

ABSTRACT

Anna A. Sinkina

Iryna M. Nikitina

<http://orcid.org/0000-0001-6595-2502>

Svetlana A. Smiian

<http://orcid.org/0000-0002-7679-2302>

Tetyana V. Babar

<http://orcid.org/0000-0002-5889-2429>

*Department of Obstetrics, Gynecology and Family Planning, Sumy State University, Sumy, Ukraine*

**FREQUENCY AND VARIANTS OF MENSTRUAL DISORDERS IN ADOLESCENTS WITH METABOLIC SYNDROME**

The problem of the correlation between reproductive disorders and metabolic syndrome (MS) is well known, but data on the frequency and nature of these disorders among adolescents are extremely limited.

**The aim of the study:** is to determine and analyze the frequency and structure of menstrual disorders in adolescent girls on the background of metabolic syndrome, as well as to study the correlation of these disorders with possible reproductive health disorders in the future.

**Materials and methods.** To achieve this goal, a retrospective analysis of randomly selected 2,000 outpatient medical records (primary registration form № 025/o) of girls aged 10 to 18 years was performed at the Sumy Regional Clinical Perinatal Center from 2011 to 2021. The menstrual cycle was assessed according to the FIGO 2018 classification. Pathological menarche was defined as early (up to 10 years) or late (after 15 years) onset of menstrual function. Polycystic ovarian syndrome (PCOS) was diagnosed according to the Rotterdam criteria (2003): oligo- or anovulation ( $\leq 6$  menstrual periods per year); clinical or laboratory hyperandrogenism (hirsutism/acne) and/or hyperandrogenemia (increased levels of free testosterone in the blood); polycystic ovaries during transvaginal ultrasound ( $\geq 15$  follicles 2–9 mm in size in each ovary).

**Results.** The results showed that in adolescent girls with overweight and MS, the frequency of menstrual dysfunction was observed in 71.1% of cases. Moreover, the most common variant of menstrual disorders in this category of patients was oligomenorrhea (60.0%), and the frequency of its manifestations was directly dependent on overweight degree. It was found that almost 82% of girls with confirmed MS had a high risk of developing polycystic ovarian syndrome (PCOS) in the future.

**Conclusion.** It was found that the incidence of obesity in children and adolescents in the population was 27.1%, and the incidence of menstrual syndrome among children and adolescents with obesity was 41.5%. A significant proportion of adolescents with menstrual syndrome had menstrual irregularities – 71.1%, which was significantly higher than in healthy girls – 19%. Among menstrual disorders in girls with menstrual syndrome and obesity, oligomenorrhea prevailed (60.0% and 52%, respectively). Moreover, the frequency of oligomenorrhea was significantly affected by the

degree of obesity. Almost 82% of girls with confirmed menstrual syndrome had at least two of the three criteria, which put them at high risk for developing polycystic ovarian syndrome in the future.

**Key words:** metabolic syndrome, adolescent reproductive health, polycystic ovarian syndrome, obesity, menstrual disorders.

**Corresponding author:** Iryna M. Nikitina, Department of Obstetrics, Gynecology and Family Planning, Sumy State University, Sumy, Ukraine  
e-mail: [nikitina1med@gmail.com](mailto:nikitina1med@gmail.com)

## РЕЗЮМЕ

Анна А. Синкіна

Ірина М. Нікітіна

<http://orcid.org/0000-0001-6595-2502>

Світлана А. Сміян

<http://orcid.org/0000-0002-7679-2302>

Тетяна В. Бабар

<http://orcid.org/0000-0002-5889-2429>

*Кафедра акушерства та гінекології, Сумський державний університет, м. Суми, Україна*

## ЧАСТОТА ТА ВАРІАНТИ ПОРУШЕНЬ МЕНСТРУАЛЬНОГО ЦИКЛУ У ПІДЛІТКІВ З МЕТАБОЛІЧНИМ СИНДРОМОМ

Проблема зв'язку репродуктивних порушень з метаболічним синдромом (МС) добре відома, проте дані щодо частоти та характеру цих порушень серед підлітків є вкрай обмеженими.

**Мета дослідження:** визначити та проаналізувати частоту і структуру порушень менструального циклу у дівчат-підлітків на тлі метаболічного синдрому, а також вивчити зв'язок цих порушень із можливими розладами репродуктивного здоров'я в майбутньому.

**Матеріали і методи.** Для реалізації поставленої мети було проведено ретроспективний аналіз випадково відібраних 2000 медичних карт амбулаторного хворого (форма первинної облікової документації № 025/о) дівчат віком від 10 до 18 років, що спостерігалися на базі консультативно-поліклінічного відділення Сумського обласного клінічного перинатального центру з 2011 по 2021 рік. Менструальний цикл оцінювався відповідно до класифікації FIGO 2018. Патологічне менархе визначалось як ранній (до 10 років) чи пізній (після 15 років) початок менструальної функції. Синдром полікістозних яєчників (СПКЯ) діагностували відповідно до Роттердамських критеріїв (2003): оліго- або ановуляція ( $\leq 6$  менструацій на рік); клінічна чи лабораторна гіперандрогенія (гірсутизм/акне) та/або гіперандрогенемія (збільшення рівня вільного тестостерону в крові); полікістозні яєчники під час трансвагінального ультразвукового дослідження ( $\geq 15$  фолікулів розміром 2–9 мм у кожному яєчнику).

**Результати.** Результати показали, що у дівчат підліткового віку з надмірною масою тіла та метаболічним синдромом частота порушень менструальної функції спостерігалася у 71,1 % випадків. Причому, найбільш частим варіантом порушень менструальної функції в цієї категорії пацієнток являється олігоменорея (60,0%), а частота її проявів має пряму залежність від вираженості зайвої ваги. Було встановлено, що майже 82 % дівчат з підтвердженим метаболічним синдромом мають високий ризик розвитку синдрому полікістозних яєчників у майбутньому.

**Висновки.** Встановлено, що частота ожиріння в дитячому та підлітковому віці в популяції склала 27,1 %, а частота менструального синдрому серед дітей і підлітків з ожирінням склала 41,5 %. Вагома частина підлітків з менструальним синдромом мала порушення менструального циклу – 71,1 %, що значно перевищувало цей показник у дівчат з нормальною вагою – 19 %. Серед порушень циклу у дівчат з метаболічним синдромом та ожирінням превалювала олігоменорея – 60,0 % та відповідно 52 %. При чому

на частоту олігоменореї суттєвий вплив мав ступінь ожиріння. Майже 82 % дівчат з підтвердженим метаболічним синдромом мали принаймні два із трьох діагностичних критеріїв, що відносять їх до групи високого ризику розвитку полікістозу яєчників у майбутньому.

**Ключові слова:** метаболічний синдром, репродуктивне здоров'я підлітків, синдром полікістозних яєчників, ожиріння, порушення менструального циклу.

**Автор, відповідальний за листування:** Ірина М. Нікітіна, кафедра акушерства та гінекології, Сумський державний університет, м. Суми, Україна

e-mail: [nikitina1med@gmail.com](mailto:nikitina1med@gmail.com)

**How to cite/ Як цитувати статтю:** Sinkina AA, Nikitina IM, Smiian SA, Babar TV. Frequency and variants of menstrual disorders in adolescents with metabolic syndrome. *EUMJ*. 2022;10(2):188-195

DOI: [https://doi.org/10.21272/eumj.2022;10\(2\):188-195](https://doi.org/10.21272/eumj.2022;10(2):188-195)

## INTRODUCTION/ВСТУП

Given the worldwide statistics on the growth of adolescent obesity, metabolic syndrome remains an extremely pressing problem in modern society. Among the gynecological diseases of puberty that lead to female infertility and are a risk factor for obstetric and perinatal complications, menstrual disorders predominate.

The increase in the global prevalence of obesity over the past 40 years has led to an increase in obesity-related diseases, including MS and polycystic ovary syndrome (PCOS) [1] This is especially true in the current realities in our country. Against the background of constant man-made and stressful stress on the body of women of reproductive age, extragenital diseases are becoming increasingly important, which will further affect the reproductive potential of the nation. Adolescents who remain most vulnerable to stressful situations are also at risk.

The prevalence of MS, according to various authors, is from 10 to 84%. This indicator depends on many factors: gender, age, ethnicity, and the use of different diagnostic criteria [2, 3]. It is difficult to estimate the prevalence of MS in children, as there are still no clearly defined criteria for children and adolescents. In various publications, the prevalence rates range from 0.2% to 38.9% [4]. According to a meta-analysis of 85 studies among children, the average prevalence of MS in whole populations was 3.3% (range from 0% to 19.2%), and overweight children were 11.9% (in the range from 2.8% to 29.3%), and in obese populations – 29.2% (in the range from 10% to 66%). For groups of people who are not obese

and not overweight, the prevalence of MS is from 0% to 1% [5]. About 90% of obese children and adolescents have at least one sign of metabolic syndrome [6].

Chronic stress and the impact of adverse environmental factors on the background of MS and obesity disrupt the mechanisms of adaptation, the work of the hypothalamic-pituitary-ovarian vertical, which leads to hormonal and reproductive disorders [7]. These disorders are especially pronounced during puberty, which is the main crisis period in the functioning of a woman's reproductive system. Dysfunction in the hypothalamic-pituitary-ovarian system in the background of MS affects the normal maturation of the follicle, disrupts adequate secretion of follicle-stimulating hormone (FSH), and luteinizing hormone (LH), alters the sensitivity of receptors to progesterone and leads to ferrogen progesterone. All this further forms a progesterone deficiency. As a result, such features of the endocrine profile in adolescent girls with MS are manifested by menstrual irregularities and chronic anovulation [8].

Hyperandrogenism and hyperinsulinism, which are characteristic of puberty, in combination with obesity provoke the development of PCOS, which is found in 80% of women with MS [9]. The pathogenesis between PCOS and MS appears to be closely related, as both of these conditions involve insulin resistance [10]. There is evidence that women with PCOS have an increased risk of developing MS [11]. It was reported that the prevalence of MS in adolescents with PCOS was probably higher than in adolescents without PCOS [12].

The analysis of the obtained data showed a high frequency of menstrual disorders among adolescent girls with MS. Therefore, it is necessary to develop a clear algorithm for the management of such patients, in order to timely identify and correct menstrual disorders, which is an important indicator of the reproductive potential of the nation.

Thus, the study of the prevalence and nature of reproductive health disorders in the background of MS is an important issue for reproducing the full picture of the pathogenesis of the syndrome, which will develop effective strategies for prevention and treatment.

**The aim of the study:** is to determine and analyze the frequency and structure of menstrual disorders in adolescent girls on the background of metabolic syndrome, as well as to study the relationship of these disorders with possible reproductive health disorders in the future.

#### Materials and methods

To achieve this goal, a retrospective analysis of randomly selected 2,000 outpatient medical records (primary registration form № 025/o) of girls aged 10 to 18 years was observed at the Sumy Regional Clinical Perinatal Center. A retrospective analysis of

medical records was conducted over the depth of 10 years.

According to the recommendations of IDF (2007) [13], the criteria for identifying the components of MS were: obesity – body mass index (BMI); arterial hypertension – arterial pressure (BP); hyperdyslipidemia – serum levels of triglycerides, total cholesterol (cholesterol), low-density lipoprotein (LDL) and high-density lipoprotein (HDL); insulin resistance (IR) – HOMA index; hyperglycemia – fasting blood glucose. The threshold for the diagnosis of obesity was BMI values > 90th percentile according to age and sex. The threshold value of hypertension was the blood pressure of 130/85 mm Hg. Art. Threshold values of the lipid profile were: triglycerides – 1.7 mmol/L, HDL – 1.03 mmol/L, cholesterol – 4.25 mmol/L, LDL – 2.75 mmol/L. Fasting hyperglycemia was considered at blood glucose levels > 5.6 mmol/L. IR was diagnosed at the HOMA index level > 2.5.

The menstrual cycle was assessed according to the FIGO 2018 classification (Table 1). Pathological menarche was defined as the early (up to 10 years) or late (after 15 years) onset of menstrual function and/or the onset of menarche later than 3 years after thelarche.

**Table 1– Characteristics of the normal menstrual cycle (FIGO 2018)**

Parameter	Normal	Abnormal	
Frequency	Absent (no bleeding) = amenorrhea		
	Infrequent (> 38 days)		
	Normal ( $\geq 24$ to $\leq 38$ days)		
	Frequent (< 24 days)		
Duration	Normal ( $\leq 8$ days)		
	Prolonged (> 8 days)		
Regularity	Normal or “Regular” (shortest to longest cycle variation: $\leq 7-9$ days)*		
	Irregular (shortest to longest cycle variation: $\geq 8-10$ days)*		
Flow Volume (patient determined)	Light		
	Normal		
	Heavy		
Intermenstrual Bleeding (IMB) Bleeding between cyclically regular onset of menses	None		
	Random		
	Cyclic (Predictable)	Early cycle	
		Mid cycle	
Late cycle			
Unsheduled Bleeding on Progestin $\pm$ Estrogen Gonadal Steroids (birth control pills, rings, patches or injections)	Not Applicable (not on gonadal steroid medication)		
	None (on gonad steroid medication)		
	Present		

PCOS was diagnosed according to the Rotterdam criteria (2003): oligo- or anovulation ( $\leq 6$  menstrual periods per year); clinical or laboratory hyperandrogenism (hirsutism/acne) and/or hyperandrogenemia (increased levels of free testosterone in the blood); polycystic ovaries during transvaginal ultrasound ( $\geq 20$  follicles 2–9 mm in size in each ovary).

All examined patients sought advice or were observed by an endocrinologist or pediatric gynecologist.

Statistical processing and analysis of the obtained data was performed using «Microsoft Excel» programs using the methods of mathematical statistics and the software package Statistica 8.0. Charts and diagrams were built using «Microsoft Excel». Mathematical processing of indicators was performed using the methods of variation statistics for comparing inhaled sets by averages using the t-Student test.

**Results.** The analysis of 2000 medical records showed that the incidence of obesity in children and adolescents in the population was 27.1% ( $n = 542$ ),

which coincides with the literature [14]. The incidence of MS among obese children and adolescents was 41.5% ( $n = 225$ ). The results show a fairly high rate of obesity among adolescents. This prevalence of this problem may be primarily due to the influence of the typical lifestyle of modern adolescents: overeating easily and usually high-calorie food, lack of physical activity, and a sedentary lifestyle. Almost half of the obese children have been diagnosed with MS, which confirms the close link between obesity and metabolic disorders.

A detailed analysis was conducted with a cohort of selected medical records of adolescents with confirmed MS. A significant proportion of adolescents with MS had menstrual irregularities – 71.1% ( $n = 160$ ). In a cohort of obese adolescents with unconfirmed MS ( $n = 317$ ), menstrual irregularities were described in 48.9% ( $n = 155$ ), which significantly exceeds the rate of these disorders in girls with normal weight ( $n = 1233$ ) – 19% ( $n = 380$ ) (Table 2). Therefore, another component of MS in adolescents can be considered menstrual irregularities.

**Table 2 – Frequency of menstrual disorders among adolescents n (%)**

	Adolescents with confirmed MS n = 225	Adolescents with obesity and unconfirmed MS n = 317	Adolescents with normal weight n = 1233
Frequency of menstrual disorders	160 (71.1)	155 (48.9)	380 (19)
Oligomenorrhea	135 (60)	165 (52)	74 (6)
Secondary amenorrhea	65 (28.9)	70 (22.1)	-
Excessive menstruation during puberty	43 (19.1)	16 (5.0)	12 (1)
Pathological menarche	23 (10.2)	32 (10.1)	-
Dysmenorrhea	72 (32.0)	95 (30.0)	86 (7)

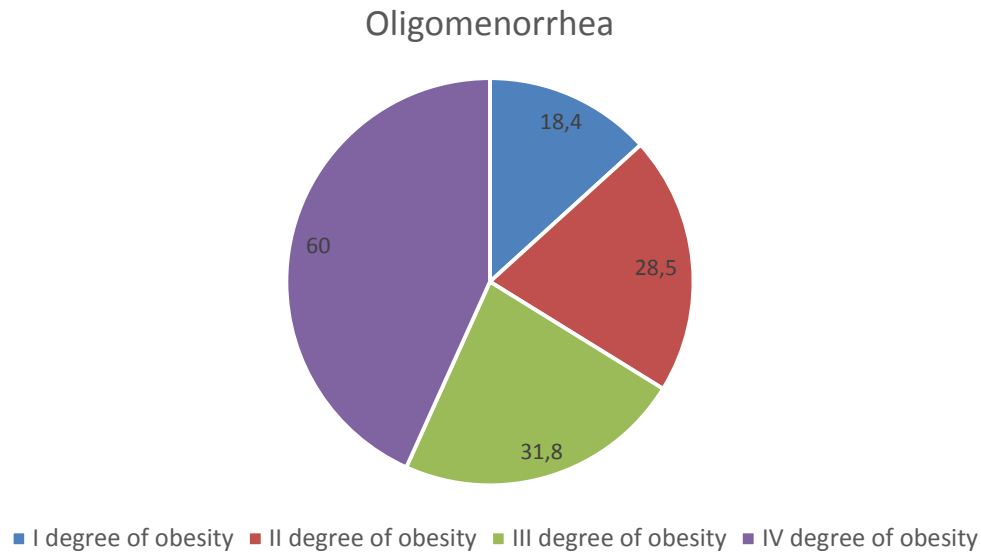
Note: \* –  $p < 0.05$  compared to adolescents with normal weight

Among menstrual disorders in girls with MS and obesity, oligomenorrhea prevailed – 60.0% ( $n = 135$ ) and 52% ( $n = 165$ ). Secondary amenorrhea was noted in 28.9% ( $n = 65$ ) of girls with MS and in 22.1% ( $n = 70$ ) – with obesity. Excessive menstruation was observed much more often in girls with MS – 19.1% ( $n = 43$ ), compared with girls with obesity and without MS – 5% ( $n = 16$ ). Pathological menarche of 10.2% ( $n = 23$ ) and 10.1% ( $n = 32$ ) and dysmenorrhea of 32% ( $n = 72$ ) and 30%, respectively, occurred with almost equal frequency in girls with MS and obesity without MS, ( $n = 95$ ), respectively. The presented menstrual disorders were

significantly different from the parameters of girls with normal weight with a high degree of reliability ( $p < 0.05$ ).

**Discussion.** Analysis of medical records of girls with MS showed that the frequency of oligomenorrhea significantly correlated with the degree of obesity. As can be seen, oligomenorrhea was present in 18.4% of girls with the first degree of obesity, in 28.5% of girls with the second degree, in 31.8% of girls with the third degree, and in 60.0% – with the fourth degree, which indicated a direct relationship between the severity of ovarian disorders and weight gain (Fig. 1).





*Figure 1 – Dependence of ovarian disorders on weight gain*

Given the contradictory physiological changes in adolescence and hormonal imbalance during maturation of the hypothalamic-pituitary-ovarian axis, as well as due to the presence of characteristic heterogeneity in ovarian morphology in adolescents, which makes

#### CONCLUSIONS/ВИСНОВКИ

1. It was found that the incidence of obesity in children and adolescents in the population was 27.1%, and the incidence of MS among children and adolescents with obesity was 41.5%.

2. A significant proportion of adolescents with MS had menstrual irregularities – 71.1%, which was significantly higher than in normal girls – 19%.

ultrasound diagnosis of polycystic ovary disease. MS was impossible. However, almost 82% (n = 184) of girls with confirmed MS had at least two of the three Rotterdam criteria (2003), which puts them at high risk of developing PCOS in the future.

3. Among menstrual disorders in girls with MS and obesity, oligomenorrhea prevailed – 60.0% and 52%, respectively. Moreover, the frequency of oligomenorrhea was significantly affected by the degree of obesity.

4. Almost 82% of girls with confirmed MS had at least two of the three Rotterdam criteria (2003), which put them at high risk for developing PCOS in the future.

#### PROSPECTS FOR FUTURE RESEARCH/ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

The high prevalence of these pathological conditions in adolescent girls with obesity and MS may indicate a close relationship between metabolic changes inherent in the pathogenesis of MS and the development of hormonal dysfunctions in the female reproductive system. Such disorders of the reproductive system in

adolescence are likely to lead to serious consequences in adulthood. Therefore, early detection, timely correction, and reasonable prevention of metabolic and menstrual disorders in adolescents are important components of the treatment of MS and prevention of its complications.

#### CONFLICT OF INTEREST/КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

#### ACKNOWLEDGEMENTS/ЗВ'ЯЗОК РОБОТИ З НАУКОВИМИ ПРОГРАМАМИ

The work is carried out within the framework of the research work “Optimization of tactics of management of patients with reproductive health disorders” (state registration number 0121U114162).

**FUNDING/ДЖЕРЕЛА ФІНАНСУВАННЯ**

None.

**AUTHOR CONTRIBUTIONS/ВКЛАД АВТОРІВ**

All authors contributed to the concept and review of the manuscript. All authors approved the final version of the manuscript.

**A B C** – Anna A. Sinkina**E F** – Iryna M. Nikitina**B** – Svetlana A. Smiian**E** – Tetyana V. Babar**A** – Work concept and design**B** – Data collection and analysis**C** – Responsibility for statistical analysis**D** – Writing the article**E** – Critical review**F** – Final approval of the article**REFERENCES/СПИСОК ЛІТЕРАТУРИ**

- Saboor Aftab SA, Kumar S, Barber TM. The role of obesity and type 2 diabetes mellitus in the development of male obesity-associated secondary hypogonadism. *Clin Endocrinol (Oxf)*. 2013;78(3):330-7. doi: [10.1111/cen.12092](https://doi.org/10.1111/cen.12092).
- Desroches S, Lamarche B. The evolving definitions and increasing prevalence of the metabolic syndrome. *Appl. Physiol., Nutr. Metab.* 2007;32(1):23-32. doi: [10.1139/h06-095](https://doi.org/10.1139/h06-095).
- Ritchie SA, Connell JMC. The link between abdominal obesity, metabolic syndrome and cardiovascular disease. *Nutr. Metab. Cardiovasc. Dis.* 2007;17(4):319-6. doi: [10.1016/j.numecd.2006.07.005](https://doi.org/10.1016/j.numecd.2006.07.005).
- Agudelo GM, Bedoya G, Estrada A, et al. Variations in the prevalence of metabolic syndrome in adolescents according to different criteria used for diagnosis: which definition should be chosen for this age group? *Metabolic Syndrome and Related Disorders*. 2014; 12(4):202-9. doi: [10.1089/met.2013.0127](https://doi.org/10.1089/met.2013.0127).
- Friend A, Craig L, Turner S. The prevalence of metabolic syndrome in children: a systematic review of the literature. *Metabolic Syndrome and Related Disorders*. 2013;11:71-80.
- Cook S, Weitzman M, Auinger P, et al. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. *Arch. Pediatric Adolescent Med.* 2013;157:821-7. doi: [10.1001/ARCHPEDI.157.8.821](https://doi.org/10.1001/ARCHPEDI.157.8.821)
- Zelinska NB. Metabolic syndrome in children. *Health of Ukraine*. 2013;6: 48-51.
- Fleming R, Hopkinson ZE, Wallace AM. [ et al.]. Ovarian function and metabolic factors in women with oligomenorrhea treated with metformin in a randomized double-blind placebo-controlled trial. *The Journal of Clinical Endocrinology and Metabolism*. 2002;87(2):569-74. doi: [10.1210/jcem.87.2.8261](https://doi.org/10.1210/jcem.87.2.8261).
- Tatarchuk TF, Kosey NV, Regeda SI. [ et al.]. [The role of reproductive health disorders in the development of metabolic syndrome in women]. *Journal of the National Academy of Medical Sciences of Ukraine*. 2019;25(1):77-87.
- Sartor BM, Dickey RP. Polycystic ovarian syndrome and the metabolic syndrome. *Am. J. Med. Sci.* 2005;330(6):336-42. doi: [10.1097/00000441-200512000-00012](https://doi.org/10.1097/00000441-200512000-00012).
- Lim SS, Kakoly NS, Tan JWJ, Fitzgerald G, Bahri Khomami M, Joham AE, et al. Metabolic syndrome in polycystic ovary syndrome: a systematic review, meta-analysis and meta-regression. *Obes. Rev.* 2019;20(2):339-52. doi: 10.1111/obr.12762.
- Fazleen NE, Whittaker M, Mamun A. Risk of metabolic syndrome in adolescents with polycystic ovarian syndrome: a systematic review and meta-analysis. *Diab. Metab. Syndr.* 2018; 12(6):1083-90. doi: 10.1016/j.dsx.2018.03.014.
- Zimmet P, Alberti KG, Kaufman FT, et al. IDF Consensus. The metabolic syndrome in children and adolescents - the IDF consensus report. *Pediatr Diabetes*. 2007;5:299-306. doi: 10.1097/00000441-200512000-00012.
- Reisinger C, Nkeh-Chungag BN, Fredriksen PM, Goswami N. The prevalence of pediatric metabolic syndrome – a critical look on the discrepancies between definitions and its clinical importance. *International Journal of Obesity*. 2021;45:12-24.

**(received 05.06.2022, accepted 16.06.2022)****(одержано 05.06.2022, затверджено 16.06.2022)****Information about the authors/Відомості про авторів**

**Anna A. Sinkina** – graduate student of the Department of Obstetrics, Gynecology and Family Planning, Sumy State University, 2 Rymkoho-Korsakova st., Sumy 40007, Ukraine.

**Iryna M. Nikitina** – Dr. Med. Sciences, Associate Professor of the Department of Obstetrics, Gynecology and Family Planning, Sumy State University, 2 Rymkoho-Korsakova st., Sumy 40007, Ukraine  
(E-mail: [nikitina1med@gmail.com](mailto:nikitina1med@gmail.com), T.: +380662947360)

**Svetlana A. Smiian** – Candidate of Med. Sciences, Associate Professor of the Department of Obstetrics, Gynecology and Family Planning, Sumy State University, 2 Rymkoho-Korsakova st., Sumy 40007, Ukraine.

**Tetyana V. Babar** – Candidate of Med. Sciences, Associate Professor of the Department of Obstetrics, Gynecology and Family Planning, Sumy State University, 2 Rymkoho-Korsakova st., Sumy 40007, Ukraine.