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THE IMPACT OF BODY MASS INDEX ON THE HORMONAL AND IMMUNOLOGICAL STATUS OF ADOLESCENT GIRLS WITH MENSTRUAL CYCLE DISORDERS

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Abstract
A study was conducted to examine the influence of body mass index (BMI) on the hormonal and immunological status of adolescent girls with menstrual cycle disorders. The research revealed that in the group of girls with high BMI and menstrual cycle disorders, hyperandrogenism, hyperinsulinemia, and reduced adiponectin levels were observed, accompanied by systemic inflammation and probable disruption of the hypothalamic-pituitary-ovarian axis. In contrast, the group of girls with low BMI and menstrual cycle disorders exhibited signs of hypoestrogenism, decreased leptin, and suppression of reproductive function, likely due to energy deficiency.

Keywords: Girls, teenagers, menstrual cycle, imbalance, testosterone, adipokines, hirsutism, hormones, body mass index.

Introduction

Adolescence is characterized by intense endocrine and metabolic changes that shape the development of the reproductive system and overall health. Menstrual cycle disorders, one of the most common reasons for seeking medical help in adolescence, can result from hormonal imbalances, metabolic changes, and immune response disturbances [1, 3].

Overweight and obesity, as well as low body weight, have a significant impact on the functioning of the hypothalamic-pituitary-ovarian axis, altering the levels of sex hormones such as estradiol, progesterone, testosterone, and gonadotropins (FSH and LH). These changes are often accompanied by systemic inflammation, altered cytokine levels, and immune balance disruptions. At the same time, girls with a low

BMI may experience hypoestrogenism, which also affects immune functions and reduces reproductive health quality [2, 4].

Given the rising prevalence of obesity and weight disorders in children and adolescents, studying the relationship between endocrine and immunological indicators is becoming increasingly important. Menstrual cycle disorders in adolescence often serve as a marker of systemic problems, including metabolic disorders, endocrine dysfunctions, and immune imbalances [7, 8].

The pathophysiology of menstrual cycle disorders in overweight or obese adolescent girls is associated with hyperinsulinemia, hyperandrogenism, and chronic low-grade inflammation, which lead to changes in normal folliculogenesis and the ovulatory cycle. In contrast, girls with low body weight experience hypogonadotropic amenorrhea, reduced estradiol and progesterone levels, which also negatively affect immune function [6, 10].

Despite the large number of studies on menstrual cycle disorders, the relationship between hormonal changes and immune response depending on BMI remains insufficiently studied. This is especially important during adolescence, when correcting such disorders can prevent the development of long-term reproductive and metabolic complications [1, 9].

Based on the above, the aim of the present study was to identify the features of hormonal and immune status in adolescent girls with different body mass indices and menstrual cycle disorders.

Materials and Methods:

The study included 68 adolescent girls aged 12 to 17. The participants were divided into three groups: the first group consisted of 23 girls with a high body mass index (BMI) and menstrual cycle disorder (MCD), the second group consisted of 18 girls with a low BMI and menstrual cycle disorder, and the third group, the control group, consisted of 27 girls with normal BMI and regular menstrual cycles. BMI diagnosis was carried out according to the age- and gender-specific standards of the World Health Organization (WHO). The body mass index (BMI) for each participant was calculated using the formula: body weight (kg) divided by the square of height (m^2). Body weight was measured with an accuracy of 0.1 kg on calibrated electronic scales, and height was measured with an accuracy of 0.1 cm using a stadiometer. BMI values were rounded to two decimal places.

The obtained values were interpreted according to the WHO age- and sex-specific standards for children and adolescents: underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), and overweight/obesity (BMI ≥ 25 kg/m^2). Based on

BMI, the participants were divided into three groups: underweight, normal BMI, and overweight.

The clinical examination included the evaluation of hirsutism using the Ferriman-Gallwey scale. Additionally, the degree of development of secondary sexual characteristics was assessed in accordance with the Tanner classification, which allowed for identifying features of puberty based on the group.

Hormonal status was evaluated based on the levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), and testosterone. Hormonal parameters were determined during the initial visit to the clinic (Samarkand city) using chemiluminescent immunoassay (CLIA).

Adipokine concentrations were studied in the laboratory of Reproductive Immunology at the Institute of Immunology and Human Genomics, Academy of Sciences of the Republic of Uzbekistan. Blood samples were collected after a thorough examination. Blood was collected in the morning on an empty stomach, serum was separated by centrifugation, and then frozen at -20°C until analysis.

The serum adipokine levels were determined using solid-phase enzyme-linked immunosorbent assay (ELISA) with test systems from BioKhiMak ST (Russia), following the manufacturer's recommendations. Quantitative assessment of results was performed by constructing a calibration curve that reflects the optical density-concentration relationship for the standard antigen, allowing for comparison with the investigated samples.

The study included adolescent girls with diagnosed menstrual cycle disorders according to WHO guidelines, aged 12–17 years. Participants with chronic inflammatory diseases, endocrinopathies (e.g., diabetes or thyroid diseases), or acute infectious processes at the time of examination were excluded.

Statistical data processing was carried out using the Student's t-test to compare quantitative indicators between groups. Values of $p<0.05$ were considered statistically significant. The results of the analysis provide a basis for interpreting the relationship between hormonal and immunological parameters in different groups of adolescent girls, taking into account their BMI and menstrual cycle status.

Results and Discussion:

The analysis of the obtained data revealed significant differences in hormonal and immunological status among adolescent girls with different BMIs and menstrual cycle disorders.

Hormonal status was characterized by analyzing the levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), and

testosterone. Follicle-stimulating hormone (FSH) is a gonadotropin hormone produced by the anterior pituitary gland that regulates the growth and maturation of ovarian follicles. FSH levels reflect the activity of the hypothalamic-pituitary-ovarian axis and play a key role in the establishment of reproductive function in adolescent girls. Changes in FSH concentration are associated with stages of puberty and can serve as markers of menstrual cycle disorders or other endocrine dysfunctions [9].

Table 1. Hormonal status of the examined adolescent girls

Indicator	Control group (n=27)	Group 1 (n=23)	Group 2 (n=18)
FSH, mIU/L	3.84 ± 0.42	4.29 ± 0.57^	2.52 ± 0.36*
LH, mIU/L	5.23 ± 0.81	9.86 ± 1.24*	3.09 ± 0.54*
TSH, mIU/L	2.57 ± 0.35	4.57 ± 0.65*	3.25 ± 0.45^
Testosterone, nmol/L	1.68 ± 0.46	3.54 ± 0.83*	0.81 ± 0.23^

Note: * - statistically significant compared to the control group ($p<0.05$-0.001). ^ - not statistically significant compared to the control group ($p>0.05$).

The analysis of FSH levels in Group 1, consisting of girls with high BMI and menstrual disorders, showed an increase to 4.29 ± 0.57 mIU/L, while the control group had an average of 3.84 ± 0.42 mIU/L. This difference was statistically insignificant ($p>0.05$), indicating that the difference with the control group is not significant. However, the slight increase in FSH levels is likely associated with compensatory activity of the hypothalamic-pituitary-ovarian system against the backdrop of hyperinsulinemia, which is characteristic of obesity, as well as disruption of the ovulatory cycle (table 1). In Group 2, which includes girls with low BMI and menstrual disorders, the FSH level was 2.52 ± 0.36 mIU/L, which was significantly lower than the values in the control group ($p<0.01$). The reduction in FSH levels by nearly 1.5 times (34.4%) indicates suppression of the hypothalamic-pituitary axis, which may be related to energy deficiency and inadequate nutrition. This condition leads to a decrease in gonadotropin production, which prevents the normal maturation of follicles and the formation of a regular ovulatory cycle (table 1).

Luteinizing hormone (LH) is a gonadotropic hormone produced by the anterior pituitary that regulates ovulation and the function of the corpus luteum. During puberty, LH levels rise, reflecting the activity of the hypothalamic-pituitary-ovarian axis. Excessive LH secretion is characteristic of polycystic ovary syndrome (PCOS) and

is associated with ovulatory dysfunction, while decreased levels are observed in hypogonadotropic states (table 1).

The analysis of LH levels in adolescent girls in Group 1, with high BMI and menstrual disorders, showed that the LH level was significantly higher than the control group ($p<0.05$), reaching 9.86 ± 1.24 mIU/L, which is 1.88 times higher than the control group (5.23 ± 0.81 mIU/L). This increase likely indicates LH hypersecretion, characteristic of PCOS, where there is an abnormal LH/FSH ratio. This pattern suggests activation of the hypothalamic-pituitary axis in the context of hyperinsulinemia and hyperandrogenism, which prevents normal follicular maturation and ovulation (table 1).

In Group 2, consisting of girls with low BMI and menstrual disorders, the LH level was significantly lower ($p<0.05$) compared to the control group, at 3.09 ± 0.54 mIU/L. This value was 1.69 times lower than the control, indicating a hypogonadotropic state (table 1). The reduction in LH levels may be related to energy deficiency, suppression of hypothalamic-pituitary activity, and impaired follicular maturation. Such changes are common in girls with low body weight and chronic nutrient deficiency, leading to amenorrhea or significant menstrual cycle disruptions.

Thyroid-stimulating hormone (TSH) is a hormone produced by the anterior pituitary that regulates the synthesis of thyroxine (T4) and triiodothyronine (T3) in the thyroid gland. It ensures metabolic balance and plays a vital role in physical and reproductive development during adolescence. Abnormal TSH levels indicate thyroid dysfunction: elevated levels are characteristic of hypothyroidism, often associated with obesity, while reduced levels indicate hyperthyroidism or hypothalamic-pituitary insufficiency.

The analysis of serum TSH levels in girls from Group 1 with high BMI and menstrual disorders showed that the TSH level was significantly higher than the control group ($p<0.05$), at 4.57 ± 0.65 mIU/L, which is nearly 1.78 times higher than the control group's level of 2.57 ± 0.35 mIU/L. This increase is likely associated with the possible development of subclinical hypothyroidism, characteristic of obesity. Elevated TSH levels may be a compensatory response to metabolic changes such as hyperinsulinemia and indicate strain on the thyroid gland due to excess body weight (table 1).

In Group 2, including girls with low BMI and menstrual disorders, the TSH level was 3.25 ± 0.45 mIU/L, which did not differ significantly from the control group ($p>0.05$). The increase in TSH levels by 1.26 times compared to the control group may indicate early signs of thyroid adaptation in the context of energy deficiency, but no significant thyroid dysfunction was observed in this group (table 1).

Testosterone is the primary androgen produced by the ovaries and adrenal glands in girls. It contributes to the development of muscle and bone mass, as well as the regulation of puberty and the ovulatory cycle. Elevated testosterone levels are characteristic of hyperandrogenic states, such as polycystic ovary syndrome (PCOS), while lower levels are associated with ovarian atrophy and energy deficiency. Testosterone is a key marker of reproductive health in adolescents.

According to the analysis of serum testosterone concentrations in girls from Group 1, with high BMI and menstrual disorders, the level of this hormone was 3.54 ± 0.83 nmol/L, significantly higher than the control group (1.68 ± 0.46 nmol/L, $p<0.05$). The value was 2.1 times higher than the control group (table 1). This increase is likely related to hyperandrogenism, commonly observed in PCOS, which is characteristic of girls with obesity. Hyperandrogenism contributes to ovulatory cycle disruptions, hirsutism, and acne, reflecting the influence of excess body weight on hormonal balance.

In Group 2, consisting of girls with low BMI and menstrual disorders, the testosterone level was 0.81 ± 0.23 nmol/L, which did not differ significantly from the control group ($p>0.05$). This value was 2.07 times lower than the control group (table 1). The decrease in testosterone levels is likely also related to energy deficiency and suppression of ovarian function, leading to reduced androgen production.

The immunological indicators included the study of serum adipokine levels.

Table 2. Adipokine Levels in the Examined Adolescent Girls

Indicator	Control Group (n=27)	Group 1 (n=23)	Group 2 (n=18)
LEP, ng/ml	18.79 ± 0.97	32.57 ± 2.13*	6.33 ± 0.71*
AdipoQ, µg/ml	8.94 ± 0.82	4.26 ± 0.59*	10.19 ± 1.24^

*Note: * - statistically significant compared to the control group (p<0.05-0.001). ^ - not statistically significant compared to the control group (p>0.05).*

Leptin (LEP) – a hormone secreted by adipose tissue that regulates energy balance, appetite, and body weight. Its level directly depends on the amount of fat tissue. Leptin stimulates the hypothalamus, suppressing hunger, and is involved in activating the hypothalamic-pituitary-ovarian axis, which makes it important for puberty. In obesity, leptin levels are elevated, which may lead to leptin resistance and reproductive function disorders. In underweight individuals, leptin reduction suppresses gonadotropin secretion, causing amenorrhea [8].

It was found that in the first group of girls with high BMI and menstrual cycle (MC) disorders, leptin levels were significantly higher, averaging 32.57 ± 2.13 ng/ml compared to the control group's 18.79 ± 0.97 ng/ml ($p<0.001$), which is 1.73 times higher than the control group. The significant increase in leptin is linked to an increase in fat mass, as leptin is a hormone secreted by adipocytes. Elevated leptin levels may lead to leptin resistance, contributing to metabolic dysfunction, hyperinsulinemia, and disruption of the hypothalamic-pituitary-ovarian axis (Table 2).

In the second group, including girls with low BMI and menstrual cycle disorders, leptin levels were significantly lower than the control, at 6.33 ± 0.71 ng/ml ($p<0.001$), which is 2.97 times lower than the control group. The reduction in leptin is associated with fat tissue deficiency, leading to energy deficiency and reproductive dysfunction. Low leptin levels suppress the secretion of gonadotropin-releasing hormone (GnRH), leading to hypogonadotropic conditions and amenorrhea, typical for girls with low body weight (Table 2).

Adiponectin (AdipoQ) – an adipokine produced by fat tissue, which increases tissue sensitivity to insulin, regulates glucose and lipid metabolism, and suppresses inflammation. Its levels decrease in obesity, contributing to insulin resistance and chronic inflammation, and may increase with low BMI, reflecting low levels of visceral fat. Adiponectin plays an important role in maintaining metabolic and reproductive health (Table 2) [7, 9].

The table presents data on adiponectin (AdipoQ) levels in adolescent girls from three groups: the control group with a normal body mass index (BMI) and regular menstrual cycles (MC), group 1 with high BMI and MC disorders, and group 2 with low BMI and MC disorders. The adiponectin level in the control group was 8.94 ± 0.82 µg/ml, reflecting a normal metabolic state and inflammatory balance (Table 2).

It was determined that in the first group of girls with high BMI and menstrual cycle disorders, the AdipoQ level was significantly lower ($p<0.05$) than the control value (8.94 ± 0.82 µg/ml), averaging 4.26 ± 0.59 µg/ml, which is 2.1 times lower than the control group. The reduction in AdipoQ is likely related to an increase in visceral fat mass, which suppresses the secretion of this adipokine.

In the second group, including girls with low BMI and MC disorders, the AdipoQ level was 10.19 ± 1.24 µg/ml, which showed no significant difference ($p>0.05$) compared to the control group, though it was 1.14 times higher than the control values. The increase in AdipoQ in girls with low BMI is likely due to the low amount of visceral fat, which promotes higher secretion. However, in the case of pronounced energy deficiency, AdipoQ levels may decrease, but this was not observed in this group.

Conclusion

The study revealed significant differences in hormonal and immunological status in adolescent girls with different body mass index (BMI) and menstrual cycle (MC) status. Girls with high BMI showed hyperandrogenemia, hyperinsulinemia, and decreased adiponectin levels, accompanied by systemic inflammation and disruptions in the hypothalamic-pituitary-ovarian axis. Girls with low BMI exhibited signs of hypoestrogenism, leptin reduction, and suppression of reproductive function, which were linked to energy deficiency. In the control group, hormonal and immune status indicators were within normal physiological limits, reflecting a balanced metabolic state and reproductive system.

Conclusions:

1. The level of follicle-stimulating hormone (FSH) was significantly reduced in girls with low BMI by 34.4%, indicating suppression of the hypothalamic-pituitary axis. Luteinizing hormone (LH) was significantly increased in girls with high BMI by 1.88 times, typical for hyperandrogenemia and polycystic ovary syndrome (PCOS).
2. The level of thyroid-stimulating hormone (TSH) was significantly increased in girls with high BMI by 1.78 times, indicating compensatory stress on the thyroid gland. In girls with low BMI, TSH levels were slightly elevated, indicating adaptation to energy deficiency.
3. Testosterone levels in the group of girls with high BMI were increased by 2.1 times, confirming hyperandrogenemia. In girls with low BMI, testosterone levels were decreased by 2.07 times, due to ovarian suppression.
4. Leptin was significantly elevated in girls with high BMI by 1.73 times and reduced in girls with low BMI by 2.97 times. This reflects the impact of fat tissue on energy and reproductive status.
5. Adiponectin levels were reduced in girls with high BMI by 2.1 times, related to insulin resistance and inflammation. In girls with low BMI, adiponectin levels exceeded the norm by 1.14 times, due to low visceral fat mass.

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