



## **THE ASSOCIATION BETWEEN AUTONOMIC NERVOUS SYSTEM DYSFUNCTION AND MENSTRUAL DISORDERS IN FEMALE ADOLESCENTS: A MULTIDISCIPLINARY EVALUATION**

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**Abstract:** Adolescence represents a critical period of physiological and psychological development, marked by significant hormonal fluctuations and the maturation of various body systems, including the autonomic nervous system (ANS) and reproductive function. During this transitional phase, the complex interplay between neurological and endocrine systems becomes particularly evident, with emerging evidence suggesting that autonomic nervous system dysfunction may play a significant role in the development and persistence of menstrual disorders among female adolescents.

**Keywords:** autonomic dysfunction, menstrual cycle, adolescent girls, neurovegetative regulation, hormonal status.

**INTRODUCTION.** The menstrual cycle status serves as a crucial health indicator for adolescent females [1, 5, 9, 13]. During periods of dysregulatory transitions, nervous system development, particularly emotional responsiveness, represents a critical component. According to multiple researchers [2, 6, 10, 14], emotional disturbances manifest in 50-80% of cases, attributed primarily to autonomic function abnormalities. When autonomic disorders remain inadequately addressed, they tend to become chronic and therapeutically resistant in adulthood. This creates a perpetuating cycle of interdependence: autonomic nervous system dysfunction compromises reproductive function in adolescent girls, while conversely, menstrual dysfunction exacerbates autonomic syndromes. The primary pathomechanism involves immature autonomic support during the development of regulatory centers, specifically the hypothalamic-pituitary system, resulting from the body's adaptive responses to impending changes and stressors [3, 7, 11]. The hypothalamus demonstrates unique anatomical and functional characteristics, exhibiting heightened reactivity to both internal and external factors compared to other neural structures [4, 8, 12]. Therefore, investigating the factors and causes underlying clinical and functional alterations in autonomic status among adolescent girls with menstrual disorders appears essential.

**STUDY OBJECTIVE.** This research aims to examine and establish the clinical and physiological characteristics of autonomic dysfunction in adolescent girls presenting with menstrual disorders.

**METHODOLOGY AND PARTICIPANTS.** The investigation was conducted across multiple clinical settings: the Multidisciplinary Clinic of Samarkand State Medical University (MC SamSMU) within pediatric neurology and gynecology departments, and the Multidisciplinary Children's Hospital in Samarkand, encompassing pediatric neurology and pediatric gynecology departments.

Study participants comprised adolescent girls with a mean age of  $17.3 \pm 1$  years. The experimental cohort included 45 participants meeting inclusion criteria of autonomic dysfunction manifestations and menstrual irregularities. A control group of 41 healthy age-matched adolescent girls was established for comparison.

The research protocol involved multiple phases: patient selection from inpatient admissions, comprehensive clinical and neurological assessments, and evaluations by pediatricians, dentists, and ENT specialists. Diagnostic procedures included: pelvic ultrasound, brachiocephalic vessel ultrasound, electrocardiography, electroencephalography, brain neuroimaging (MRI) with sella turcica visualization, standard biochemical blood analyses, and hormonal assessments (progesterone, estradiol, testosterone, cortisol, leptin). Psychological evaluation utilized the Spielberger-Khanin questionnaire. Statistical analysis employed standard software packages with Student's criteria on personal computers.



## RESEARCH FINDINGS

The primary study group consisted of 45 adolescent girls (mean age  $17.2 \pm 1$  years) with average menarche at  $15 \pm 0.4$  years. Menstrual cycle disturbances persisted for 2-6 months, with menstrual duration averaging  $9 \pm 1$  days characterized by scanty discharge.

Initial presentations universally featured headaches of varying intensity, duration, and distribution. Cephalgia typically worsened with fatigue (mental or physical exertion). Emotional lability, manifesting as tearfulness or aggressiveness, ranked as the second most frequent complaint. Sleep disturbances with daytime somnolence disrupting normal activity patterns were also commonly reported.

Continuous blood pressure and heart rate monitoring revealed variable changes in both parameters among study participants, contrasting with the healthy control group ( $n=41$ ). Objective examination identified distinct patterns: 26 girls exhibited vagotonic symptoms, while 19 displayed sympathetic manifestations. This led to subgroup classification: Subgroup 1 (26 patients with vagotonia) and Subgroup 2 (19 patients with sympatheticotonia).

**Subgroup 1 (Vagotonic):** Blood pressure remained low ( $\le 100/60$  mmHg), heart rate approximately 70 bpm. The Kerdo vegetative index averaged  $5.20 \pm 0.10$  (negative value), with minute blood circulation volume of  $2035.7 \pm 50$  ml.

**Subgroup 2 (Sympatheticotonic):** Elevated blood pressure ( $\ge 130/80$  mmHg), heart rate 83-85 bpm. Kerdo index averaged  $7.58 \pm 0.2$  (positive value), with minute circulation volume of  $4900.90 \pm 58.1$  ml.

Comprehensive examinations revealed subgroup-specific manifestations. Subgroup 1 predominantly experienced gastrointestinal complaints (poor appetite, nausea, borborygmi, frequent diarrhea) and ENT pathology (allergic rhinitis, ear pain). Subgroup 2 girls more frequently presented with excessive weight.

Cardiovascular-respiratory system relationships (normal 3-5) averaged 2.5-2.8 in Subgroup 1 and 4.9-5.1 in Subgroup 2. ECG abnormalities manifested differently: Subgroup 1 averaged 48 units in lead II, while Subgroup 2 averaged 162 units.

**NEUROIMAGING RESULTS.** EEG analysis revealed bioelectric brain activity patterns with both common and distinctive features between subgroups. Subgroup 1 demonstrated uncertain brain structure functioning with alpha range peaks (average frequency 12 Hz, amplitude 55 mV). Similar parameters occurred less frequently in Subgroup 2. Approximately 30% of cases in each subgroup showed slow/sharp waves or alpha/gamma zone synchronization in bilateral or frontal regions, confirming hypothalamic-cortical nervous system

dissociation due to increased brain bioelectric activity and cerebral dysfunction.

Brain MRI using 1.5T tomography (General Electric, USA, 2018) focused on sella turcica regions revealed: 3.6% scattered pituitary changes, 2.1% "empty sella" signs, 19.5% microadenomas ( $<10$  mm), and one benign neoplasm (Rathke's cyst). Total MRI abnormalities comprised 25.2% of cases.

Adolescent girls in the study group demonstrated menstrual cycle disorders with neuroimaging abnormalities detected in only 25.2% of cases. Inter-subgroup comparison revealed a 7.4% difference favoring the vagotonic subgroup, suggesting the need for contrast-enhanced or functional neuroimaging components for enhanced diagnostic accuracy. The serum level of leptin was determined in all the examined adolescents. It is known that hormones are involved in the mechanism of the reproductive system, but leptin plays the main role in the metabolism and regulation of other gonadotropic hormones and in a woman's body it proportionally depends on the mass of adipose tissue. Thyroid hormones inhibit lipogenesis and disrupt the maturation of reproductive function, in addition, they are involved in the development of neuroendocrine diseases. Thus, when examining the level of leptin in the blood serum of the examined adolescent girls, there was a significant decrease in the 1st group (adolescent girls with a lower body weight), which was statistically different from the 2nd group, where  $P < 0.05$ , and the difference with the control group, where  $P < 0.01$ .

The indicator of the degree of leptin in the blood differed from the control group (in adolescent girls with normal body weight), and averaged 12.01 ng/ml, while in 1P the indicator had a low level of 3.3 ng/ml on average, and in 2P it was higher than normal, with an average of 16.04 ng/ml of changes. Analysis of the results of laboratory parameters of leptin in adolescent girls, in a comprehensive examination with other indicators, confirms the commonality and collaboration with other hormones in the pathomechanism of menstrual dysfunction.

The characteristic of the examined teenage girls, in addition to vegetative changes, was the fact of menstrual cycle disorders, so it was logical to study the issue of hormonal background, the main ones: estradiol, testosterone and progesterone, cortisol. The difficulty in determining the results of the analysis was the absence of a menstrual cycle, since according to the standard it is necessary to fix the hormonal assessment with the level of the menstrual cycle phase. In this regard, based on the initial onset of menarche, the period of the menstrual cycle was conditionally determined, thus the division of the cycle phase was also conditional. In



addition, hormone levels were evaluated with the results of a group of healthy teenage girls for comparison. The indicators of hormonal changes were as follows: in both subgroups, estradiol and testosterone were higher than the norm; progesterone in both subgroups was lower than normal; cortisol exceeded the norm, and by much higher, naturally, the intensity of cortisol is aimed at increasing stress, which reduces the effectiveness of adaptation in the body, and as a result increases the anxiety-depressive process and It is the root cause of menstrual rhythm disorders.

Therefore, it was appropriate to conduct, as a subsequent stage, an assessment of the psychoemotional state of adolescent girls using the traditional (accessible) Spielberger-Khanin questionnaire to determine the level of anxiety and depression. The result of the analysis of the Spielberger-Khanin questionnaire demonstrated high levels of personal and situational anxiety, in addition, an increased result of emotional lability in both subgroups. At the same time, the correlation analysis between these indicators was directly proportional and depends on the heart rate. In comparison between the data of clinical laboratory, instrumental research methods and psychoemotional analyses, the predominance of emotionally disturbing personality characteristic disorders directly affecting the cardiovascular system was noted.

**CONCLUSIONS:** The research findings demonstrate that adolescent females experiencing autonomic imbalance and menstrual irregularities exhibit significantly elevated psychoemotional disturbance rates. Notably, the predominance of sympatho-adrenal responses serves as a reliable indicator of severe stress conditions in this population. The multidisciplinary evaluation approach, incorporating clinical assessments, laboratory investigations, instrumental diagnostics, neuroimaging studies, and neuropsychiatric evaluations, successfully elucidates and validates the systemic dysfunction underlying the pathophysiological mechanisms. This comprehensive analysis reveals interconnected alterations affecting both central and autonomic nervous systems, as well as major organ systems in adolescent girls presenting with menstrual cycle disturbances and autonomic dysfunction.

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