testosterone levels, increases estrogen levels, and increases scrotal heat, impairing sperm quality (Silvestris et al., 2018; Kahn & Brannigan, 2017). Treatment of obesity-related infertility includes weight loss, a healthy diet, and regular physical activity. Basic treatment methods include cycle monitoring, ovulation induction, and intrauterine insemination (IUI). Advanced methods include IVF (In vitro fertilization), ICSI (Intracytoplasmic sperm injection), and IVM (In vitro maturation of oocytes) (ASRM, 2021). In the IVM process, oocytes are collected at an immature stage and matured in the laboratory, avoiding the high use of hormones typically required in conventional IVF. During maturation, oocytes progress from the immature stage to the MII stage, where they are ready for fertilization (Vuong et al., 2020). The key difference is that in vivo, the oocyte matures naturally inside the ovary under hormonal control, whereas in vitro, the oocyte matures in the laboratory without extensive hormonal stimulation (Vuong et al., 2020). Female infertility main causes include: Problems with ovulation; Ovarian dysfunction; Blockage of the fallopian tubes; Uterine dysfunction; Hormonal disorders; Advanced age (Loma Linda Fertility) Male infertility main causes include: Low sperm count; Poor sperm motility; Abnormal sperm morphology; Hormonal problems; Varicocele or infections (Loma Linda Fertility) Obesity disrupts hormonal balance and reduces pregnancy chances in both sexes. In females, obesity increases

insulin and androgen levels, causing anovulation and menstrual disorders, reduces oocyte quality, and decreases responsiveness during fertility treatments. In males, obesity reduces testosterone levels, increases estrogen levels, and increases scrotal heat, impairing sperm production and quality. Treatment of obesity-related infertility includes weight loss, a healthy diet, regular physical activity, and treatment of metabolic disorders. Severe obesity may require medical therapy or surgical interventions (Loma Linda Fertility). Basic Methods: Cycle monitoring, Ovulation induction, Intrauterine insemination (IUI) Advanced Methods: IVF (In vitro fertilization), ICSI (Intracytoplasmic sperm injection), IVM (In vitro maturation of oocytes) (Loma Linda Fertility). Oocytes are collected at an immature stage and matured in the laboratory. This process avoids the high use of hormones that are typically required in conventional IVF. During oocyte maturation, the oocytes progress from the immature stage to the MII stage, where they are ready for fertilization. While this process usually occurs in the ovary, it can also be carried out in the laboratory. The difference between in vitro maturation (IVM) and in vivo maturation is that in vivo, the oocyte matures naturally inside the ovary under hormonal control, whereas in vitro, the oocyte matures in the laboratory without the need for extensive hormonal stimulation (Lavor.K et al., 2023).

2. Materials and Methods

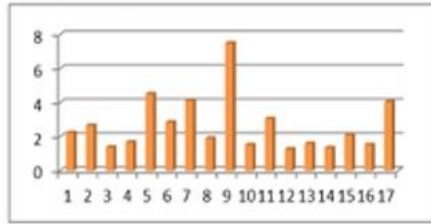
As the material used to determine differences in reproductive hormone levels related to infertility, statistical data provided by the Health Center in Kumanovo were used, while their statistical processing was carried out using computer software. Health Center “Zdravstven Dom” Kumanovo – Laboratory

JZU „ZDRAVSTVEN DOM“ KUMANOVO LABORATORIJA			
Pacient			
Analiza	Rezultat/Eдиници		Referentna vrednost
TSH (Vidas)	/	mIU/L	0.46 - 4.68
FT4 (Vidas)	/	pmol/L	9 - 20
ESTRADIOL (Vidas)	pg/mL	ženi: folikularna faza: 18-147 Ovularna faza: 93-573 Lutealna faza: 43-214 Postmenopauza: <38 muži: <62	
LH (Vidas)	mIU/mL	ženi: folikularna faza: 1.5-8.0 Lutealna faza: 0.2-6.5 Postmenopauza: 8-33 muži: 1-7.0	
FSH (Vidas)	mIU/mL	ženi: folikularna faza: 2.9-12.0 Ovularna faza: 6.3-24 Lutealna faza: 1.5-7.0 Postmenopauza: 17-95 muži: 1.7-12	
PROLAKTIN (Vidas)	ng/mL	ženi: 5.0-35.0 muži: 3.0-25.0	
TESTOSTERON (Vidas)	ng/mL	ženi: 0.1-0.9 muži: 3.0-10.6	
Datum:			

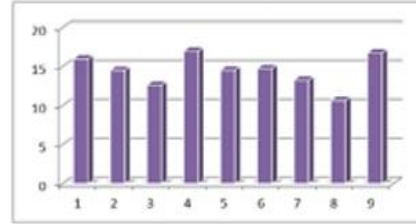
3. Results and Discussion

The analysis of 30 samples shows that the mean values of TSH (2.66 mIU/L) and FT4 (14.47 pmol/L) are within the reference ranges, suggesting normal thyroid gland function. FSH (8.51 mIU/mL) and LH (10.24 mIU/mL) show individual variability but remain mostly within physiological limits. Prolactin has a mean value of 21.41 ng/mL, with some individual elevations but no significant group-level deviations. The mean testosterone level (0.59 ng/mL) is low, while estradiol (77.40 pg/mL) shows expected biological variation. Overall, the analyzed hormonal profile appears balanced, with no evident disorders at the group level.

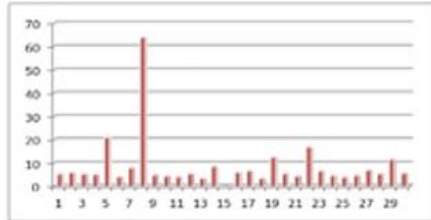
Hormoni refer. Nr.	TSH (mIU/L) 0.46-4.68	FT4 (pmol/L) 9-20	FSH (mIU/mL) variron	LH (mIU/mL) variron	PRL (ng/mL) variron	TST (ng/mL) variron	E2 (pg/mL) variron
1.	/	/	5.26	4.14	32.71	0.86	73.95
2.	/	/	5.92	5.16	28.06	0.29	55.91
3.	/	/	5.24	4.38	32.98	1.25	65.86
4.	/	/	5.11	4.30	13.58	0.23	46.06
5.	/	16.01	21.08	16.17	21.03	0.62	95.58
6.	/	/	4.25	2.23	35.38	0.44	73.88
7.	/	/	7.93	6.14	19.85	0.24	16.77
8.	2.24	14.55	64.12	37.32	9.08	/	31.52
9.	2.66	/	4.94	4.46	27.90	1.16	71.05
10.	/	/	4.49	2.63	11.52	0.67	64.77
11.	1.38	12.64	4.16	7.23	14.90	0.97	51.21
12.	1.69	17.00	5.54	2.95	17.30	0.58	51.35
13.	4.51	14.57	3.46	1.43	28.38	0.26	131.68
14.	/	/	8.50	4.08	24.89	0.48	26.35
15.	/	/	0.10	0.10	10.45	0.34	36.12
16.	/	/	6.14	4.11	43.30	0.48	38.58
17.	2.85	/	6.78	2.68	/	/	127.83
18.	4.12	14.77	3.37	11.01	17.35	0.69	86.99
19.	1.91	13.28	12.64	5.51	17.21	0.39	395.35
20.	7.51	10.68	5.58	4.28	30.85	0.61	57.97
21.	/	/	4.46	10.29	7.16	0.94	96.01
22.	1.53	/	16.94	5.11	17.74	/	103.61
23.	3.06	/	6.54	1.54	/	/	42.28
24.	1.28	/	4.65	3.79	15.36	0.48	31.77
25.	1.60	/	3.92	3.70	10.27	0.20	117.05
26.	1.34	/	4.61	3.81	16.32	/	38.92
27.	/	/	6.97	3.99	32.79	0.44	51.95
28.	2.10	/	5.55	7.1	20.39	/	164.75
29.	1.53	16.77	11.67	2.03	/	0.82	32.77
30.	4.04	/	5.65	4.98	/	0.75	43.90
Mesatarja	2.66	14.47	8.51	10.24	21.41	0.59	77.40



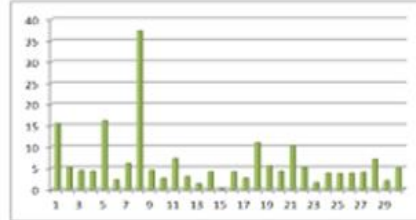
Grafikoni 1. TSH



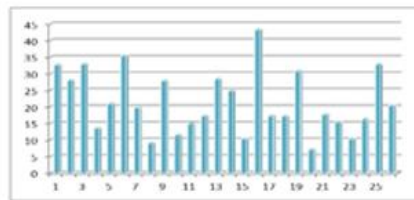
Grafikoni 2. FT4



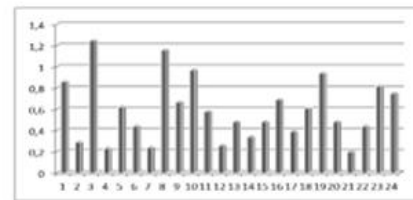
Grafikoni 3. FSH



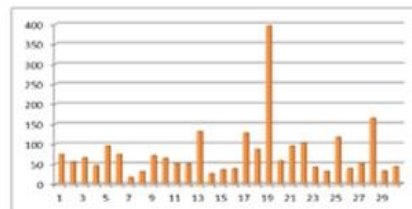
Grafikoni 4. LH



Grafikoni 5. PRL



Grafikoni 6. TST



Grafikoni 7. E2

4. Conclusions

These charts present the results of laboratory measurements for different hormones in a sample group (patients or consecutive tests). Each chart shows the variation of a specific hormone. Here is a simple explanation for each of them: 1. Thyroid Hormones • Chart 1. TSH (Thyroid-Stimulating Hormone): This hormone regulates the function of the thyroid gland. Most values are below 4, but a marked increase is observed in sample 9 (close to 8), which may indicate reduced thyroid activity (hypothyroidism) in that case. • Chart 2. FT4 (Free Thyroxine): This is the main hormone produced by the thyroid. The values appear relatively stable between 10 and 18, which is generally considered within normal laboratory ranges. 2. Reproductive Hormones (Cycle and Fertility) • Chart 3. FSH (Follicle-Stimulating Hormone): It helps stimulate egg development in females. A very high peak is observed in sample 8 (above 60). Such a high value may be related to the ovulatory phase or, in other cases, to menopause. • Chart 4. LH (Luteinizing Hormone): It works together with FSH for ovulation. Here, a clear peak is also seen in sample 8 (close to 37),

confirming a hormonal surge (LH surge) that usually occurs right before ovulation. • Chart 7. E2 (Estradiol): This is the main type of estrogen. A massive increase is seen in sample 19 (close to 400), indicating high ovarian activity at that point in the cycle. 3. Other Hormones • Chart 5. PRL (Prolactin): The milk-production hormone. The values fluctuate significantly, with a high peak in sample 16 (above 40). Elevated prolactin can be influenced by stress, sleep, or certain medical conditions. • Chart 6. TST (Testosterone): This chart shows testosterone levels. The values are mostly low (below 1.2), suggesting that these measurements were taken in females (since male values are much higher).

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