

# Mizaj's Relationship with Luteinizing Hormone and Follicle-Stimulating Hormone in Young Females

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**Abstract: Background:** Unani medicine introduces the concept of Mizaj, representing an individual's inherent temperament and constitution. This study explores the intriguing connection between Mizaj and the levels of two crucial reproductive hormones, Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH), in women.

**Methods:** The study involved 120 women, categorized into four distinct Mizaj types: Balghami, Damvi, Safravi, and Saudavi. Mizaj assessment was conducted using the Ajnas-e-Ashra classification system. Hormonal assays for FSH and LH were performed on day 3 of the menstrual cycle.

**Results:** The study revealed a significant correlation between Mizaj types and FSH and LH levels. Balghami Mizaj women exhibited markedly higher FSH and LH levels in comparison to Safravi and Damvi Mizaj types, while no substantial differences were observed between Balghami and Saudavi Mizaj.

**Discussion:** These findings underscore the profound impact of Mizaj on the regulation of FSH and LH levels in women. The results prompt intriguing questions about the implications of Mizaj's assessment in understanding factors influencing fertility and reproductive health.

**Conclusion:** This study illuminates the intricate relationship between Mizaj and hormonal levels, particularly in Balghami Mizaj women who exhibited significantly higher FSH and LH levels. These findings hold the potential to enhance our comprehension of women's health and guide future research in this area.

**Keywords:** Mizaj, FSH, LH, Women's Health, Hormonal Balance, Unani Medicine.

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## 1. INTRODUCTION

The concept of Mizaj, an essential component of traditional Unani medicine, represents an individual's inherent temperament and constitution. It serves as the foundation of health and plays a significant role in the diagnosis, prevention, and treatment of various health conditions. The principles of Unani medicine have been meticulously developed over centuries, drawing from ancient Greek, Persian, and Indian medical traditions. Hippocrates (460 B.C.), a Unani physician, presents the doctrine of body fluids (i.e., Humors or Akhlat, [singular khilt]) in his book "Human Nature." He maintains that the human body contains four major kinds of humour—i.e., Dam (blood), Balgham (Phlegm), Safra (yellow bile), and Sauda (black bile). According to quality and quantity, an accurate proportion and mixing of these elements (homeostasis) constitutes health. Thus, this humoral theory states that if homeostasis is maintained inside the body the person will remain healthy, and if this homeostasis is disturbed, then the disease will develop. Hence, this hemostasis of Akhlat deals with every aspect of the disease (i.e., etiology, pathology, prevention, and treatment). Internal and external causes influence the hemostasis of the human body leading to sue' Mizaj that ultimately inflicts the whole body or a specific organ

in the form of the disease. The principle of management of the disease is to correct the altered Mizaj. Thus, before commencing any treatment, the Mizaj of a patient or organ must be evaluated.<sup>1</sup>

A functional hypothalamic-pituitary axis is essential for mammalian reproduction. The hypothalamus secretes the decapeptide, gonadotropin-releasing hormone (GnRH) that is responsible for initiating the cascade of events that regulate the gonads.<sup>2</sup> Pituitary gonadotropes, in turn, express receptors specific to GnRH. Activation of these receptors by GnRH initiates intracellular signal transduction pathways to induce synthesis and release of the gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH).<sup>2</sup> Human FSH can be defined in molecular terms as a heterodimeric glycoprotein hormone consisting of two noncovalently linked subunits designated  $\alpha$  and  $\beta$ , which consist of 92 amino acids and 111 amino acids,<sup>3</sup> respectively, and which are products of different genes. Each subunit of FSH has two N-linked glycosylation sites. The sites are located on Asn 52 and Asn 78 for the  $\alpha$ -subunit and Asn 7 and Asn 24 for the  $\beta$ -subunit. The glycosylation sites are essential for the expression of FSH bioactivity. In females, FSH is necessary for the selection and growth of ovarian follicles and the production of estrogens from androgen substrates.

LH is a heterodimeric glycoprotein. Each monomeric unit is a glycoprotein molecule. The full, functional protein is made up of one alpha and one beta subunit. The alpha subunits of LH, FSH, TSH, and hCG are identical and contain 92 amino acids in humans. The beta subunits, however, vary. LH has a beta subunit of 120 amino acids (LHB), which confers its specific biological action and is responsible for the specificity of the interaction with the LH receptor. LH and FSH are the hormones that encourage ovulation. The mean values for women before ovulation are around (3.8-8.8) IU/L. After ovulation, these levels drop to between (1.8 - 5.1) IU/L.<sup>4</sup> At the middle of the menstrual cycle it reaches its highest value, between (4.5-22.5) IU/L. During menopause, the values go up even more, between (16.74-113.59) IU/L. For men, the mean values are around (16.74-113.59) IU/L.<sup>5,6,7</sup> LH and FSH usually range between 5 and 20 IU/mL (Sterling 2015). In most women, LH and FSH are present in equal amounts in the early part of their life. However, there is a surge in LH levels about 24 hours before ovulation, during which the amount of LH increases to about 25-40 IU/mL. Once the egg is released from the ovary, the LH level goes back down. FSH triggers the growth of follicles and stimulates the granulosa cells of the follicles to secrete both estrogens and progesterone. These cells develop LH receptors as a result of this process.<sup>8</sup> LH has a predominant role in the trigger of ovulation of the Graffian follicle as well as its luteinisation. FSH and LH levels are regulated by the steroid hormones through feedback loop mechanisms; estrogenic exerts negative feedback on FSH secretion and both negative and delayed positive feedback effects on LH secretion which in turn results in increased progesterone secretion and LH surge.<sup>9</sup>

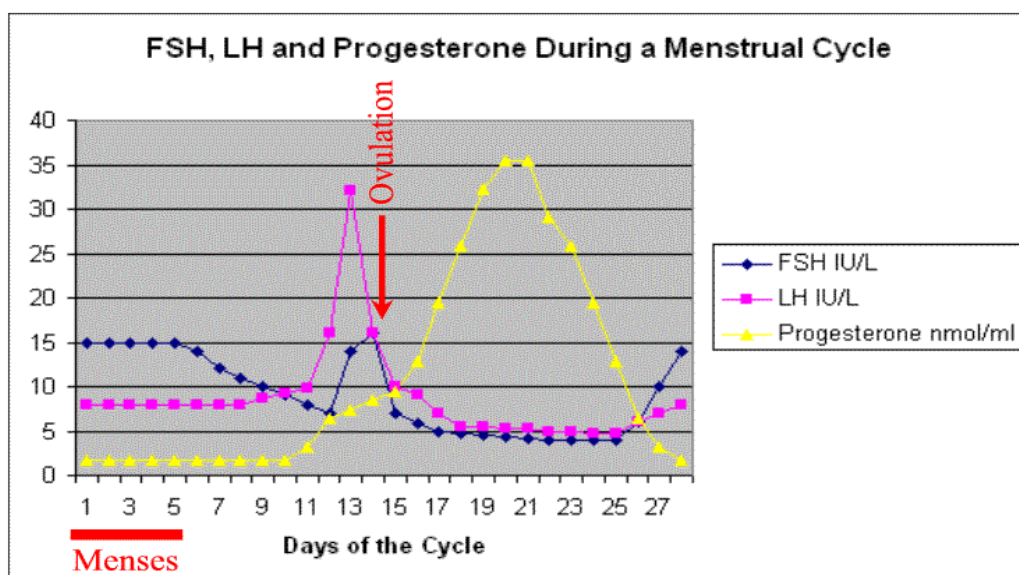


Fig 1: FSH and LH levels during the menstrual cycle

The present research aims to shed light on the relationship between Mizaj and the levels of LH and FSH by conducting a comprehensive study that encompasses both theoretical and empirical investigations. It is our aspiration that this research will contribute to the expansion of knowledge in the field of traditional medicine, offering new perspectives on the intricate connections between an individual's Mizaj and their reproductive hormone levels.

## 2. METHODOLOGY

### Study Design:

**Place of Study:** The study was conducted at the Department of Amraz-e-Niswan wa Qabalat at A & U Tibbia College Hospital in Karol Bagh, New Delhi, **Study Type:** Descriptive observational study. **Duration:** The study was conducted over 1.5 years, **Sample Size:** A total of 120 subjects participated, **Sampling Technique:** Subjects were selected using a simple random technique.

### Inclusion Criteria:

Female patients aged 18 to 45 years, including both married and unmarried, Both nulliparous and multiparous patients, and Patients with complaints of lower abdominal pain and lower backache.

### Exclusion Criteria:

Patients with menstrual irregularities (infrequent cycles, scanty bleeding, oligomenorrhea, amenorrhea, and irregular bleeding), Patients with diagnosed cases of ovarian cysts ranging in size from 10 mm to 30 mm, Patients with a history of AIDS, syphilis, or gonorrhoea, Patients with a history of cardiovascular, renal, or liver diseases, Patients with diabetes (Type 1 or Type 2), Patients with systemic diseases or malignancies, Patients with endocrine disorders other than ovarian cysts, Individuals engaged in alcohol or other intoxicating substance abuse, and Pregnant females.

### Informed Consent:

Patients who met the inclusion criteria were provided with an information sheet detailing the study, and the study procedures, Patients had the opportunity to ask questions and were given time to review the information, and Informed consent forms were signed by patients who voluntarily agreed to participate.

### Assessment of Mizaj (Temperament):

Mizaj (temperament) was assessed using the Ajnas-e-Ashra, a classification system consisting of 10 classical principles as per the Unani system of medicine. The four types of temperament assessed were Damwi (Sanguine), Balghami (Phlegmatic), Safrawi (Bilious), and Saudawi (Melancholic).

### Investigations Required:

Complete Blood Count (CBC) with Erythrocyte Sedimentation Rate (ESR) and Hormonal assay FSH, LH on day 3 of the menstrual cycle.

## 3. RESULTS AND OBSERVATIONS

Unlocking the Secrets of Mizaj: A Journey into FSH and LH Levels in Women

**Data Descriptions:** This comprehensive investigation involved 120 women, with each mizaj group comprising balghami 64, damvi 18, safrawi 31, and saudawi 7 participants. The mizaj-specific mean FSH levels were as follows: Mizaj Balghami (M = 15.009, SD = 6.208), Mizaj Safrawi (M = 10.8174, SD = 3.61998), Mizaj Damvi (M = 10.975, SD = 3.182), and Mizaj Saudawi (M = 13.4157, SD = 8.36309). The corresponding LH levels for each group were: Mizaj Balghami (M = 10.7958, SD = 5.54863), Mizaj Safrawi (M = 8.0023, SD = 2.93180), Mizaj Damvi (M = 7.1089, SD = 1.85572), and Mizaj Saudawi (M = 10.1500, SD = 6.11983).

Table 1

	MIZAJ	Mean FSH	MEAN LH
1.	DAMWI	10.975 ± 3.182	7.108 ± 1.855
2.	BALGHAMI	15.009 ± 6.208	10.79 ± 5.548
3.	SAFRAWI	10.817 ± 3.6199	8.002 ± 2.931
4.	SAUDAWI	13.4157 ± 8.363	10.15 ± 6.119

**Key Statistical Results:** Our study unearthed compelling evidence of a pivotal connection between mizaj types (balghami, damvi, safrawi, and saudawi) and hormone levels in women. The ANOVA test uncovered a statistically significant difference in FSH levels among mizaj types ( $F(3, 116) = 5.357, p = 0.02$ ). In parallel, LH levels were also found to be significantly impacted by mizaj types ( $F(3, 116) = 4.409, p = 0.006$ ).

Table 2

		ANOVA				
		Sum of Squares	df	Mean Square	F	Sig.
FSH	Between Groups	472.877	3	157.626	5.357	.002
	Within Groups	3412.937	116	29.422		
	Total	3885.814	119			
LH	Between Groups	198.735	3	66.245	2.741	.046
	Within Groups	2803.269	116	24.166		
	Total	3002.004	119			

**Group Comparisons:** Delving deeper, post hoc analyses, including Tukey's Honestly Significant Difference (HSD) test, illuminated the distinctiveness of each mizaj type. Women with Mizaj balghami demonstrated markedly higher FSH levels ( $M = 15.0009$ ,  $SD = 6.208$ ) compared to Mizaj safravi ( $M = 10.8174$ ,  $SD = 3.61998$ ,  $p = 0.003$ ) and Mizaj damvi ( $M = 10.975$ ,  $SD = 3.182$ ,  $p = 0.032$ ). Meanwhile, no statistically significant differences were observed between mizaj balghami and saudavi ( $M = 13.4157$ ,  $SD = 8.36309$ ,  $p = 0.883$ ).

Intriguingly, a similar pattern emerged for LH levels, with women of Mizaj balghami showing a significant LH level elevation ( $M = 10.7958$ ,  $SD = 5.54863$ ) compared to Mizaj safravi ( $M = 8.0023$ ,  $SD = 2.93180$ ,  $p = 0.033$ ) and Mizaj damvi ( $M = 7.1089$ ,  $SD = 1.85572$ ,  $p = 0.018$ ), while no significant differences were discerned between mizaj balghami and saudavi ( $M = 10.1500$ ,  $SD = 6.11983$ ,  $p = 0.985$ ).

Table 3

Multiple Comparisons Tukey HSD					
Dependent Variable	(I) Mizaj	(J) Mizaj	Mean Difference (I-J)	Std. Error	Sig.
FSH	Balghami	Damvi	4.02538*	1.44716	.032
		Safravi	4.18352*	1.18693	.003
		Saudavi	1.58522	2.15936	.883
LH	Balghami	Damvi	2.47023	1.31155	.241
		Safravi	1.39997	1.07571	.564
		Saudavi	4.60292	1.95701	.092

**Hypothesis Testing:** Our initial hypothesis, suggesting that mizaj types impact FSH and LH levels, was met with partial support. Mizaj balghami emerged as a pivotal factor, with significantly higher FSH and LH levels compared to safravi and damvi, while no substantial differences were detected between mizaj balghami and saudavi.

**Implications and Observations:** These compelling findings invite us to consider the role of mizaj in the intricate regulation of FSH and LH levels. Understanding this profound connection holds the promise of identifying critical factors influencing fertility and reproductive health in women.

#### 4. DISCUSSION

The Mizaj of an individual is characterized by the fluid element (Akhlāt) and its physiological effects, expressed by the preponderance of a particular Khilt in the body. A person may be Damwi (sanguineous), Balghami (phlegmatic), Safrawi (choleric), or Saudawi (melancholic) based on the preponderance of Dam, Balgham, Safra, or Sauda, respectively.<sup>10,11</sup>

In mammalian ovaries, LH induces androgen biosynthesis, while FSH stimulates aromatase activity.<sup>12</sup> A study revealed no correlation between Mizaj types and free T3 and T4, but thyroid-stimulating hormone (TSH) was significantly higher in Balghami Mizaj, suggesting a potential association with khilt-e-balgham and Barid-Ratab Mizaj.<sup>13</sup> Follicle stimulating hormone and Luteinizing hormone is a glycoprotein hormone-like TSH and has similar alpha subunit. Additionally, LH has been identified to increase thyroid adenylate cyclase activity.<sup>14,15,16</sup> The link between balghami Mizaj and LH/FSH levels results in our study prompts critical explanations regarding LH and FSH hormone's potential form as balghami khilt.

Rofas (98-171 AD) noted that obese women, dominated by khilt balgham, may face challenges in conception, with an increased risk of abortion or difficult labor.<sup>17</sup> Majoosi (930-994 AD) mentioned that if temperament of women becomes

cold(balghami), it causes zo'afe jigar causes liver dysfunction and inability of conversion chyme into blood, rather it forms tenacious phlegm which is major cause of amenorrhoea. Obesity exacerbates these effects, narrowing blood vessels and reducing uterine blood supply.<sup>18</sup> Abnormality in quality and quantity of *Madda* in *Su-i-Mizaj Maddi* can also lead to *ihitbas al-tamth(amenorrhoea)*.<sup>19</sup> Sue mizaj barid causes uterine vasoconstriction (which leads to amenorrhoea)<sup>20,21,23,24</sup> & spasm of fallopian tubes so that nutfa (gamete) fails to reach the uterus, placental insufficiency which ultimately leads to infertility.<sup>20,21,23,28</sup> Ibn Sina states that sue mizaj rated results in infertility due to zo'afe quwwate jaziba and Masika of the uterus, which leads to decreased endometrial receptivity and failure of embryonic implantation.<sup>20,21,25,26,27,28</sup> Al Majoosi cited that ghalbae balgham, causes infertility, due to the dominance of khilte balgham.<sup>20,30</sup> when ihtibas al-tamth (amenorrhea) occurs, it leads to different kinds of disorders [19]. Unani scholars state at this age, the mizaj of the woman changes more towards burudat. The production of blood in the liver gets decreased, whatsoever is produced that too declines towards coldness [3,17]. Hence, the causes of ihtibas al-tamth at this age may be burudat al-rahim or ghalaba al-burudat (dominance of coldness), sudda urooq al-rahim (closer of the uterus or its vessels due to obstruction), or increased viscosity of blood [4,17]. In ghalaba al-burudat, ghaleez akhlat (viscos The above concepts of different Unani scholars reflect that FSH/LH can cause khilt-e-balgham and a cold temperament (barid Mizaj). Hormones are classified into three types based on their chemical nature.<sup>27,42</sup>, i.e. Protein hormones (growth hormones, thyroid stimulating hormones, Adrenocorticotrophic hormone, Follicle-stimulating hormone, Luteinizing hormone, Antidiuretic hormone), Steroid hormones (Aldosterone, Testosterone, Cortisol, Progesterone), and Derivatives of the amino acid called tyrosine(Thyroxine, Triiodothyronine, Epinephrine, Norepinephrine and Dopamine.<sup>34,35,36,37,38</sup> Our research results have unveiled a compelling association between Balghami Mizaj and the levels of LH and FSH as levels were highest in balghami women. Our research establishes a significant association between Balghami Mizaj and higher LH and FSH levels in women.

## 5. CONCLUSION

In conclusion, our study has unveiled a significant and captivating relationship between mizaj types and FSH and LH levels in women. These findings beckon further exploration into the underlying mechanisms, as well as the tantalizing prospect of clinical applications in the realm of women's health.

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**Conflicts of Interest:** The authors declare no conflict of interest.

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**Limitations of the study:** The study's limitations include a modest sample size, a single-centre design limiting generalizability, subjective Mizaj assessment, exclusion criteria restricting diverse representation, cross-sectional nature hindering causal inference, hormonal assays limited to day 3, and a lack of comprehensive covariate adjustment.

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