

ASSOCIATION OF CORTISOL WITH ANXIETY AND DEPRESSIVE CONDITIONS IN STUDENTS AT VARIOUS STAGES OF TRAINING

Tarasov AV¹✉, Rakhmanov RS², Razgulin S², Skoblina NA³, Kiselev SV⁴

¹ Immanuel Kant Baltic Federal University, Kaliningrad, Russia

² Privolzhsky Research Medical University, Nizhny Novgorod, Russia

³ Pirogov Russian National Research Medical University, Moscow, Russia

⁴ Burdenko Voronezh State Medical University, Voronezh, Russia

The students' cortisol levels reflecting stress are associated with the anxiety and depression manifestations, which is important in terms of the educational process hygienic optimization. The study aimed to assess the correlation on students' blood levels of cortisol with anxiety and depressive conditions at various stages of training. A total of 200 1st-year students, who were taught during the academic year 2023–2024, took part in the comparative cross-sectional study. Serum cortisol levels were determined by enzyme immunoassay (ELISA), and the HADS scale was used to detect anxiety and depressive disorders. Signs of anxiety depression at training stages were detected in 34.4–43.6% ($p = 0.189$) and 18.2–24.7% ($p = 0.256$) of students. In the end of the academic year the share of clinical form in the structure of anxiety increased by 19.3% and that in the structure of depression increased by 4.3%. The cortisol levels associated with anxiety were higher in spring, than on autumn — 32.3% ($p = 0.001$), including 35.3% with subclinical form ($p = 0.001$), 28.4% with clinical form ($p = 0.028$); the values associated with depression were 53.9% higher in spring ($p = 0.001$), including 55.4% with subclinical form ($p = 0.001$), 45.6% with clinical form ($p = 0.052$). There was no association of cortisol levels with anxiety in autumn ($r = 0.07$, $p = 0.488$), there was a moderate positive one in spring ($r = 0.51$, $p = 0.001$), including the following: girls in autumn had $r = 0.03$, $p = 0.771$, in spring $r = 0.49$, $p < 0.001$, while boys in autumn had $r = 0.18$, $p = 0.296$, in spring $r = 0.57$, $p = 0.001$, respectively. A nonlinear log model showed a significant effect of anxiety ($F = 16.26$, $p < 0.001$), explaining 7.7 % of variance. The findings are important for the development of preventive programs focused on stress management in students.

Keywords: students, autumn, spring, anxiety, depression, cortisol, relationship

Author contribution: Rakhmanov RS — study concept and design, manuscript writing; Tarasov AV — primary data acquisition and systematization, statistical data processing, manuscript writing; Razgulin SA — literature review; Skoblina NA — data interpretation, manuscript writing; Kiselev SV — literature data acquisition.

Compliance with ethical standards: the study was compliant with the ethical standards of the World Medical Association Declaration of Helsinki. It was approved by the Ethics Committee of the Immanuel Kant Baltic Federal University (protocol No. 38 dated March, 2023). Each subject submitted the informed consent to take part in the study and for personal medical information to be published in an anonymized form.

✉ **Correspondence should be addressed:** Andrey V. Tarasov

A. Nevsky Str. 14, Kaliningrad, 2360241, Russia; drup1@yandex.ru

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АССОЦИАЦИЯ КОРТИЗОЛА С ТРЕВОЖНО-ДЕПРЕССИВНЫМИ СОСТОЯНИЯМИ У СТУДЕНТОВ НА РАЗЛИЧНЫХ ЭТАПАХ ОБУЧЕНИЯ

А. В. Тарасов¹ ✉, Р. С. Рахманов², С. А. Разгулин², Н. А. Скоблина³, С. В. Киселев⁴

¹ Балтийский Федеральный университет имени И. Канта, Калининград, Россия

² Приволжский исследовательский медицинский университет, Нижний Новгород, Россия

³ Российский национальный исследовательский медицинский университет имени Н. И. Пирогова, Москва, Россия

⁴ Воронежский государственный медицинский университет имени Н. Н. Бурденко, Воронеж, Россия

Отражающий стресс уровень кортизола у студентов связан с проявлениями тревожности и депрессии, что важно с точки зрения гигиенической оптимизации учебного процесса. Целью исследования было оценить взаимосвязь уровня кортизола в крови студентов с тревожно-депрессивными состояниями на разных этапах обучения. В сравнительном поперечном исследовании приняли участие 200 студентов 1-го курса, обучавшихся в 2023–2024 учебном году. Уровень кортизола в сыворотке крови определяли методом иммуноферментного анализа (ИФА), для выявления тревожно-депрессивных состояний использовали шкалу HADS. Признаки тревоги и депрессии по этапам обучения выявлены у 34,4–43,6% ($p = 0.189$) и 18,2–24,7% ($p = 0.256$) студентов. В конце года обучения доля клинически выраженной формы в структуре тревоги увеличилась на 19,3%, в структуре депрессии — на 4,3%. Показатели кортизола при тревоге весной выше, чем осенью, — на 32,3% ($p = 0.001$), в том числе при субклинической форме на 35,3% ($p = 0.001$), при клинически выраженной форме на 28,4% ($p = 0.028$); при депрессии весной они выше на 53,9% ($p = 0.001$), в том числе при субклинической форме на 55,4% ($p = 0.001$), при клинически выраженной форме на 45,6% ($p = 0.052$). Ассоциация уровня кортизола с тревогой осенью отсутствует ($r = 0.07$, $p = 0.488$), весной она умеренная прямая ($r = 0.51$, $p = 0.001$), в том числе у девушек осенью $r = 0.03$, $p = 0.771$, весной $r = 0.49$, $p < 0.001$, а у юношей осенью $r = 0.18$, $p = 0.296$, весной $r = 0.57$, $p = 0.001$ соответственно. Нелинейная логарифмическая модель показала значимый эффект тревожности ($F = 16.26$, $p < 0.001$), объясняющий 7,7 % дисперсии. Результаты исследования имеют значение для разработки профилактических программ, направленных на управление стрессовой нагрузкой студентов.

Ключевые слова: студенты, осень, весна, тревога, депрессия, кортизол, взаимосвязь

Вклад авторов: Р. С. Рахманов — концепция и дизайн исследования, написание текста статьи; А. В. Тарасов — сбор, систематизация первичного материала, статистическая обработка данных, написание текста статьи; С. А. Разгулин — анализ литературы; Н. А. Скоблина — интерпретация данных, написание текста статьи; С. В. Киселев — сбор данных литературы.

Соблюдение этических стандартов: исследование проведено с соблюдением этических норм Хельсинкской декларации Всемирной медицинской ассоциации. Получено одобрение этического комитета БФУ им. И. Канта (протокол № 38 от 31 марта 2023 г.). Каждый участник исследования дал письменное добровольное информированное согласие на участие в исследовании и публикацию персональной медицинской информации в обезличенной форме.

✉ **Для корреспонденции:** Андрей Вячеславович Тарасов

ул. А. Невского, д. 14, г. Калининград, 2360241, Россия; drup1@yandex.ru

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Modern students experience significant psycho-emotional stress associated not only with gaining independence and the educational process specifics, but also with the need to adapt to new social conditions, as well as the professional and personal identity development [1, 2]. The transition to adulthood increases stress: students face high academic demands, competition, and expectations of success; some have to combine study with work, live away from family, and arrange their daily lives [3–6]. The complex influence of factors leads to the increased mental health vulnerability, contributing to susceptibility to anxiety disorders, depression, and chronic stress [7, 8]. Thus, the study of the body's stress responses is becoming especially important, and data on the prevalence of such conditions and the factors influencing those become necessary for the development of adequate preventive measures [9, 10].

The conditions that lead to the development of chronic stress also negatively affect the body's physiological parameters, in particular the of the hypothalamic-pituitary-adrenal (HPA) axis activity. Cortisol is a key hormonal marker of stress, reflecting the HPA axis activation and ensuring the body's adaptive responses to psycho-emotional stimuli [11]. Studying the relationship between cortisol levels and manifestations of anxiety and depression makes it possible to determine the stress response biological mechanisms, identify groups at risk, and develop preventive measures to maintain the students' psycho-emotional and physical health [12].

Previous research suggests that women and men may respond differently to stressful stimuli, and seasonal fluctuations affect hormonal levels and psycho-emotional state [13]. However, the data on the relationship between anxiety, depression, and cortisol levels in students, considering these factors, remain limited and contradictory.

The study aimed to assess the correlation between the student's blood levels of cortisol and anxiety and depressive conditions at various stages of training.

METHODS

A comparative cross-sectional study was conducted involving two independent groups of 1st-year students assessed in the beginning (autumn, $n = 99$) and in the end of the academic year (spring, $n = 101$). A total of 200 students (140 girls and 60 boys), whose average age was 19.8 ± 0.6 years, took part in the study. All participants had previously undergone a medical examination and were in good health. Inclusion criteria: no earlier diagnosed anxiety or depressive disorder with the confirmation of belonging to the first or second health group. Exclusion criteria: the third health group and the diagnosis of mental disorder. The representative sample was calculated using the Epi Info software tool (<http://www.cdc.gov/epiinfo/>) with the 95% confidence level. The minimum sample size was 174 subjects, based on the number of 1st-year university students in the academic year 2023–2024.

No specific assessment of dietary patterns, dietary restrictions, and physical activity was conducted in the period immediately preceding the study. To standardize the testing conditions, blood samples were collected by puncture of the cubital vein in the fasting state from 8 to 9 a.m. by the nurse at the university clinic. Serum cortisol levels were determined by enzyme-linked immunoassay (ELISA; ELISA Test for Quantitative Determination of Cortisol in Human Serum. Human GmbH, REF 55050; Germany) with the minimal sensitivity of 2.5 ng/mL. Optical density was measured using the AMR-100 microplate reader (Allsheng; China) at a wavelength of 450 nm using an automatic Bio-Plex Pro II Wash Station (Bio-Rad; Austria).

The Hospital Anxiety and Depression Scale (HADS) representing a clinical instrument allowing one to detect and quantify symptoms of anxiety and depression was used to assess psycho-emotional state. The method includes two subscales (each of 7 items) focused on anxiety and depression, respectively. For each item, the respondent assigns a score ranging from 0 to 3 points, after which a total score is calculated for each subscale (maximum score 2). The results are interpreted based on three ranges: 0–7 points indicate that there are no symptoms, 8–10 points correspond to a subclinical form, and 11 points or higher indicate a clinical form of the disorder. Thus, HADS provides a differentiated assessment of anxiety and depression severity, increasing the accuracy of the emotional state diagnosis [14].

Statistical data processing was performed using the STATISTICA 12.0 software (StatSoft, Inc.; USA). The sample distribution was tested for normality using the Kolmogorov–Smirnov test. Mean values were compared using the Student's *t*-test for independent samples, the analysis of share differences was conducted using the Z-test, and the Spearman's rank correlation coefficient was used to assess the correlation between continuous variables. The differences were considered significant at $p < 0.05$. The 95% confidence intervals (95% CI) were calculated for quantitative indicators.

A general nonlinear log model was constructed using sigma-restricted parameterization to assess the impact of psychosocial, biological, and climatic factors on blood cortisol levels in students. Severity of anxiety and depression on the HADS scale, gender, season, and the "gender – season" interaction were included in the model as independent variables. The model made it possible to assess the contribution of each factor to the variability of cortisol levels.

RESULTS

Testing showed that the proportion of students with no signs of anxiety was significantly (1.6 times) higher than the proportion of students with anxiety symptoms. Among girls, it was 1.4 times higher than in individuals with anxiety, while among boys, it was 2.2 times higher. In autumn, the proportion of students without anxiety was 1.9 times higher, while in spring, there were no significant differences in the proportional distribution of individuals having and not having anxiety symptoms. Furthermore, only in the cohort examined in autumn was the subclinical form of anxiety encountered 1.8 times more often, than the clinical form (Table 1).

Among the examined individuals, no signs of depression were observed 3.7 times more often, than depressive symptoms. Furthermore, the proportion of individuals with the subclinical depression form was 2.9 times higher, than the proportion of individuals with the clinical form. Depression was diagnosed 4.4 times less often in girls. In individuals with depression, the subclinical form occurred 4.2 times more often, than the clinical one. Among boys, the proportion of individuals without depression was 2.5 times higher, than that of individuals with depressive symptoms. No significant differences in the prevalence of depressive symptoms or the distribution of subclinical and clinical forms between girls and boys were found. In autumn, the proportion of students with no signs of depression was 4.5 times higher, than that of students with depression, while the subclinical form was reported 3.5 times more often, than the clinical one. In spring, the proportion of students with no signs of depression was 3.0 times greater, than the proportion of those with depressive symptoms. Furthermore, the subclinical form

Table 1. Structure of student distribution based on the presence of anxiety signs, %

Comparison groups	No signs of anxiety	Signs of anxiety	including the form		p^*
			subclinical	clinical	
	1	2	3	4	
Sample size	61	39	53.8	46.2	$p_{1-2} < 0.001$ $p_{3-4} = 0.336$
Girls	57.9	42.1	55.9	44.1	$p_{1-2} = 0.008$ $p_{3-4} = 0.197$
Boys	68.3	31.7	47.4	52.6	$p_{1-2} < 0.001$ $p_{3-4} = 0.988$
p^{**}	0.163	0.177	0.512	0.536	
Spring	56.4	43.6	45.4	54.6	$p_{1-2} = 0.393$ $p_{3-4} = 0.793$
Autumn	65.6	34.4	64.7	35.3	$p_{1-2} < 0.001$ $p_{3-4} = 0.015$
p^{**}	0.181	0.189	0.09	0.452	

Note: * — significance of differences for groups with various anxiety severity; ** — significance of differences for groups of males and females and for seasons of the year.

occurred 4.0 times more often, than the clinical one. Seasonal differences in the detection rates of anxiety and depressive conditions, as well as subclinical and clinical forms, were non-significant (Table 2).

Cortisol levels were significantly (1.3 times) higher in individuals with anxiety, than in those without it ($p < 0.001$); with the subclinical form, it was 1.3 times higher than in individuals with no signs of anxiety ($p < 0.001$), and with the clinical form it was 1.3 times higher ($p < 0.001$). There were no differences in levels between the subclinical and clinical forms.

It was found that cortisol levels of girls with anxiety were higher compared to that of girls with no anxiety: by 34.7%. There were no differences in hormone levels between the subclinical and clinical forms. An increase in cortisol levels (by 22.3%) was also observed in boys with anxiety. In cases of subclinical anxiety, cortisol levels did not differ from those in the group without anxiety, whereas in individuals with the clinical form these were significantly higher—by 28.5%. The values did not differ between the subclinical and clinical forms.

Intergroup differences in blood cortisol levels (between males and females) were significant only in the group without signs of anxiety, where boys had higher cortisol levels. No differences between gender groups were found regarding the presence of the assessed signs, including in the subclinical and clinical forms.

In autumn, there were no differences in cortisol levels between individuals with and without anxiety (including subclinical and clinical forms). In spring, Students with anxiety had cortisol levels 56.8% higher, than students without anxiety. This same ratio was true for both subclinical and clinical anxiety: cortisol levels exceeded those in the group without anxiety by 58.5% and 55.5%, respectively. At the same time, seasonal differences proved to be significant: in autumn, cortisol levels in the group of students showing no signs of anxiety were 1.1 times higher, than in spring. An opposite trend was observed in the group of students showing signs of anxiety: cortisol levels were 1.3 times higher in spring, than in autumn, in individuals with both subclinical and clinical forms of anxiety (Table 3).

Students with signs of depression had significantly higher cortisol levels than students without depression (by 24.3%). In individuals with subclinical depression, the levels were 1.3 times higher than in those without depression, whereas in cases of clinical depression, the differences from the group with no depression were non-significant. The values did not differ between the subclinical and clinical forms.

Cortisol levels in female students with depression were significantly higher (by 28.2%), than in those without depression. In individuals with subclinical depression, these 31.3% higher compared to that in individuals with no depression, whereas no differences were reported for the clinical form. Cortisol

Table 2. Structure of student distribution based on the presence of depression signs, %

Comparison groups	No signs of depression	Signs of depression	including the form		p^*
			subclinical	clinical	
	1	2	3	4	
Sample size	78.5	21.5	74.4	25.6	$p_{1-2} < 0.001$ $p_{3-4} < 0.001$
Girls	81.4	18.6	80.8	19.2	$p_{1-2} < 0.001$ $p_{3-4} < 0.001$
Boys	71.7	28.3	64.7	35.3	$p_{1-2} < 0.001$ $p_{3-4} = 0.095$
p^{**}	0.123	0.128	0.912	0.085	
Spring	75.3	24.7	72	18	$p_{1-2} < 0.001$ $p_{3-4} < 0.001$
Autumn	81.8	18.2	77.7	22.3	$p_{1-2} < 0.001$ $p_{3-4} = 0.015$
p^{**}	0.258	0.256	0.675	0.66	

Note: * — significance of differences for groups with various depression severity; ** — significance of differences for groups of males and females and for seasons of the year.

Table 3. Cortisol levels in individuals showing and not showing signs of anxiety, nmol/L, $M \pm \sigma$ (95% CI)

Comparison groups	No signs of anxiety	Signs of anxiety	including the form		p^*
			subclinical	clinical	
	1	2	3	4	
Girls	316.5 $\pm$ 14.1 (288.3–344.7)	426.5 $\pm$ 16.8 (392.8–460.2)	421.2 $\pm$ 19.4 (381.6–460.9)	433.3 $\pm$ 29.5 (372.5–494.0)	$p_{1-2} < 0.001$ $p_{1-3} < 0.001$ $p_{1-4} < 0.001$ $p_{3-4} = 0.724$
Boys	365.6 $\pm$ 17.8 (329.4–401.7)	447.3 $\pm$ 26.8 (390.9–503.6)	422.3 $\pm$ 43.9 (320.9–523.7)	469.7 $\pm$ 32.7 (395.6–543.7)	$p_{1-2} = 0.013$ $p_{1-3} = 0.196$ $p_{1-4} = 0.011$ $p_{3-4} = 0.393$
p^{**}	0.04	0.535	0.978	0.488	
Spring	307.9 $\pm$ 19.4 (269.0–346.8)	482.9 $\pm$ 17.7 (447.2–518.7)	488.1 $\pm$ 20.1 (446.0–530.3)	478.7 $\pm$ 28.2 (420.3–537.0)	$p_{1-2} < 0.001$ $p_{1-3} < 0.001$ $p_{1-4} < 0.001$ $p_{3-4} = 0.793$
Autumn	355.0 $\pm$ 12.2 (330.6–379.4)	365.0 $\pm$ 17.8 (328.7–401.4)	360.8 $\pm$ 21.6 (315.9–405.7)	372.8 $\pm$ 32.7 (300.7–444.9)	$p_{1-2} = 0.637$ $p_{1-3} = 0.812$ $p_{1-4} = 0.575$ $p_{3-4} = 0.753$
p^{**}	0.037	< 0.001	< 0.001	0.028	

Note: * — significance of differences for groups with various anxiety severity; ** — significance of differences for groups of males and females and for seasons of the year.

levels did not differ between subclinical and clinical forms of depression. Differences in the levels of this hormone in males having and not having depression, including with various depression severity, were non-significant. There were no differences in cortisol levels in gender groups.

In autumn, cortisol levels did not differ based on the fact of having or not having depression; however, in spring, the levels were significantly higher (by 50.7%) in individuals with depression compared to those with no depression. The differences compared to data for subclinical and clinical depression reached 55.6% and 38.1%, respectively, whereas there were no differences between the data for the subclinical and clinical forms. Furthermore, in spring, cortisol levels in individuals with depression exceeded the levels measured in autumn by 53.9%, including by 55.4% with the subclinical form (Table 4).

The correlation analysis revealed a significant association between cortisol levels and the fact of having anxiety: the association was positive, of moderate strength ($r_s = 0.33$; $p < 0.001$). Moderate positive correlations were found in both girls and boys. No significant correlation was detected in autumn. The most pronounced association was observed in spring: a moderate-to-strong, positive association (Table 5). A positive association was also reported for individuals with depression: a positive one of moderate strength. The associations were positive, of moderate strength in the groups of both females and males. In autumn, there was no significant correlation between cortisol levels and depressive symptoms; moderate-to-strong, positive correlation was reported in spring (Table 5).

When constructing a nonlinear regression model to test the influence of psychosocial and demographic factors on blood cortisol levels in students, high overall model significance was determined ($F = 214.00$, $p < 0.001$). In general, the model explained 62.5% of cortisol level variance, and 37.5% of variance were not taken into account. Anxiety proved to be the most significant factor: the statistical significance was achieved for it ($F = 16.26$, $p < 0.001$). As for depression, no significant association with cortisol levels was revealed ($F = 0.16$, $p = 0.691$). Gender demonstrated borderline statistical significance ($p = 0.049$) and explained 2.0% of cortisol level variance. Other factors included in the model were non-significant. However, it should be noted that the model residual variance

turned out to be rather high ($SS = 3\,031\,396.73$, $MS = 15\,625.76$), which suggests that there are unaccounted-for factors capable of influencing cortisol levels, including dietary habits, sleep quality, physical activity, chronic stress, and individual characteristics of HPA axis regulation.

DISCUSSION

The study results demonstrate a complex pattern of correlations between the students' psycho-emotional state and cortisol levels. Thus, in the combined sample, the proportion of individuals with signs of anxiety was 1.8 times higher than the proportion of individuals with signs of depression ($p < 0.001$), including the proportion of students with subclinical signs of anxiety was 1.4 times lower than the proportion of students with subclinical signs of depression ($p = 0.026$), and the proportion of students with clinical signs of anxiety was 1.8 times higher than the proportion of students with clinical signs of depression ($p = 0.027$). The average HADS scores were significantly higher in spring, than in autumn: 1.1 times higher for anxiety показатель ($p = 0.040$), 1.2 times higher for depression ($p = 0.031$).

Cortisol levels were higher in individuals showing signs of anxiety, than in those showing signs of depression. A significant positive correlation and a significant contribution to the model's variance indicated that students with higher anxiety levels had elevated stress hormone levels. These data confirm the results of previous studies, in which a strong correlation between the depression severity and the HPA axis activation was reported [15, 16].

In contrast to anxiety, depression did not have a significant effect on cortisol levels within the nonlinear model, although correlation analysis showed moderate positive associations. This suggests that in healthy students, mild and subclinical manifestations of depression may not lead to pronounced HPA axis activation. This finding is consistent with other research results, according to which subclinical depressive symptoms showed a weak correlation with the cortisol concentration [17].

Data on the prevalence of anxiety among the students in the studied cohort confirm that anxiety symptoms are more common in the student population, than depressive symptoms [18]. Seasonal differences reflected by the fact that average

Table 4. Cortisol levels in individuals showing and not showing signs of depression, nmol/L, $M \pm \sigma$ (95% CI)

Comparison groups	No signs of depression	Signs of depression	including the form		p^*
			subclinical	clinical	
	1	2	3	4	
Girls	344.7 $\pm$ 12.4 (320.1–369.4)	442.3 $\pm$ 27.2 (386.1–498.4)	452.5 $\pm$ 32.1 (385.5–519.5)	399.5 $\pm$ 43.8 (277.8–521.2)	$p_{1-2} = 0.001$ $p_{1-3} = 0.001$ $p_{1-4} = 0.365$ $p_{3-4} = 0.455$
Boys	374.6 $\pm$ 17.5 (339.3–401.7)	434.0 $\pm$ 30.9 (368.5–499.5)	440.7 $\pm$ 44.1 (342.3–539.0)	421.7 $\pm$ 38.3 (323.1–520.3)	$p_{1-2} = 0.085$ $p_{1-3} = 0.108$ $p_{1-4} = 0.114$ $p_{3-4} = 0.850$
p^{**}	0.195	0.844	0.688	0.71	
Spring	341.3 $\pm$ 17.6 (306.2–376.4)	514.4 $\pm$ 19.5 (474.0–554.8)	531.2 $\pm$ 25.8 (476.6–585.8)	471.3 $\pm$ 12.9 (439.7–502.3)	$p_{1-2} < 0.001$ $p_{1-3} < 0.001$ $p_{1-4} < 0.028$ $p_{3-4} = 0.174$
Autumn	363.8 $\pm$ 11.1 (341.8–385.8)	334.2 $\pm$ 17.8 (283.9–384.5)	341.9 $\pm$ 23.8 (277.5–406.3)	323.8 $\pm$ 60.0 (132.5–515.0)	$p_{1-2} = 0.258$ $p_{1-3} = 0.458$ $p_{1-4} = 0.439$ $p_{3-4} = 0.780$
p^{**}	0.274	< 0.001	< 0.001	0.052	

Note: * — significance of differences for groups with various depression severity; ** — significance of differences for groups of males and females and for seasons of the year.

anxiety and depression severity was higher in spring, than in autumn, which was probably due to academic workload and stressful events of the academic year, as well as general seasonal factors affecting emotional well-being [19].

Cortisol levels in students with anxiety were significantly higher than in those without it. This effect was reported for both subclinical and clinical anxiety forms. In girls, anxiety was associated by a similar rise in cortisol levels in both forms, whereas in boys, a significant increase was reported only in cases of clinical anxiety. Seasonal analysis showed that differences between the groups with and without anxiety were more pronounced in spring, than the autumn, which was consistent with the correlation analysis data: there was

a positive correlation (moderate-to-strong) in spring, whereas no significant correlation was observed in autumn. These findings are in line with the data of previous studies, in which elevated cortisol levels were observed in students and young adults under conditions of anxiety and stress [20].

In the context of depression, cortisol levels in students with the subclinical form were higher compared to the group without depression. There were no gender differences in the groups with depression. Seasonality was evident only in spring, when the correlation was moderate and significant, whereas no association was observed in autumn. The findings are consistent with the results of the earlier study, in which a correlation between symptoms of depression and anxiety and the characteristics

Table 5. Characteristics of correlations between the students' blood cortisol levels and the signs of anxiety and depression

Comparison groups	Spearman's rank correlation coefficient, r_s	Correlation strength and direction	Significance, p
Anxiety			
Total sample	0.33	Moderate positive	< 0.001
Girls	0.35	Moderate positive	< 0.001
Boys	0.37	Moderate positive	0.003
Spring	0.51	Moderate positive	< 0.001
Autumn	0.07	No	0.488
Girls spring	0.49	Moderate positive	< 0.001
Boys spring	0.57	Moderate positive	0.001
Girls autumn	0.03	No	0.771
Boys autumn	0.18	No	0.296
Depression			
Total sample	0.25	Moderate positive	< 0.001
Girls	0.22	Moderate positive	0.007
Boys	0.30	Moderate positive	0.016
Spring	0.45	Moderate positive	< 0.001
Autumn	0.02	No	0.180
Girls spring	0.39	Moderate positive	< 0.001
Boys spring	0.62	Moderate positive	< 0.001
Girls autumn	0.08	No	0.509
Boys autumn	0.03	No	0.841

of the cortisol response to stressful situations was identified in young people, even in those having no clinical diagnosis [21].

The nonlinear model confirmed the findings of the correlation analysis: anxiety was the most significant predictor of cortisol levels, while the gender factor showed borderline significance. Furthermore, the residual variance was 37.5%, which suggested that there were additional factors, not included in the analysis, such as dietary habits, chronic stress, sleep quality, physical activity, and individual features of the HPA axis regulation. These findings are in line with the reported data showing that physiological stress responses in students, including the HPA axis activation and elevated cortisol levels, were associated with emotional and psychological manifestations of stress, such as anxiety and depression, particularly in the context of academic demands [22].

Thus, the results obtained demonstrate that the students' cortisol levels are strongly associated with the anxiety severity and are less dependent on depression. Despite the fact that the cortisol level increase absolute values were within the reference ranges, these provided important information. Cortisol has a systemic effect on the body: it intensifies catabolic processes associated with the increased consumption of proteins, fat, vitamins, and minerals. This can deplete energy resources and reduce the body's adaptive capabilities [23]. Long-term adverse changes may manifest as the muscle mass loss, the development of osteoporosis, visceral fat accumulation, and the increased

risk of cardiovascular disease, effects on the immune, reproductive, and nervous systems, cognitive decline, and emotional instability [24–28].

In the university settings, preventive work may include the early detection of anxiety signs, the optimization of work-rest regime, and measures to reduce stress. The reported strengthening of the association between anxiety and cortisol levels in spring indicates the feasibility of closer monitoring of students' psycho-emotional state during periods of increased academic workload. Preventive measures in the university settings may include the early detection of anxiety signs, psychological support for students, the work-rest regime optimization, and measures to reduce stress.

CONCLUSIONS

Signs of anxiety were detected more often than signs of depression among 1st-year students, with no significant seasonal differences in their prevalence. In spring, cortisol levels associated with anxiety and depression were higher, than in autumn, and the association between cortisol and anxiety and depressive symptoms was more pronounced. The most significant correlation reported was between cortisol levels and anxiety, as confirmed by the nonlinear model results. The obtained data justify the importance of early detection of anxiety states and the reduction of stress among students, particularly at the end of the academic year.

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