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Original Scientific Paper

FAMILY-RELATED STRESS IN EUTHYROID ADOLESCENTS WITH HASHIMOTO'S THYROIDITIS AND ELEVATED LEVELS OF ANTI-THYROID ANTIBODIES

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SUMMARY – Stress response is a complex, adaptive reaction to various endogenous or exogenous stimuli. Psychological stress (PS) may trigger inflammation, disrupt hormone balance and affect the immune and other body systems. PS is discussed in the literature when considering autoimmunity as a possible external factor influencing its development. Furthermore, chronic PS, including family-related stress (FRS), can contribute to autoimmune thyroid diseases like Hashimoto's thyroiditis (HT). The present research was conducted as a randomized study to explore the response to and coping with FRS in 88 euthyroid adolescents with HT and elevated levels of anti-thyroid antibodies (ATA) (case group) compared to 88 healthy adolescents (control group), as well as to present, discuss and compare the obtained results with the literature published so far. The multidimensional Response to Stress Questionnaire for children and adolescents was used to examine the level of FRS. We found that the case group's exposure to FRS was lower than the control group's, but no statistically significant difference was established. According to the results of our study, the mutual connection between exposure to FRS and coping with FRS in adolescents with HT and elevated levels of ATA cannot be confirmed.

Keywords: *Adolescent*; *Stress*; *Hormones*

Introduction

Stress disrupts homeostasis through the activity of various types of stressors of psychosomatic origin[1]. Coping with psychologically stressful events involves complex, adaptive mechanisms directed towards different types of external and internal stimuli, which aim

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to re-establish homeostasis[1,2]. They can be voluntary (controlled coping) and involuntary (automatic reaction), while the stress response can be engaged (active coping with stressful situations, e.g. using emotional expressions) and disengaged (avoidance of stressful events)[3]. The impact of psychological stress (PS) on the autonomous nervous system is manifested through two basic neuroendocrine axes: sympathetic-adrenal-medullary (SAM) and hypothalamic-pituitary-adrenal (HPA)[1,4,5]. During stressful events, within the SAM-axis, the hypothalamus generates and transmits impulses to various body organs, releasing several hormones and other messengers (primarily catecholamines) into the bloodstream, further increasing the effects of sympathetic arousal. Through the feedback axis regulated by the hypothalamus and pituitary gland, the secretion of adrenocorticotropic hormone (ACTH), cortisol, thyrotropin (TSH), prolactin (PRL), antidiuretic hormone (ADH) and oxytocin (OXY) increases, which maintains excitation and the HPA-axis[4]. The abovementioned mechanisms lead to further metabolic, circulatory, immunological, endocrinological, neurological and other body changes that manifest in various organs, tissues and cells[1,4,6].

PS is discussed in the literature when considering autoimmune disorders as a possible external factor influencing their development. The mechanisms underlying the connection between PS and autoimmunity are complicated and insufficiently studied. They include mutual pathophysiological interactions of polygenic, immunological and environmental risk factors[7-10]. Furthermore, PS may be associated with the development and exacerbation of autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, Graves' disease (GD) and Hashimoto's thyroiditis (HT)[11-17]. Pathophysiologically, humoral and/or cytotoxic immunity mechanisms are predominantly involved[18]. Although the connection between PS and the development of GD is largely clear, the mechanisms of the impact of PS on the development of HT are still not fully elucidated; it is known that T-cell mediated cytotoxic immunity plays a more important role in the development of HT, while humoral immunity mechanisms are more pronounced in GD[12,19]. In addition to the euthyroid form of HT (with normal values of TSH, total thyroxin/free-thyroxin (T4/fT4), and total triiodothyronine/free triiodothyronine (T3/fT3)), HT can also be encountered in clinical practice in the form of subclinical hypothyroidism (increased TSH value and normal values of T4/fT4 and T3/fT3) and clinical hypothyroidism (increased TSH value and decreased values of T4/fT4 and T3/fT3). Unfortunately, research studies on PS and family-related stress (FRS) in euthyroid subjects with HT are mostly focused on middle-aged and elderly individuals. This issue among adolescents has been assessed, but to a significantly lesser extent. Therefore, as the goal of our study, we set out to explore the response to and coping with FRS in euthyroid adolescents diagnosed with HT (with elevated levels of anti-thyroid antibodies (ATA): 1. thyroid peroxidase antibodies (TPOAb) and/or 2. thyroglobulin antibodies (TgAb)) compared to healthy adolescents, as well as to present, discuss and compare the obtained results with the literature data published so far.

Subjects and methods

Initially, 236 randomly selected respondents (adolescents) aged 10-18 years, of both sexes and of Southeastern European origin participated in the study. All of them had been followed up in an outpatient pediatric setting for > 1 year. The case group consisted of 109 adolescents with elevated levels of ATA, diagnosed with the euthyroid form of HT by clinical and echo-sonographic examination and laboratory tests before inclusion in the study. Twenty-one of them were subsequently excluded from the study. The control (healthy) group consisted of 127 euthyroid adolescents, in whom the above-mentioned clinical work-up excluded the diagnosis of HT. Thirty-nine of them were subsequently excluded from the study. Consequently, both groups had an equal number of adolescents (N = 88; 65 girls (73.86%) and 23 boys (35.1%)) with equal distribution by sex. The study and control groups were tested without a time limit, in groups, or individually. The testing included: 1. the collection of demographic data (sex and age at the time of testing); 2. the presence of other diseases/disorders/conditions, such as autoimmune diseases, attention-deficit/hyperactivity disorder (ADHD) and post-traumatic conditions; 3. laboratory testing of blood samples for TSH (normal value 0.729-4.402 mIU/L), fT4 (normal value 10-28.2

pmol/L), fT3 (normal value 4.26-8.1 pmol/L), TPOAb (normal value < 5.60 IU/mL) and TgAb (normal value < 4.20 IU/mL); 4. completing a questionnaire for determining stress in children and adolescents (Response to Stress Questionnaire – RSQ). Exclusion criteria for both groups included: 1. incomplete anamnestic data; 2. intellectual disabilities; 3. the presence of any autoimmune diseases (except HT in the test group); 4. disrupted values of TSH, fT4 and fT3 in the examined group; 5. disrupted values of TSH, fT4, fT3, TPOAb and TgAb in the control group; and 6. incompletely filled in RSQ. We examined the level of FRS with the multidimensional RSQ for children and adolescents, which assesses the conscious and voluntary regulation of emotions, cognition, behavior and physiology in situations and circumstances which are stressful for the individual[20] (Additional File 1). The authors of the questionnaire, Compas et al. from Vanderbilt University in Nashville, USA, approved the use of the RSQ for this study. The RSQ consists of 3 coping factors and 2 stress responses: 1. Primarily engaged coping (e.g., problem-solving, expression and modulation of emotions); 2. Secondary engaged coping (e.g., positive thinking, cognitive restructuring, acceptance, distraction); 3. Avoidant coping (e.g., procrastination, denial); 4. Involuntary engaged stress response (e.g., psychological arousal, worry); and 5. Involuntary avoidant stress response (e.g., emotional numbing). At the beginning of the RSQ, there is a list of 12 family-related stressors. Each is scored on a scale of 1-4 (1 – Not at all, 2 – A little, 3 – Somewhat, and 4 – Very much). This is followed by 57 items (three items for 10 voluntary FRS and 9 categories for involuntary FRS responses). For each item, one of four possible answers is selected. They are scored on a scale of 1–4 in the following order: 1 – Not at all, 2 – A little, 3 – Some, 4 – A lot. For each of the three coping factors and two stress responses, five coping scales are used. Scores are calculated as the ratio of the effect for each factor to the total impact of the RSQ.

The research was conducted with the approval of the Ethics Committee and followed the principles of the 1964 Declaration of Helsinki and all its subsequent amendments. All respondents and their parents/legal guardians signed an informed consent and agreed to participate in the research, as well as to the publication of its results.

Statistical analysis

Before proceeding with data processing, the normality of the distribution of the obtained results was checked. A statistically significant difference was taken at $P < 0.05$ and a confidence interval of (CI) > 95%. Parametric tests were applied for independent variables with a normal distribution (t-test) or the Mann-Whitney U test for variables with asymmetric distribution (Z-value). Statistical analysis was performed using the statistical program SPSS, version 20.0 (IBM, Armonk, NY, USA). Categorical variables were expressed as absolute and relative frequencies (number and percentage). An *a priori* analysis of the test's statistical power was also performed in the G*Power 3.0 program, using the estimated mean effect size for all statistical tests. With $\alpha = 0.05$, desired power $\beta = 0.95$ and assumed medium effect size $d = 0.5$, a sample size of $N = 176$ subjects (88 in the case group and 88 in the control group) was calculated and used to test the primary hypothesis of this study.

Results

Within the case group, isolated elevated TPOAb levels were found in 9 adolescents (10.23%), while isolated elevated TgAb levels were found in 32 adolescents (36.36%). Simultaneously elevated values of both ATA were found in 47 adolescents (53.41%).

Exposure to FRS

The case group's exposure to FRS was lower than that of the control group (1.63 (1.63-1.87) vs. 1.69 (1.66-1.89)), but no statistically significant difference was noticed ($Z = -0.48$; $N = 88$; $P = 0.63$) (Figure 1).

Coping with FRS

1. Voluntary coping with FRS

1.1. Voluntary (primary) engaged coping with FRS for the case group was lower compared to the control group ($\bar{X} = 0.177$; $SD = 0.033$ vs. $\bar{X} = 0.185$; $SD = 0.033$), without a statistically significant difference ($t = -1.61$; $N = 88$; $P = 0.11$).

1.2. Voluntary (secondary) engaged coping with FRS for the case group was higher compared to the control group and amounted to 0.250 (0.243-0.262) vs. 0.230 (0.230-0.247) with a statistically significant

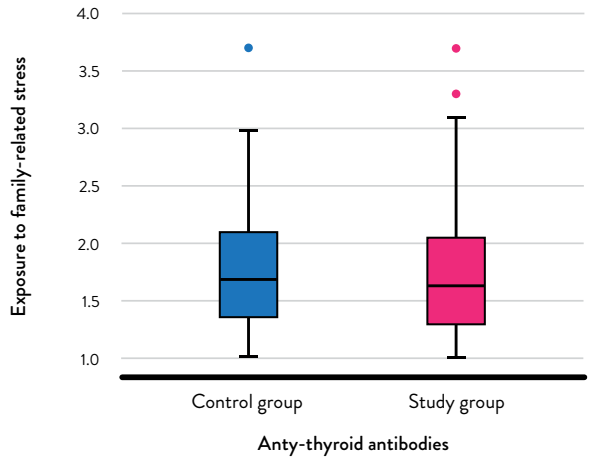

Figure 1. Exposure to FRS in the study and control group of adolescents.

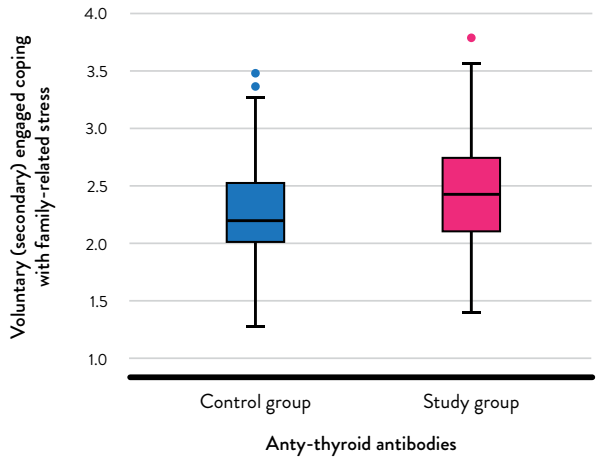

Figure 2. Voluntary (secondary) engaged coping with FRS in the study and control group of adolescents.

difference (Z = -2.48; N = 88; *P* = 0.01; r = 0.19) (Figure 2) (Table 1). However, a statistically significant difference was observed only in male subjects, i.e. boys in the case group experienced more secondary FRS compared to boys in the control group (0.273 (0.044) vs. 0.213 (0.013)) with statistical significance (Z = -6.36; N = 23; *P* < 0.01; r = 0.48) (Table 1).

The groups were compared using the Student's t-test for a variable with a normal distribution (t-value) or Mann-Whitney's U test for a variable with an asymmetric distribution (Z-value). If a statistically significant difference was found, the effect size was measured by calculating the Pearson correlation coefficient (r) for a variable with an asymmetric distribution, or partial eta-squared (η^2) for a variable with a normal distribution.

1.3. Voluntary disengaged coping with FRS was slightly higher in the case group compared to the control group (0.155 (SD=0.025) vs. 0.150 (SD=0.025)), but without statistical significance (t = 1.29; *P* = 0.20).

2. Involuntary coping with FRS

2.1. Involuntary engaged coping with FRS was lower in the case group compared to the control group (0.240 (0.231-0.248) vs. 0.255 (0.245-0.261))

Table 1. A comparison of voluntary (secondary) engaged coping with FRS between the study and control group of adolescents concerning ATA and sex.

DV	IV	G		N	$\bar{X}$/M	SD/CI	t/Z	*P*	r/ η^2
FCF2	ATA	T		88	0.250	0.243-0.262	**-2.48**	**0.01**	**0.19**
		C		88	0.230	0.230-0.247			
	ATA*S	M	T	23	0.273	0.044	**-6.36**	**<0.01**	**0.48**
			C	23	0.213	0.013			
		F	T	65	0.250	0.235-0.256	-0.10	0.92	
			C	65	0.250	0.237-0.258			
			C	41	0.249	0.046			

Labels and abbreviations: DV – dependent variable; FCF2 – voluntary (secondary) engaged coping with FRS; IV – independent variable; ATA – anti-thyroid antibody level; S – sex; G – group; T – case group; C – control group; M – male; F – female; N – number of subjects; $\bar{X}$ – mean; M – median; SD – standard deviation; CI – 95% confidence interval.

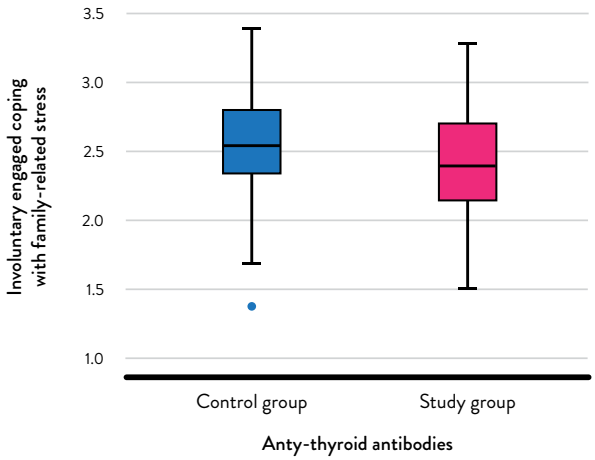

Figure 3. Involuntary engaged coping with FRS in the study and control group of adolescents.

with a statistically significant difference with a small effect size (Z = -2.37; N = 88; *P* = 0.02, r = 0.18) (Figure 3). Again, a statistically significant difference was observed only in boys, i.e. boys in the case group had a lower involuntary engagement response to FRS than boys in the control group (0.250 (0.212-0.249) vs. 0.270 (0.261-0.278)) with a statistical significance (Z = -3.52; N = 23; *P* < 0.01, r = 0.52) (Table 2).

The groups were compared using the Student's t-test for a variable with a normal distribution (t-value) or Mann-Whitney's U test for a variable with an asymmetric distribution (Z-value). If a statistically significant difference was found, the effect size was measured by calculating the Pearson correlation coefficient (r) for a variable with an asymmetric distribution, or partial eta-squared (η^2) for a variable with a normal distribution.

2.2. Involuntary disengaged coping with FRS was only slightly higher in the case group compared to the control group (0.170 (0.169-0.182) vs. 0.170 (0.167-0.180)). The difference was not statistically significant (Z = -0.30; N = 88; *P* = 0.77).

Discussion

In the present paper, we investigated the exposure to, coping with and response to PS, i.e. FRS, in euthyroid adolescents with elevated levels of ATA diagnosed with HT. The case group included more girls (73.86%) than boys (35.1%) in a ratio of 2.8:1 in favor of girls, which would approximately correspond to previously conducted studies with a ratio of 2:1 of female and male respondents in the pediatric population, since HT is more common in females[21]. Considering the results of previous studies that explored the relationship between PS and autoimmune thyroid diseases, a connection between stress and GD was noticed. Intriguingly, the relation between PS and the occurrence of HT was questionable[22]. The prevalence of elevated TPOAb in patients with HT is > 80%, but TPOAb can also be detected with a lower prevalence (about 50%) in patients with GD[23]. However, patients

Table 2. A comparison of involuntary engaged coping with FRS between the study and control groups of adolescents concerning ATA and sex.

DV	IV	G		N	$\bar{X}$/M	SD/CI	t/Z	*P*	r/ η^2
FCF4	ATA	T		88	0.240	0.231-0.248	**-2.37**	**0.02**	**0.18**
		C		88	0.255	0.245-0.261			
	ATA*S	M	T	23	0.250	0.212-0.249	**-3.52**	**<0.01**	**0.52**
			C	23	0.270	0.261-0.278			
		F	T	65	0.240	0.233-0.253	-0.82	0.42	
			C	65	0.250	0.237-0.257			
			C	41	0.250	0.237-0.264			

Labels and abbreviations: DV – dependent variable; FCF4 – involuntary engagement response to FRS; IV – independent variable; ATA – anti-thyroid antibody level; S – sex; G – group; T – test; C – control; M – male; F – female; N – number of subjects; $\bar{X}$ – mean; M – median; SD – standard deviation; CI – 95% confidence interval.

with GD under PS had lower TPOAb concentrations compared to patients with GD who were not exposed to stressful events[24]. There are some difficulties in considering the research on the association between HT and PS, because the clinical picture of HT develops gradually, sometimes even years after the appearance of elevated levels of ATA[23]. During a five-year follow-up of 790 subjects with a positive family history of autoimmune thyroid disease (study by Effraimidis et al.), elevated TPOAb levels were found in only 81 subjects, suggesting that PS and HT are not associated[25]. Also, in a study by Striedor et al., no statistically significant difference was observed between individuals exposed to PS with elevated or normal TPOAb levels[26]. In his research, Martin-du Pan concluded that neither PS nor pregnancy are triggers for the development of HT[27]. Intriguingly, a study by Vaivode et al. observed a positive correlation between TPOAb levels and the number of stressful events in 7–12 months before clear symptoms of HT. In this case, the authors even suggested monitoring the level of TH12 cytokines as a marker of the development of autoimmune disease[28]. In addition, Vita et al. presented an isolated case of a patient with a long-term diagnosis of HT, in whom PS provoked the appearance of hashitoxicosis. At the time of diagnosis of hashitoxicosis, TPOAb values were 3 times higher compared to previous years, while elevated levels of TgAb and thyrotropin stimulating antibodies (TRAb) were not detected[29]. Agha-Hosseini et al. found increased concentrations of cortisol, one of the typical representatives of hormones that are secreted in increased amounts in stressful events, in 40 patients with HT, which was statistically significant compared to the control group[30]. Markomanolaki et al. observed that after eight weeks of stress management training, subjects experienced a decrease in TgAb levels and a reduction in PS, depression and anxiety[31]. Several other authors describe cases of conversion of HT to GD as a rare occurrence in adults and children. For example, Gonzalez-Aguilera et al. describe 24 patients with HT with a transition to GD. Although they did not describe PS as a possible factor, 3 out of 24 patients had gastritis, in one patient the conversion occurred in the first trimester of pregnancy and in the third patients it occurred 3 months after delivery[32]. Two girls with a conversion of HT to GB are also described as case reports in adolescence. However, even with them, PS is not defined as a possible cause[33].

In our study, in addition to exposure to PS, i.e. FRS, we also studied coping with FRS (primarily and secondarily engaged and disengaged) in adolescents with and without elevated ATA levels. In primarily engaged coping with FRS, problem-solving is actively approached through emotional regulation and expression[34]. We found no differences in primary coping with FRS regardless of the presence of elevated ATA levels and the subjects' sex. Secondary coping (e.g., adaptive coping, cognitive restructuring, acceptance, distraction) with FRS was statistically significantly higher in boys in the case group compared to the control group. When we consider willingly engaged and disengaged, and involuntarily engaged and disengaged coping with FRS, the only statistical difference was found for the involuntarily engaged response. The involuntarily engaged response to FRS for the case group was lower compared to the control group. Again, a statistically significant difference was observed only in boys, i.e. boys in the case group had less involuntary engagement in response to FRS than boys in the control group. According to research on coping with PS in chronic illnesses, secondary coping indicates successful adaptation in children and adolescents. By contrast, disengaged (avoidant) coping is associated with poor adaptation to PS[35]. Different ways of coping with PS is also linked to physiological differences. Secondary coping is associated with lower HPA axis activity compared to avoidant coping[36]. According to some studies, depression in children and adults is associated with HPA axis dysregulation[37]. Subjects who use engaged coping with PS (primary and secondary coping with PSs) have been observed to have fewer behavioral problems and emotional disturbances[38]. Although primary and secondary engaged coping is compatible, there is a difference depending on whether the effect is a controllable or less controllable stressor. During the action of a controllable stressor, primary engaged coping is more adaptive, while secondary engaged coping is more adaptive during the action of an uncontrollable stressor. The more controllable the stressor, the better the active coping with PS, and when the stressor is less controllable, the better the acceptance and adaptation to PS, i.e. secondary engaged coping with PS[35]. In a study of coping with chronic

PS in children with recurrent abdominal pain, it was observed that primary and secondary engaged coping was associated with lower levels of anxiety, depression and somatization. In secondary coping with PS, a lower level of pain was also observed compared to subjects who coped with PS primarily[39]. Jaser et al. investigated coping with FRS in children whose parents suffered from depression. Children who coped with FRS secondarily showed fewer symptoms of depression and anxiety[40]. Disengaged coping (avoidance coping) is associated with poor adaptation to PS[34]. In a study by Yiliz et al., which included euthyroid subjects with HT (mostly women — 91% of subjects with an average age of about 37 years), the correlation between coping with PS and symptoms of depression and anxiety was studied. Their results indicate that coping focused on emotions and the problem was negatively correlated with depression[41].

Autoimmune thyroid diseases such as HT and GD are often found to be more common in individuals with symptoms of various psychiatric disorders, especially depression. Depression can be the first symptom of hypo- or hyperthyroidism, and it can also occur in euthyroid subjects with elevated ATA levels. A study by Kirim et al. showed an elevated frequency of depression and a higher rate of severe depression in patients with euthyroid chronic autoimmune thyroiditis. The respondents were mostly women (only 2 male subjects were included in the control and case groups). Due to the significantly lower incidence of HT in men, there are significantly fewer scientific publications investigating HT in the male population[42]. However, it should be emphasized that our study was about adolescents, while the previously cited studies were about adults. In our study, a statistically significant difference was observed in boys; male adolescents with elevated ATA levels were more likely to deal with FRS secondarily, while adolescents in the control group, also boys, had a statistically significantly higher involuntary response to FRS.

Furthermore, the response to PS is associated with various psychosomatic and psychiatric disorders. Men and women react differently to PS biologically and psychologically. Due to sex and different responses to PS, a different spectrum of diseases can be found in male and female patients. Thus, arterial hypertension, aggressive behavior and substance use disorders are more frequently found in men, while autoimmune diseases, depression and pain syndromes are diagnosed more frequently in women. Also, less engaged and more disengaged coping with PS, as well as an involuntary stress response, are associated with depression in adolescence[43]. Men are less sensitive to PS than women (men have greater activation of the HPA axis and greater secretion of ACTH), while women have greater sensitivity to the adrenal cortex[44,45]. Jucevičiūtė et al. examined the association of autoimmune thyroid diseases with depression and bipolar disorder in their study. They found that euthyroid subjects with HT and elevated TPOAb levels were more prone to depression, but no difference in the incidence of depression was reported concerning sex[46]. Women have more pronounced dysregulation of the HPA axis compared to men. Throughout life, not only HT but also depression and PTSD develop more frequently in women than in men, although both sexes are exposed to approximately the same level of PS. Some studies have linked this to the pro-inflammatory effects of estrogen, while androgen hormones have the opposite, anti-inflammatory effect. It is known that dysregulation of the HPA axis also occurs in subjects suffering from depression. Therefore, most studies associate the occurrence of HT with depression in women[47,48]. Worldwide, the estimated global prevalence of clinical depression is around 5.8% in women and around 3.5% in men, which is significantly lower, but still not negligible. It should be noted that in some segments, depression in men manifests with a different clinical presentation compared to the female population. In men, we often find symptoms such as violence, aggression and addiction, with men seeking medical help less frequently. Sometimes the diagnosis of depression can be incorrectly recorded as an addiction disease, because there is significant overlap in the clinical presentation[49,59]. Precisely because of the lower incidence of both autoimmune diseases and depression in men, previous studies have not included men with the disorders mentioned above and research was predominantly performed on women. Around the age of 13, the rate of depression increases more in girls, while it decreases in boys. In late adolescence, the rate of depression is twice as high in girls, which would approximately correspond to adulthood. Even

when exposed to the same stressor, women are twice as likely to develop depression compared to men. The tendency for depression in girls is explained by differences in the response to PS and hormonal changes during puberty, regardless of increased or decreased levels of estrogen. However, although the female sex is twice as likely to develop depression, suicide is four times more common in males. Nevertheless, we did not thematically address depression or the socioeconomic status of adolescents in our study. Still, it is important to note that PS is also associated with poorer socioeconomic status, which should also be considered in research. Although worse financial aspects play a significant role in this sense, families with poorer socioeconomic status also have higher levels of domestic violence and psychopathology in the form of depression and addiction.

Conclusion

During our study, we did not observe a difference in adolescents' exposure to PS i.e. FRS, regardless of the presence of ATA. Adolescents with HT and elevated levels of ATA coped more actively with FRS using positive thinking, cognitive restructuring and acceptance compared to healthy adolescents. According to our study results, the mutual connection between exposure to FRS and coping with FRS in adolescents with HT and elevated levels of ATA cannot be confirmed. However, coping with FRS in euthyroid adolescents with HT involves addressing both the physical and emotional aspects of the condition. Understanding HT, considering the emotional and psychological needs of adolescents, promoting healthy coping mechanisms (PS management, physical activities, hobbies, involving the family in supportive roles), peer support, optimizing nutrition and lifestyle, and empowering adolescents (helping them to take an active role in managing their health and PS, setting boundaries, communicating their needs and learning problem-solving skills) are a good and recognizable mechanism to lower overall PS levels and ensure a better quality of life.

Limitations

The study's limitations are reflected in the relatively small number of respondents with a higher proportion of females and the cohort of only one geographical area (Southeastern Europe), which makes inter-geographical comparability of the respondents impossible. Socioeconomic indicators and psychiatric indicators such as depression and substance use/addiction were also not considered.

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Sažetak

OBITELJSKI STRES KOD EUTIROIDNIH ADOLESCENATA S HASHIMOTOVIM TIREOIDITISOM I POVIŠENIM RAZINAMA ANTITIREOIDNIH PROTUTIJELA

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Odgovor na stres predstavlja složenu, adaptivnu reakciju na različite endogene i egzogene podražaje. Psihološki stres (PS) može biti povezan s upalnim procesima, remetiti hormonsku ravnotežu i utjecati na imunosni sustav i druge tjelesne sustave. Kada govorimo o autoimunosti, PS se u literaturi navodi kao mogući vanjski čimbenik koji utječe na njen razvoj. Nadalje, kronični PS, uključujući obiteljski-povezani stres (OPS), može doprinijeti autoimunim bolestima štitnjače poput Hashimotovog tireoiditisa (HT). Ovo istraživanje provedeno je kao randomizirana studija ispitivanja odgovora na OPS i suočavanja s OPS-om u 88 eutireoidnih adolescenata s HT-om i povišenim razinama antitireoidnih protutijela (ATP) (ispitivana skupina) u usporedbi s 88 zdravih adolescenata (kontrolna skupina). Dodatni ciljevi bili su prikazati, raspraviti i usporediti dobivene rezultate s do sada objavljenim literaturnim podacima. U ispitivanju razine OPS-a korišten je višedimenzionalni upitnik odgovora na stres za djecu i adolescente. Utvrdili smo nižu razinu izloženosti OPS-u u ispitivanoj skupini u odnosu na kontrolnu skupinu, pri čemu nije utvrđena statistički značajna razlika. Sukladno rezultatima naše studije, nije potvrđena povezanost između izloženosti OPS-u i suočavanju s OPS-om u adolescenata s HT-om i povišenim razinama ATP-a.

Ključne riječi: *Adolescent; Stres; Hormoni*