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Physical development of adolescents with type 1 diabetes mellitus and the impact of the war in Ukraine on its impairment

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Abstract

Purpose: To determine the characteristics of physical development (PD) of adolescents with type 1 diabetes mellitus (T1DM) and the impact of the war in Ukraine on its nature.

Material and methods: The nature of physical development (PD) was assessed in adolescents with T1DM aged 14–18 years, examined before the start of the war on 24.02.2022 (*main group*, n = 114) and after 01.10.2022 (*comparison group*, n=76). The study was conducted in accordance with the principles of the Declaration of Helsinki and accepted by the Committee on Bioethics and Deontology. The examination of patients was carried out in accordance with the standards of medical care "Diabetes mellitus in children", approved by Order of the Ministry of Health No. 413 of February 28, 2023 (Order of the Ministry of Health of Ukraine, 2023) and

protocol for providing medical care to children in the specialty "pediatric endocrinology" (Order of the Ministry of Health of Ukraine, 2013).

Results: It was proven that 29,1% of modern adolescents 14-17 years old, patients with T1DM, had a disharmonic PD, the nature of which depended on gender and the state of glycemic control. Girls were more likely to have impaired growth (21,0%) and overweight (12,8%), while boys were diagnosed with tall stature (8,9%) and underweight (8,9%). More often, PD disturbances were observed in the case of stable decompensation of carbohydrate metabolism with a decrease in the time spent in the target range and high levels of glycemic variability during the day.

Among adolescents with T1DM during the period of hostilities in Ukraine, the number of adolescents with disharmonious PD increased (36,7%, P<0,05), which may be due to a deterioration in glycemic control. In boys, an increase in the percentage of patients with underweight (20,0%, P<0,05) and with short stature (4,0%, P<0,05) was recorded, and in girls - with overweight (29,9 %, P<0,05).

Conclusions: confirms the negative impact of T1DM on RF, especially when socio-economic conditions worsen during armed conflicts. The relationship between the nature of risk factors, gender, the state of glycemic control and unfavorable living conditions during the war in Ukraine was determined.

Key words: adolescents, physical development, type 1 diabetes mellitus, war in Ukraine

Introduction

Physical development (PD) of adolescents is a complex of morpho-functional characteristics that characterize the age-related level of biological development (Osadchuk, & Sergeta, 2012).

It has been proven that among the etiopathogenetic factors influencing the developmental processes of a child, a significant role belongs to the state of his health, somatic and mental pathology. The features of physical and sexual development disorders in school-age children suffering from psychosomatic pathology were determined (Lebets, et al, 2021)

Among the chronic somatic diseases in the city, diabetes mellitus (DM) is a severe, disabling pathology of the endocrine system. Data were obtained on changes in risk factors in children and adolescents during the manifestation of type 1 diabetes mellitus (DM), the incidence of which has been significantly increasing in recent years (Chumak, et al, 2021)

It was established that the nature of changes in body weight during the period of manifestation of T1DM was accompanied by certain features of the characteristics of carbohydrate metabolism. Thus, in the group of patients with overweight (OW), at the onset of the disease there was less pronounced decompensation of metabolism with lower levels of glycated hemoglobin (HbA1) and smaller fluctuations in glycemia than in the group of patients with underweight (UW) (Budreiko, 2010).

It is assumed that the presence of OW in some children in the initial period of the disease can serve as confirmation of the "accelerator hypothesis" and the connection between the onset of diabetes and accelerated physical development the day before. It was shown that in case of unsatisfactory compensation of carbohydrate metabolism, stable decompensation of metabolism with the formation of complications and the presence of comorbid diseases at puberty may lead to a violation of somatofield development (Budreiko, 2006; Kostenko, 2022).

As a result of carbohydrate metabolism disorders caused by insulin deficiency, the processes of growth and puberty are disrupted. It is noted that insulin is the most important growth and anabolic factor, one of the mediators of somatotropic effects, which are very important for the body of adolescents. Thus, when studying the functional state of the growth hormone/insulin-like growth factor type 1 (GH/IGF-1) system, it was found that in adolescents with type 1 diabetes during puberty there was an increase in the level of growth hormone (GH) and insulin-like growth factor type 1 (IGF -1), but their performance was lower than that of healthy peers. The functional state of the GH/IGF-1 system in adolescents with T1DM depends on gender, level of sexual development, duration of diabetes and the state of compensation of carbohydrate metabolism (Turchina, et al., 2022a).

The negative impact of disorders of the pituitary-thyroid system on the somato-sexual development of adolescents with diabetes has been determined, especially during early puberty, when the number of patients with signs of hypothyroidism is likely to increase (23,5%). It has been proven that the progression of thyroid failure is accompanied by a decrease in the levels of GH and IGF-1 (Turchina, et al., 2023b)

This became the basis for improving methods of prevention and treatment of disorders of somato-sexual development in adolescents with T1DM due to the correction of thyroid dysfunction (Turchina, et al., 2023a) and vitamin-microelement imbalance (Turchyna, et al., 2022b; Volkova, et al., 2023).

A comprehensive examination of children and adolescents with T1DM identified disturbances in the course of puberty and the development of menstrual function in girls. In 2/3 of those examined, disharmonious development occurred (Turchina, et al., 2019).

Thus, the lack of adequate treatment for a child with diabetes mellitus has a negative impact on growth processes with the formation of a disharmonious PD. The introduction of new types of insulin, the use of

modern insulin administration regimens, and the formation of motivation for treatment in the process of learning self-control contributed to the improvement of compensation for diabetes mellitus in adolescence (Turchina, et al., 2020a; Turchina, et al., 2020b).

It should be noted that the PD of children and adolescents is not only one of the important integral indicators of their health, but also an indicator of the state of the child's living environment. It has been proven that the nature of PD at each stage of ontogenesis depends on a number of different factors: socio-economic, environmental and hygienic, nutritional status, physical and psychological stress, adaptation of the body to learning conditions and educational load, which affect the growth of the child (Fedorenko, & Kitsula, 2011).

Among the negative socio-economic factors, an important city is occupied by military conflicts and the associated deterioration of the child's living conditions and the state of medical care, which leads to an increase in the incidence of mental and somatic pathologies with an unfavorable course. A study of the nature of PD in school-age children affected by the armed conflict in eastern Ukraine in 2014-2021 made it possible to establish that the formation of disharmonious physical development in children and adolescents is influenced by the nature of endocrinopathy and the age at which the patient experienced the active effects of negative factors, associated with the armed conflict (Turchina, & Kostenko, 2018a; Turchina, & Kostenko, 2018b).

But the question remains how the unfavorable conditions of the full-scale war in Ukraine, which began on February 24, 2022, influenced the development of children with type 1 diabetes, who received modern rehabilitation technologies in the last pre-war years.

Conflict and violence stemming from the military invasion of Ukraine in late February 2022 and ongoing fighting have affected the lives of hundreds of thousands of civilians. In war conditions, the emotional state of people is generally unstable and emotions change rapidly during the day. As the researchers note, now it is especially important to pay attention to the study, first of all, of states of emotional response caused by the consequences of military operations, such as fear, anxiety, anger, irritation, etc. not only of an individual, but also, in general, of the Ukrainian people (Gubar, 2023).

As a result of the hostilities, infrastructure, houses, hospitals, and schools were damaged. This social and humanitarian crisis has led to a depletion of healthcare resources to care for patients with chronic

pathology, namely T1DM. The consequences of military conflict affect different areas of T1DM treatment. First, delivery services and pharmacies were disrupted, leading to shortages of vital medications, particularly insulin. There was a shortage of materials for monitoring blood glucose levels, and access to specialized endocrinological care was limited. Without receiving appropriate treatment, especially for T1DM in children and adolescents, there was a risk of developing acute complications such as ketoacidosis and hypoglycemic conditions. Secondly, impaired food distribution contributed to elevated blood sugar levels due to non-adherence to dietary treatment. Third, the impact on the mental health of these patients has increased significantly.

Considering the fact that PD objectively reflects the state of somatic and mental health of children and adolescents, research aimed at identifying factors influencing the growth of a sick child in war conditions, deepening the understanding of the mechanisms of disorders of somato-sexual development in patients with T1DM in these difficult conditions is relevant with the aim of improving methods of their treatment and rehabilitation.

Purpose of the work.

To determine the nature of the physical development of adolescents with type 1 diabetes mellitus (T1DM) and the impact on the nature of the war in Ukraine.

Material and methods of research.

Participants

Adolescents 14-17 years old, who have had T1DM for more than a year and were in the endocrinology department of the State Institution "Institute of Health Care for Children and Adolescents of the National Academy of Medical Sciences of Ukraine" (State Institution "INPN of NAMS", Kharkiv) for examination and treatment.

The main group - 103 patients with T1DM 14-17 years old were examined during 2020-2021 before the start of the war in Ukraine (until February 24, 2022);

Comparison group - 49 patients with T1DM aged 14-17 years, examined during the war in Ukraine after October 1, 2022, when it became possible to conduct a comprehensive examination in the conditions of the endocrinology department State Institution "INPN of NAMS".

The study was conducted in accordance with the principles of the Declaration of Helsinki and accepted by the Committee on Bioethics and Deontology. Parents and patients provided written informed consent to participate in the study.

Research design

Clinical-anamnestic and laboratory-instrumental examination of

patients was carried out in accordance with the standards of medical care "Diabetes mellitus in children" (Ministry of Health of Ukraine, 2023) and protocol for providing medical care to children in the specialty "pediatric endocrinology" (Ministry of Health of Ukraine, 2013).

Anthropometric studies were carried out (height, body weight, BMI was determined in kg/m^2, which was calculated using the formula (Kalmykova, et al., 2018; Kalmykova, et al., 2021)):

$$\mathbf{BMI = m/h^2}$$

where m is body weight (kg); h is height (m).

PD was assessed by comparing the main anthropometric indicators by age standards in accordance with the protocols for providing medical care to children in the specialty "Pediatric Endocrinology" (Ministry of Health of Ukraine, 2013). The assessment of the patients' body height was carried out according to the centile growth chart for children, taking into account age and gender. Underweight was diagnosed if BMI was below the 5th percentile, and overweight was above the 85th percentile.

The state of carbohydrate metabolism was assessed by the level of glycemia during the day and the indicators of glycosylated hemoglobin (HbA1c). Optimal glycemic control (GC) was defined as HbA1c less than 7.0%, suboptimal - HbA1c 7.0 - 9.0%, and high-risk GC with HbA1c > 9,0% (DiMeglio, et al., 2018). The coefficient of glycemic variability (CV) was calculated (Bolli, 2006). Based on glucose monitoring data, the time spent in the target range (TIR - time-in-range) was determined (Monnier, et al., 2017).

Serum analysis

Glucose and HbA1c levels were determined on an empty stomach. Glucose monitoring was also carried out throughout the day. Blood glucose was determined by a photometric biochemical method. HbA1c level – by ion-exchange high-performance liquid chromatography.

Statistical analysis

The creation of the database and statistical processing of the results were carried out using Microsoft Excel and SPSS 26.0 application packages. All data were subject to normal distribution. For the summary assessment of quantitative variables, the mean ± standard deviation/error of the mean (M(SD), M(m)) was used. Nominal data were characterized using the number of observations (n) and frequency (%). Comparison of data between groups was performed using one-way analysis of variance (ANOVA). The significance level was set at $p<0,05$.

Results of the research.

Individual analysis of anthropometric indicators and BMI in adolescents 14-17 years old with

T1DM examined during 2020-2021. before the start of the war in Ukraine (main group), made it possible to diagnose harmonious PD (HPD) in 70,0% of the examined. Every third patient had disharmonious PD (DPD) due to high (9,7%) or short stature (5,8%). Overweight and underweight were diagnosed with almost the same frequency (7,8 and 7,1%); Figure 1.

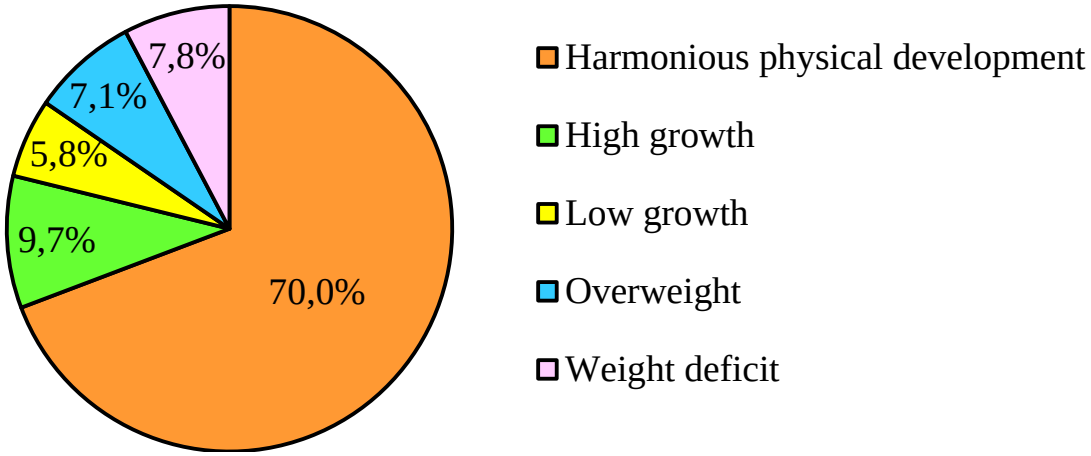

Figure 1. Pattern of physical development (PD) in adolescents with T1DM (main group).

Sexual characteristics in the nature of PD in patients with T1DM were determined. Girls were more likely to be diagnosed with DPD than boys (36,2% compared to 23,2%, respectively $p<0,05$). Among girls there was a greater percentage of patients who were short and overweight (10,6% and 3,6%, respectively) than among boys (1,8% and 3,6%, respectively, $p<0,05$). Children were slightly more likely to be underweight (8,9% compared to 6,4% in girls, $p<0,05$); Figure 2.

An analysis of PD was carried out depending on the level of compensation of carbohydrate metabolism. Accordingly, modern recommendations for the monitoring and treatment of T1DM in children and adolescents are especially important to monitor not only the HbA1c level, but also the variability of glycemia during the day (pre-, postprandial, night), calculate the CV coefficient, time spent in the target range (TIR- time -in-range) and time spent in hypo- and hyperglycemia.

The study of these indicators revealed that only 11.7% of patients had optimal GC (HbA1c < 7.0%), 39.8% had suboptimal (HbA1c – 7,0 – 9,0%), 48,5% had CG with high risk (HbA1c – 7.0 – 9.0%). Only 36.1% of

subjects were in the target range (TIR-time-in-range) state more than 50% of the time. In the majority of patients (84,3%), high variability of glycemia was recorded during the day with a CV of more than 36%. Individual analysis of GC indicators in adolescents with HPD and DPD identified probably higher CV values specifically in patients with DPD.

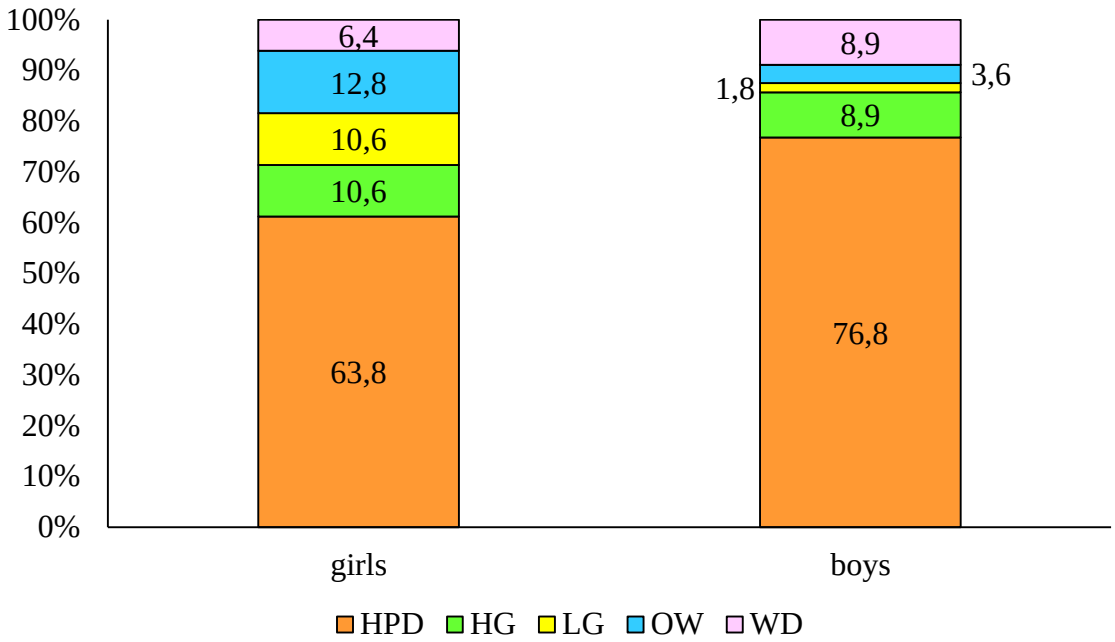

Figure 2. The nature of physical development (PD) in girls and boys with type 1 diabetes mellitus (main group).

Notes: Harmonious physical development (HPD); High growth (HG); High growth (HG); Low growth (LG); Overweight (OW); Low growth (LG)

Analysis of the structure of DPD in patients with different levels of compensation for carbohydrate metabolism made it possible to establish that at the optimal level of compensation, predominantly high growth was recorded (38,5%); Figure 3.

Patients with optimal control were most often diagnosed with high stature (26,3%) and underweight (15,8%). Among adolescents who were in a state of stable decompensation, the percentage of patients with underweight (18,4%), overweight (10,5%) and underweight (13,2%) increased. Regardless of the state of carbohydrate metabolism compensation, children are more likely to be tall and underweight.

Thus, it has been proven that 30,0% of modern adolescents aged 14-

17 years, suffering from T1DM, had DPD, the nature of which depended on gender and GC status. Girls were more likely to be short of height and overweight, boys were tall and underweight. With optimal GC compensation, 2/3 of those examined had HPD, 1/3 had high growth. In the case of stable decompensation, the percentage of adolescents with HPD was three times lower and the percentage of adolescents with overweight and underweight was twice as high.

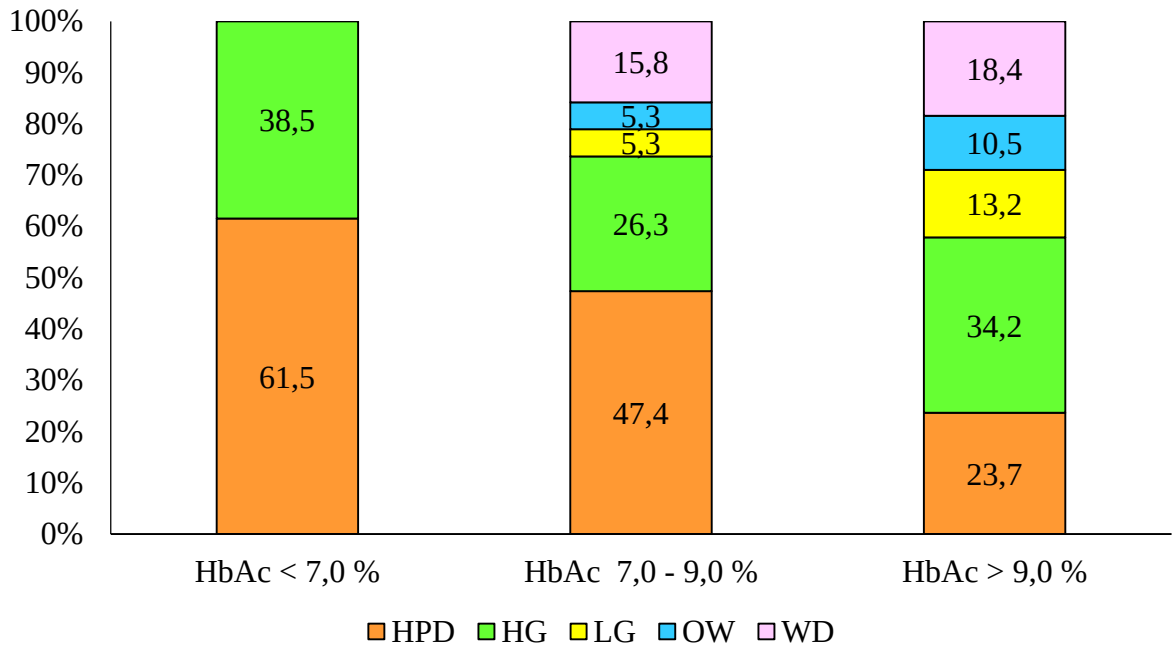

Figure 3. The nature of physical development (PD) in adolescents with type 1 diabetes mellitus, depending on compensation of carbohydrate control

Notes: Harmonious physical development (HPD); High growth (HG); High growth (HG); Low growth (LG); Overweight (OW); Low growth (LG).

In order to determine the impact of unfavorable conditions of martial law on the territory of Ukraine, the results of examination of patients 14-17 years old with T1DM before the start of the war (*main group*) and peers examined after 10.01.2022 (*comparison group*) were compared.

When assessing the PD of adolescents 14-17 years old in the *comparison group*, an increase in adolescents from DPD was registered (36,7% compared to 29,1% in the *main group*, P<0,05). There have also been changes to the DPD structure. The percentage of patients with high stature (4,1%, P<0,05) significantly decreased

and increased with short stature (8,1%, P<0,05), overweight (16,4%, P<0,05) and underweight (12,1%, P<0,05).

Among boys, an increase in the percentage of patients with underweight (20,0%, P<0,05) and short stature (4,0%, P<0,05) was registered, and among girls - with excess weight (29,2%, P<0,05). Also, short height was determined somewhat more often in girls (12,5%, P < 0,1) and there were no girls with tall height (Figure 4).

Figure 4. Characteristics of risk factors in adolescents with T1DM, the *main group* and the *comparison group*

Notes: Harmonious physical development (HPD); High growth (HG); High growth (HG); Low growth (LG); Overweight (OW); Low growth (LG).

Individual analysis of CV coefficient indicators determined a likely increase in the number of patients with high CV indicators (26,5% compared to 15,7% at the beginning of the war in Ukraine, P <0,05). Among adolescents in the comparison group with DPD, a higher level of CV was more often determined than in patients with HPD (33,3% compared to 22,6%, respectively, P<0,05). Patients with HPD were more likely to have optimal TIR scores than adolescents with HPD (64,5 compared to 55,6%, respectively, P<0,05).

Discussion

In modern conditions, there are significant changes in the nature of the

physical and sexual development of adolescents with T1DM and these changes, according to scientists, are associated with the use of new treatment technologies (Aliyeva, 2010; Yagasaki, et al., 2010)

This study made it possible to determine the characteristics of PD in modern adolescents with T1DM, who in the pre-war years received complex treatment with the prescription of short- and long-acting analog insulins, staged rehabilitation with the involvement of a multidisciplinary team, group and individual psychotherapy, and training in the principles of self-control of T1DM (Turchina, et al., 2020a)

Based on a comprehensive study conducted in previous years, the most significant unfavorable factors of impaired somato-sexual development in adolescents with T1DM were identified and methods of prevention and treatment of patients with T1DM with an unfavorable prognosis for puberty were improved (Turchina, et al., 2023c).

Prevention and treatment of disorders of somato-sexual development is based on certain mechanisms and significant prognostic factors, namely: achieving optimal GC through self-control and correction of insulin therapy; correction of thyroid dysfunction; carrying out general stimulating therapy using vitamins and essential microelements.

The introduction of the developed technology into the clinical activities of medical institutions made it possible to evaluate its effectiveness in carrying out this study and to study the nature of risk factors in adolescents aged 14-17 years, who during 2019-2022 were treated on the basis of the endocrinology department of the State Institution “INPN of NAMS”. It was confirmed that in adolescents 14-17 years old with T1DM examined before the start of the war, DPD developed in every third patient (30,0%). More often, PD disturbances were observed in the case of persistent decompensation of carbohydrate metabolism with a decrease in time in the target range (TIRg) and high levels of glycemic variability (CV).

As in previous years, a significant percentage of patients with tall stature (9.8%) was registered among teenagers with T1DM. This may be the result of an increase in the level of GH and IGF-1 in adolescents with T1D, especially during puberty itself (Turchina, et al., 2022a).

It is assumed that the increased growth rate is a consequence of the use of insulin analogues. The use of various insulin regimens, insulin analogues, and new technologies including insulin pumps and Continuous glucose monitoring (CGM) has been shown to result in more physiological blood insulin concentrations, normalization of GH and IGF-1 levels, and growth

performance, independent of GC (Donaghue, et al., 2003; Giannini, et al., 2014).

Considering the negative impact of thyroid dysfunction both on the state of the GH/IGF-1 system and on the somato-sexual development of adolescents with T1DM (Turchina, et al., 2023b), the inclusion of methods of its correction in treatment also had a positive effect on indicators of somato-sexual development.

As for determining the influence of unfavorable conditions in which adolescents were during military operations on the territory of Ukraine, preliminary studies conducted at the State Institution "INPN of NAMS" made it possible to establish a connection between the presence and nature of endocrinopathies, the risk of developing DPD and age at the beginning of the anti-terrorist operation (ATO) in Ukraine. It has been proven that the risk group for the formation of DPD are children under 9 years of age, regardless of the form of endocrine pathology, adolescents 11-13 years old with thyropathies and adolescents 14-16 years old with T1DM. The nature of DPD depended on the form of endocrine pathology and the age of the patient before the onset of ATO: in young children, growth disorders were most often determined, in adolescents 9-13 years old with thyropathies and patients with T1DM - excessive or insufficient body weight, in adolescents 14-16 years old with thyropathies – growth disturbance, and in adolescents 14-16 years old, patients with T1DM – overweight (Turchina, & Kostenko, 2018b).

That is, as in the previous study, unfavorable conditions of military operations on the territory of Ukraine are an unfavorable factor in PD impairment in adolescents with T1DM, which may be a consequence of worsening GC due to an increase in glycemic variability during the day and a decrease in the time spent in the target range.

This confirms the negative impact of T1DM on PD, especially in the case of worsening socio-economic conditions during armed conflicts. Under these conditions, the nature of PD is an integral indicator of the course of T1DM in adolescence, which is influenced by both biomedical and social factors.

Continuing research to determine the leading mechanisms of the unfavorable course of T1DM during the war in Ukraine and the post-war period in order to improve the technology of treatment and rehabilitation is a relevant area of modern research.

Conclusions.

1. It has been proven that 30,0% of modern adolescents 14-17 years old with T1DM had DPD, the nature of which depended on gender and HC status.

2. Girls were more likely to have impaired growth and overweight, while boys were more likely to be tall and underweight.

3. More often, PD violations were observed in the case of persistent decompensation of carbohydrate metabolism with a decrease in the time spent in the target range (TIRg) and high levels of glycemic variability (CV).

4. Among adolescents with T1DM during the period of hostilities on the territory of Ukraine, the number of adolescents from DPD increased, which may be due to the deterioration of the GC condition. Among boys, an increase in the percentage of patients with underweight and short stature was recorded, and among girls - with overweight.

Authors' contribution

Conceptualization, S.T; methodology, S.T; check, S.T, Y.K and S.K; formal analysis, S.T and O.V; investigation, S.T, A.K and O.V; data curation,S.K and Y.K; writing - rough preparation, A.K and O.V; writing - review and editing, S.T, Y.K and S.K; project administration, S.T. All authors have read and agreed with the published version of the manuscript.

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Conflict of interest

The authors declare no conflict of interest.

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