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Type 1 diabetes mellitus in children at the prehospital stage. The difficulties of diagnosis

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ABSTRACT. Introduction. The total number of patients with type 1 diabetes (T1D) under the age of 18 in the Russian Federation as of December 31, 2023, was 61,318 (208 per 100,000 child population), with an incidence of 8,009 (28 per 100,000 child population). In most countries, including Russia, the incidence of type 1 diabetes in childhood is increasing. Given the epidemiological indicators and social significance of this disease, as well as the importance of timely diagnosis of diabetes in children, an analysis was conducted of the difficulties at the prehospital stage in diagnosing type 1 diabetes onset. **The aim of the study** – to analyze complex cases in the diagnosis and management of children with new-onset type 1 diabetes at the prehospital stage of emergency and urgent medical care. **Materials and methods.** We analyzed 121 medical records of children with clinical and/or laboratory-confirmed type 1 diabetes onset who were emergently hospitalized via emergency and urgent medical care at the Clinic of St. Petersburg State Pediatric Medical University in 2022–2023. Blood glucose levels at the time of admission and clinical manifestations of the disease were assessed. **Results.** The highest blood glucose levels were found in children aged 1–3 years (27.9 ± 2.6 mmol/L); however, glycemia levels did not correlate with the presence of “major symptoms” of type 1 diabetes, which is attributed to the polymorphic clinical presentation. It was revealed that the mean age of type 1 diabetes onset in children with a history of perinatal hypoxia was earlier (6.98 ± 0.47 years), compared to those without such history (8.98 ± 0.5 years). **Conclusions.** Type 1 diabetes in children often presents under the “masks” of acute respiratory viral infections, intestinal or genitourinary infections, leading to delayed diagnosis and the development of ketoacidosis. Adolescents have the longest period from first symptoms to laboratory confirmation of type 1 diabetes. Systematic training of outpatient physicians on the clinical and diagnostic criteria of type 1 diabetes needs to be improved.

KEYWORDS: *diabetes mellitus, children, pre-hospital stag, tactical and diagnostic measures*

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Сахарный диабет 1-го типа у детей на догоспитальном этапе. Сложности диагностики

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РЕЗЮМЕ. Введение. Общая численность пациентов с сахарным диабетом 1-го типа в возрасте до 18 лет в Российской Федерации на 31.12.2023 года составляла 61 318 человек (208 на 100 тыс. детского населения), заболеваемость — 8009 (28 на 100 тыс. детского населения). В большинстве стран, включая Россию, регистрируется нарастание заболеваемости сахарным диабетом 1-го типа в детском возрасте. Учитывая эпидемиологические показатели и социальную значимость данного заболевания, а также важность своевременной диагностики сахарного диабета у детей, проведен анализ сложностей догоспитального этапа в диагностике дебюта сахарного диабета 1-го типа. **Цель исследования** — провести анализ сложных случаев диагностики и тактики ведения детей с дебютом сахарного диабета на догоспитальном этапе оказания скорой и неотложной медицинской помощи. **Материалы и методы.** Проанализирована 121 медицинская карта детей за 2022–2023 гг. с клиническим и/или лабораторным дебютом сахарного диабета 1-го типа, госпитализированных в экстренном порядке по скорой и неотложной медицинской помощи в Клинику Санкт-Петербургского государственного педиатрического медицинского университета. Проведен анализ показателей гликемии на этапе поступления ребенка с дебютом сахарного диабета 1-го типа в стационар, рассмотрены клинические проявления заболевания. **Результаты.** Самый высокий уровень глюкозы крови выявлен у детей 1–3 лет ($27,9 \pm 2,6$ ммоль/л), при этом уровень гликемии не соотносится с наличием «больших симптомов» сахарного диабета 1-го типа, что связано с полиморфизмом клинических проявлений. Выявлено, что средний возраст дебюта сахарного диабета 1-го типа у детей с отягощенным анамнезом по перинатальной гипоксии наступал в более ранние сроки и составил $6,98 \pm 0,47$ года, возраст дебюта у детей с неотягощенным анамнезом составил $8,98 \pm 0,5$ года. **Выводы.** Сахарный диабет 1-го типа у детей часто дебютирует под «масками» ОРВИ, кишечной или мочеполовой инфекции, что приводит к поздней диагностике и развитию кетоацидоза. У подростков самый длительный период от первых симптомов до лабораторного подтверждения сахарного диабета 1-го типа. Необходимо улучшить систематическое обучение врачей амбулаторного звена клиническим и диагностическим критериям сахарного диабета 1-го типа.

КЛЮЧЕВЫЕ СЛОВА: сахарный диабет, дети, догоспитальный этап, тактико-диагностические мероприятия

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

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INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a disease resulting from autoimmune destruction of insulin-producing β -cells of the pancreas, leading to the development of absolute insulin deficiency.

According to the International Diabetes Federation (IDF) data for 2021, the total number of children and adolescents (under 19 years of age) with type 1 diabetes worldwide exceeds 1.2 million people. The total number of patients with T1DM under the age of 18 in the Russian Federation as of December 31, 2023, was 61,318 (208 per 100,000 pediatric population) [1].

Type 1 diabetes mellitus is a multifactorial disease; however, the specific mechanisms of interaction between genetic predisposition, environmental factors, and the state of the immune system underlying T1DM remain unclear. Environmental triggers (infectious, dietary, or chemical) that initiate β -cell destruction are still unknown.

Typical complaints of type 1 diabetes mellitus (T1DM) at disease onset include thirst, frequent urination with nocturnal and daytime urinary incontinence in young children, weight loss or unexplained failure to gain weight (in infants), weakness, fatigue, and recurrent skin infections, as well as inflammatory diseases of the external genital organs.

With the development of ketoacidosis, the above complaints are accompanied by dry skin and mucous membranes, the smell of acetone in the exhaled air, vomiting, impaired consciousness up to coma, and regular deep breathing with a loud inspiration and forceful expiration (Kussmaul breathing) [2, 3]. It should be noted that from the appearance of autoantibodies to the onset of clinical manifestations, several years may pass, and the symptoms are highly heterogeneous, which may lead to delayed diagnosis of T1DM at the stage of ketoacidosis development [4–6].

AIM

To analyze complex cases involving the diagnosis and management of children with newly diagnosed type 1 diabetes mellitus during the prehospital phase of emergency and urgent medical care.

Research objectives

1. To study the age structure of children at the onset of diabetes mellitus.

2. To assess the level of newly diagnosed hyperglycemia in children at the onset of diabetes mellitus depending on age.

3. To identify diagnostic difficulties in providing medical care to children with newly diagnosed diabetes mellitus at the prehospital stage.

MATERIALS AND METHODS

An analysis was performed of 121 medical records of children for the years 2022–2023 with a clinical and/or laboratory onset of type 1 diabetes mellitus (T1DM), who were urgently admitted via emergency medical services to the Clinic of the Federal State Budgetary Educational Institution of Higher Education “Saint Petersburg State Pediatric Medical University” of the Ministry of Health of the Russian Federation (SPbSPMU).

The retrospective analysis of medical histories included the assessment of initial and final diagnoses, the age of hospitalized children, the duration from the detection of clinical and/or laboratory signs of T1DM to hospitalization, as well as the level of hyperglycemia, and the nature of diagnostic and therapeutic measures at the prehospital stage.

For statistical processing, mean values and standard deviations of quantitative indicators were calculated ($M \pm m$), intergroup differences were assessed using Student's t-test, and a probability of error of less than 5% ($p \leq 0.05$) was considered statistically significant.

RESULTS AND DISCUSSION

All patients were divided into groups according to age: from 1 to 3 years ($n=17$), from 4 to 7 years ($n=33$), from 8 to 12 years ($n=41$), from 13 to 17 years ($n=30$). The mean age of the children was 8.93 ± 0.39 years, including 62 boys and 59 girls (Fig. 1).

When analyzing differences between age groups in relation to sex distribution, no statistically significant differences were found ($p > 0.05$).

The reasons for emergency hospitalization at the onset of type 1 diabetes mellitus in children were clinical manifestations and/or detected laboratory abnormalities – hyperglycemia and/or glucosuria.

Complaints of children and/or parents regarding the child's health were classified as follows: “major symptoms of diabetes mellitus” – polyuria, polydipsia, and weight loss – in 85.9% of cases ($n=104$), as well as dry mouth, lethargy, and

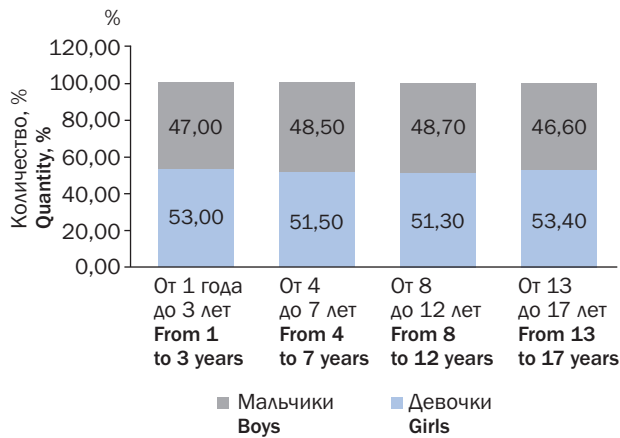


Fig. 1. The ratio of boys and girls with type I diabetes onset in different age groups in the study (the figure is prepared by the authors using their own data)

Рис. 1. Соотношение мальчиков и девочек с дебютом сахарного диабета 1-го типа в различных возрастных группах (рисунок подготовлен авторами по собственным данным)

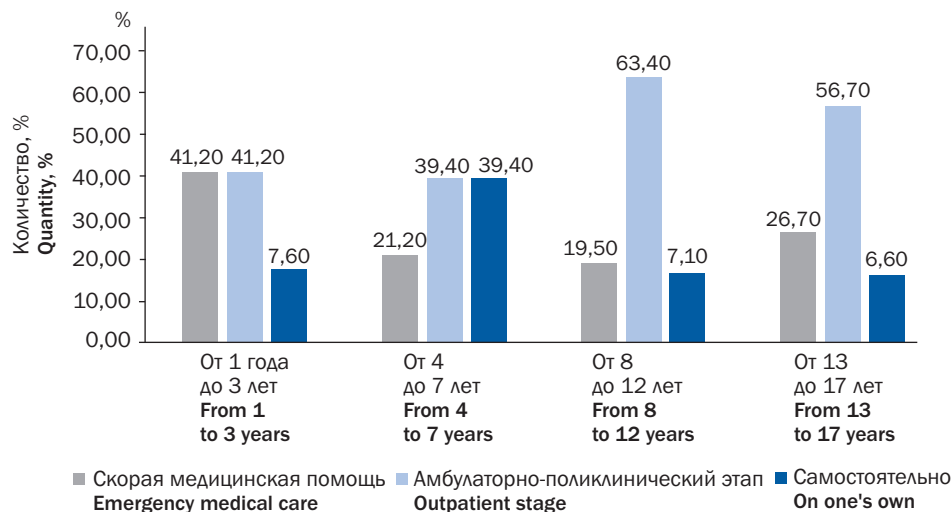


Fig. 2. The number of cases of hyperglycemia detection during the onset of type I diabetes in children at various stages of medical care and during self-admission to the hospital (the figure is prepared by the authors using their own data)

Рис. 2. Количество случаев выявления гипергликемии при дебюте сахарного диабета 1-го типа у детей на различных этапах оказания медицинской помощи и при самостоятельном обращении в стационар (рисунок подготовлен авторами по собственным данным)

drowsiness in 14.8% (n=18), nausea and vomiting in 12.4% (n=15), urinary disturbances (dysuria, nocturia, enuresis) in 6.7% of cases (n=8), abdominal pain in 5.8% (n=7), and less frequently headache and dizziness (n=3), acetone odor from the mouth (n=2), and oral candidiasis (n=1).

Hyperglycemia was initially detected at the primary care setting, at the stage of emergency medical care, and during self-referral (Fig. 2).

In children aged 1 to 3 years, hyperglycemia was more often detected during emergency medical care or at the primary care setting. In the group of children aged 4 to 7 years, hyperglycemia was also predominantly detected at the primary care setting or by parents themselves. Among children aged 8 years and older, hyperglycemia was most frequently detected at the primary care setting.

It was found that blood glucose levels at the onset of type 1 diabetes mellitus in children varied depending on age: in the 1–3 years group, higher values were observed – 27.9 ± 2.6 mmol/L; in older age groups, lower values were recorded: in children aged 4–7 years – 19.77 ± 1.65 mmol/L, 8–12 years – 21.34 ± 1.53 mmol/L, and 13–17 years – 20.3 ± 1.44 mmol/L ($p \leq 0.05$). This is most likely related to the absence of specific complaints in the child, as well as the inability to clearly articulate them due to younger age.

The duration from the onset of initial symptoms to laboratory confirmation of existing hyperglycemia or glucosuria was 16.5 ± 3.78 days in the 1–3 years group, 16.53 ± 2.9 days in the 4–7 years group, 19.05 ± 2.37 days in the 8–12 years group, and 28.29 ± 5.2 days in the 13–17 years group ($p > 0.05$).

Table 1. Analysis of blood glucose levels in children with various clinical manifestations at the onset of diabetes mellitus**Таблица 1.** Анализ уровня глюкозы крови у детей с различными клиническими проявлениями при дебюте сахарного диабета

Уровень глюкозы крови, ммоль/л Blood glucose level, mmol/l	Возраст детей Age of children			
	1–3 года 1–3 years	4–7 лет 4–7 years	8–12 лет 8–12 years	13–17 лет 13–17 years
Имели «большие симптомы сахарного диабета», уровень гликемии Had “major symptoms of diabetes mellitus”, glycemic level	27,50±2,84	19,84±1,67	22,72±1,75	20,28±6,43
Не имели «больших симптомов сахарного диабета», уровень гликемии Did not have “major symptoms of diabetes mellitus”, glycemic levels	29,93±6,43	10,85±1,70	14,13±2,99	12,56±4,37

The table is based on data from the authors' own research

Таблица составлена по данным собственного исследования авторов

A comparative analysis of glycemia levels was performed in children with “major symptoms of diabetes mellitus” and in children without corresponding specific symptoms of T1DM (Table 1).

The results show that in children under 3 years of age, glycemia levels do not correlate with the presence of “major symptoms” of T1DM, which is associated with difficulties in timely diagnosis of diabetes mellitus in this age group.

Among all analyzed medical records of children with newly diagnosed type 1 diabetes mellitus, half had a complicated medical history in the form of perinatal hypoxia during the prenatal development period. It was found that the mean age of T1DM onset in children with a history of perinatal hypoxia occurred earlier and was 6.98 ± 0.47 years, whereas in children without such a history the age of onset was 8.98 ± 0.5 years ($p \leq 0.05$).

Notably, 74% of children were admitted to the hospital in a state of diabetic ketoacidosis (mild or moderate severity) (mild – 15%). Such a high rate of ketoacidosis, according to the analysis of medical documentation, was associated with several reasons.

1. Lack of clinical suspicion for T1DM due to the polymorphism of clinical manifestations (differential diagnosis of the causes of existing complaints was performed, including infectious causes in cases of abdominal pain, vomiting, weakness, and headache in the child; urinary tract infection was also excluded).

2. Delayed presentation of the child's legal guardians for medical care (attempts at self-treatment).

3. In many cases, at the outpatient stage, after detection of glucosuria or moderate hyperglycemia, further confirmatory investigations were performed in the outpatient setting instead of hospitalizing the child.

CONCLUSION

Currently, it is known that several years may pass from the appearance of autoantibodies to the clinical manifestation of type 1 diabetes mellitus. At the same time, the symptoms of the disease are highly heterogeneous and may be masked by different “clinical disguises”: from signs of acute respiratory or intestinal infection to manifestations of the genitourinary system, which at the initial diagnostic stage may lead to delayed verification of T1DM at the stage of developing ketoacidosis. In addition, a trend toward a younger age of diabetes onset is observed, including the first years of life. Infants and preschool children are unable to clearly formulate their complaints due to age-related features (emotional lability, difficulties in verbal communication, use of diapers), and their apparent well-being may mislead both parents and outpatient clinicians, preventing adequate and timely assessment of the child's condition severity. All these factors lead to delayed diagnosis of T1DM in this group of children, with pronounced hyperglycemia and ketoacidosis. Adolescents, in turn, often conceal their complaints from relatives, which is associated with the longest interval between the onset of initial symptoms and laboratory confirmation of T1DM in this age group.

Considering all of the above, in order to ensure timely diagnosis of diabetes mellitus, systematic training of outpatient healthcare personnel is required regarding the clinical presentation and diagnosis of diabetes mellitus. It is necessary to consider expanding the indications for emergency bedside glucometry at the prehospital stage in a number of cases, in addition to the detection of typical clinical symptoms of diabetes mellitus, in diagnostically unclear or doubtful situations: fever without obvious catarrhal symptoms, emotional lability in young children, sudden or progressive lethargy, altered level of consciousness, seizure syndrome, abdominal pain, vomiting, candidal lesions of the oral mucosa, pruritus of the skin or mucous membranes, complaints of headache, presence of dysuria/nocturia/enuresis, as well as in cases of dyspnea or noisy breathing. If laboratory abnormalities are detected – hyperglycemia, glucosuria, or ketonuria – hospital admission of the child to an endocrinology department is recommended.

It is also necessary to inform the population about socially significant diseases, including type 1 diabetes mellitus, through the placement of public awareness campaigns. A high level of awareness regarding this disease will help reduce the rate of complications, including severe ketoacidosis at the stage of T1DM diagnosis.

ADDITIONAL INFORMATION

Authors' contribution. I.Yu. Melnikova – analysis and writing of the article; D.I. Shaytor,

A.V. Emelyanova, O.L. Yezhova, Yu.A. Demchuk – collection of material for writing the article; V.M. Shaytor – analysis and writing of the article; K.V. Skobeleva – preparation of graphic materials; A.V. Yakovlev – analysis of the material.

All authors contributed, read and approved the final version before publication.

Competing interests. The authors declare that they have no competing interests.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. И.Ю. Мельникова – анализ и написание статьи; Д.И. Шайтор, А.В. Емельянова, О.Л. Ежова, Ю.А. Демчук – сбор материала для написания статьи; В.М. Шайтор – анализ и написание статьи; К.В. Скобелева – подготовка графических материалов; А.В. Яковлев – анализ материала.

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