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CONGENITAL METABOLIC AND ENDOCRINE DISORDERS IN INFANTS HOSPITALIZED IN CRITICAL CONDITION

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Abstract

Congenital metabolic and endocrine disorders, many of which are inherited, are characterized by disturbances in biochemical pathways and, when not diagnosed early, may lead to life-threatening metabolic decompensation. The limited implementation of neonatal screening programs may result in delayed diagnosis of these conditions and the development of critical illness. The aim of this study was to analyze the structure and clinical characteristics of metabolic and endocrine disorders identified in children under one year of age admitted to the intensive care unit in critical condition.

Retrospective and prospective data of 1,256 patients under one year of age admitted to the intensive care unit in critical condition and diagnosed with congenital anomalies during the period 2019–2022 were analyzed. Among these patients, congenital metabolic and endocrine disorders were confirmed in 90 cases (7.2%). These disorders were most frequently detected in the age group of 29 days to 6 months (52.2%). Boys constituted 65.6% of the patients. In 80% of cases, the diagnosis was established in the intensive care unit. Among metabolic and endocrine disorders, cystic fibrosis (31.1%), glucose-6-phosphate dehydrogenase deficiency (25.5%), congenital hypothyroidism (14.4%), and congenital adrenal hyperplasia (6.7%) predominated. The mortality rate was 15.6%.

Metabolic and endocrine disorders, if not diagnosed early, may lead to the development of critical illness during infancy and are associated with a high risk of mortality. Expansion of neonatal screening programs and improvement of early laboratory diagnostic capabilities may play a crucial role in reducing hospitalizations due to metabolic decompensation and lowering mortality risk.

Keywords: congenital metabolic and endocrine diseases; neonatal screening; critical condition.

INTRODUCTION

According to the classification of the World Health Organization, congenital anomalies are divided into two main groups: structural and functional defects. Congenital metabolic and endocrine diseases, many of which are inherited, represent a group of functional anomalies and are considered one of the major causes of life-threatening clinical conditions in early childhood.

According to various epidemiological studies, the overall incidence of congenital metabolic disorders, many of which are inherited, is estimated to be approximately 50.9 per 100,000 live births (approximately

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one case per 2,000 newborns) [1]. Epidemiological data indicate that the prevalence of inherited metabolic disorders, a subset of congenital metabolic diseases, varies by type: amino acid disorders occur in approximately 1 in 8,257 newborns, organic acidemias in 1 in 18,165, and fatty acid oxidation defects in about 1 in 7,569 newborns [2]. The implementation of early neonatal screening programs plays a crucial role in the timely detection of these diseases.

Inherited metabolic disorders, a subset of congenital metabolic conditions, are characterized by defects in multiple biochemical pathways and comprise a broad and heterogeneous nosological spectrum. These conditions include disorders of amino acid metabolism (phenylketonuria, maple syrup urine disease, tyrosinemia, and homocystinuria), carbohydrate metabolism disorders (glycogen storage diseases, galactosemia, fructose intolerance, and fructose-1,6-bisphosphatase deficiency), congenital disorders of protein glycosylation, lysosomal storage diseases, mucopolysaccharidoses, oligosaccharidosis, sphingolipidoses, mitochondrial diseases, peroxisomal enzyme deficiencies, and carnitine transport defects [3]. These pathologies may affect multiple organs and systems and can lead to severe metabolic decompensation at an early stage of life.

In Azerbaijan, the lack of full implementation of expanded neonatal screening programs for metabolic disorders—particularly the absence of systematic mass screening using the heel-prick blood test—often leads to delayed diagnosis of these conditions. As a result, a significant proportion of patients are admitted to intensive care units later in life in critical condition due to metabolic decompensation. Systematic national statistical data on this issue remain limited. However, a report presented by UNICEF indicates noticeable fluctuations in the indicators of endocrine system diseases, metabolic disorders, and nutritional disorders among children aged 0–13 years during the period of 2017–2022, highlighting the growing relevance of metabolic health problems [4]. These findings emphasize the importance of studying the causes of hospitalizations associated with metabolic decompensation and the need for early diagnosis.

The aim of this study was to analyze metabolic disorders detected in children under one year of age admitted to the intensive care unit in critical condition, based on retrospective and prospective data during the period 2019–2022.

MATERIAL AND METHODS

Retrospective and prospective data of 1,256 patients under one year of age admitted to the intensive care unit in critical condition and diagnosed with congenital anomalies between 2019 and 2022 were analyzed. Among the studied cohort, congenital metabolic and endocrine disorders were confirmed in 90 patients (7.2%), and the present study was based on the analysis of these cases.

RESULTS

Congenital metabolic and endocrine disorders were confirmed in 90 patients (7.2%).

The distribution of these disorders according to age at diagnosis showed that 30 cases (33.3%) were identified within the first 28 days of life, 47 cases (52.2%) between 29 days and 6 months, and 13 cases (14.4%) between 6 and 12 months of age ($P\chi^2 < 0.001$). The mean age at admission to the intensive care unit was 48 days (range: 18–116 days).

According to gestational age, 21 patients (23.3%) were born prematurely, while 69 patients (76.7%) were born at term. In terms of sex distribution, males predominated, accounting for 59 cases (65.6%), while females constituted 31 cases (34.4%) ($P\chi^2 = 0.426$).

Analysis of the causes of admission to the intensive care unit showed that 54 patients (60%) were hospitalized for reasons unrelated to the underlying metabolic and endocrine disorders, 32 patients (35.6%) were admitted due to complications associated with these conditions, and 4 patients (4.4%) were hospitalized with suspected congenital anomalies. Regarding the location of diagnosis, these disorders were identified in 18 patients (20%) in maternity hospitals, whereas in 72 patients (80%) the diagnosis was established in the intensive care unit.

Table 1. Structure of metabolic and endocrine disorders identified in the study (n = 90).

Metabolic disorder	N	%
Cystic fibrosis	28	31.1
Glucose-6-phosphate dehydrogenase deficiency	23	25.5
Congenital hypothyroidism	13	14.4
Congenital adrenal hyperplasia	6	6.7
Other metabolic disorders	20	22.3

Analysis of the nosological structure of functional anomalies demonstrated that cystic fibrosis was identified in 28 patients (31.1%), glucose-6-phosphate dehydrogenase deficiency in 23 patients (25.5%), congenital hypothyroidism in 13 patients (14.4%), congenital adrenal hyperplasia in 6 patients (6.7%), and other metabolic disorders in the remaining cases. Compared with the practically healthy control group, these indicators were statistically significantly higher ($P_U < 0.001$) (Table 1). In some cases, extended metabolic investigations could not be performed due to the severity of the clinical condition or technical limitations. In addition, rare pathologies were combined under the category of “other metabolic disorders” in order to ensure statistical reliability.

According to the structural characteristics of the anomalies, isolated metabolic and endocrine disorders were observed in 68 patients, whereas a combination of structural anomalies and metabolic and endocrine disorders was identified in 22 patients. Among the associated structural anomalies, congenital heart defects were detected in 12 patients (13.3%), digestive system anomalies in 8 patients (8.9%), nervous system anomalies in 3 patients (3.3%), and syndromic conditions, including Down syndrome, in 3 patients (3.3%).

The mean duration of stay in the intensive care unit was 8 days ($p = 0.303$). Among patients with metabolic and endocrine disorders, mortality was observed in 14 cases (15.6%) ($P\chi^2 = 0.594$).

Most cases were of metabolic origin and were associated with clinical manifestations such as neurological impairment, metabolic decompensation, and signs of multiple organ dysfunction at the time of admission.

DISCUSSION

Congenital metabolic and endocrine disorders, many of which are inherited, when not diagnosed at an early stage, are

often accompanied by life-threatening episodes of metabolic decompensation and represent a significant cause of hospitalization in critical condition. Neonatal screening programs play a crucial role in the early detection of these disorders. Heel-prick blood screening in newborns is considered the primary method for initial diagnosis; however, the composition of screening panels varies between countries. In suspected cases, diagnostic confirmation may require a range of laboratory investigations, including blood glucose, serum ammonia, acid–base balance, electrolytes, lactate, liver function tests, serum amino acids, tandem mass spectrometry, carnitine levels, acylcarnitine profile, and urinary organic acids.

Patients with metabolic disorders have been reported to have an increased risk of mortality, particularly during the neonatal period, when metabolic decompensation and multiple organ dysfunction are most likely to occur. However, only a proportion of deaths are directly attributable to the underlying metabolic disorder.

According to national data, congenital anomalies account for a substantial proportion of intensive care admissions, among which metabolic diseases represent approximately 7.2% of cases.

The results of the present study demonstrated that congenital metabolic and endocrine disorders were identified in 7.2% of children under one year of age admitted to the intensive care unit in critical condition. The fact that more than half of the cases were detected within the first six months of life indicates that these disorders frequently manifest with early clinical decompensation. The observation that a considerable proportion of patients were initially hospitalized for reasons unrelated to congenital anomalies but were subsequently diagnosed with metabolic disorders highlights the non-specific clinical presentation and associated diagnostic challenges.

In the present study, 80% of diagnoses were established in the intensive care unit, reflecting limited availability of early screening and primary diagnostic capabilities. This finding suggests that critical conditions often develop as a consequence of delayed detection and underscores the importance of expanding neonatal screening programs.

Among metabolic and endocrine disorders, cystic fibrosis, glucose-6-phosphate dehydrogenase deficiency, congenital hypothyroidism, and congenital adrenal hyperplasia were the most prevalent conditions. In some cases, etiological clarification remained incomplete due to limited diagnostic resources. The association of these conditions with neurological impairment, metabolic acidosis, hypoglycemia, and multiple organ dysfunction requiring intensive care is consistent with previously reported findings. The mortality rate of 15.6% observed in the present study confirms that metabolic and endocrine disorders are associated with a high risk of adverse outcomes. Compared with previously reported data, these findings further emphasize the importance of intensive care management in this patient population.

CONCLUSION

The present study demonstrated that congenital metabolic and endocrine disorders constitute a significant proportion of cases among children under one year of age admitted to the intensive care unit in critical condition. The predominance of early clinical manifestations highlights the critical importance of timely diagnosis. The fact that the majority of diagnoses were established in the intensive care unit indicates the insufficient implementation of

neonatal screening programs and early diagnostic strategies. The non-specific clinical presentation contributes to delayed recognition and the development of critical conditions.

Expansion of neonatal screening programs, improvement of early diagnostic capabilities, and implementation of a multidisciplinary approach are essential for reducing morbidity and mortality in this patient population.

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KRITIK VƏZIYYƏTDƏ HOSPITALIZASIYA OLUNAN KÖRPƏLƏRDƏ ANADANGƏLMƏ METABOLIK VƏ ENDOKRIN POZĞUNLUQLAR

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Xülasə

Anadangəlmə metabolik və endokrin pozğunluqların əksəriyyəti irsi xarakter daşıyır, biokimyəvi metabolik yolların pozğunluğu ilə xarakterizə olunur və erkən diaqnostika olunmadıqda həyati təhlükə yaradan metabolik dekompensasiya ilə nəticələnə bilər. Neonatal skrininq proqramlarının məhdud tətbiqi bu patologiyaların gec diaqnostikasına və kritik vəziyyətlərin inkişafına səbəb ola bilər. Tədqiqatın məqsədi kritik vəziyyətdə reanimasiya şöbəsinə qəbul edilən 1 yaşadək uşaqlarda aşkar olunan metabolik və endokrin pozğunluqların strukturunu və klinik xüsusiyyətlərini təhlil etmək olmuşdur.

2019–2022-ci illər ərzində kritik vəziyyətdə reanimasiya şöbəsinə qəbul edilmiş və anadangəlmə anomaliya diaqnozu qoyulmuş 1 yaşadək 1256 xəstənin retrospektiv və prospektiv məlumatları təhlil edilmişdir. Bu xəstələrin 90-da (7,2%) anadangəlmə metabolik və endokrin pozğunluqlar təsdiqlənmişdir. Bu pozğunluqlar ən çox 29 gün–6 ay yaş intervalında aşkarlanmışdır (52,2%). Xəstələrin 65,6%-ni oğlanlar təşkil etmişdir. Halların 80%-də diaqnoz reanimasiya şöbəsində qoyulmuşdur. Metabolik və endokrin pozğunluqlar arasında kistik fibroz (31,1%), qlükoza-6-fosfatdehidrogenaza çatışmazlığı (25,5%), anadangəlmə hipotireoz (14,4%) və anadangəlmə adrenal hiperplaziya (6,7%) üstünlük təşkil etmişdir. Letallıq göstəricisi 15,6% olmuşdur.

Metabolik və endokrin pozğunluqlar erkən diaqnostika olunmadıqda südəmər dövrdə kritik vəziyyətlərin inkişafına və yüksək ölüm riskinə səbəb ola bilər. Neonatal skrininq proqramlarının genişləndirilməsi və erkən laborator diaqnostika imkanlarının artırılması metabolik dekompensasiya ilə əlaqədar hospitalizasiya və ölüm riskinin azaldılmasında mühüm rol oynaya bilər.

Açar sözlər: anadangəlmə metabolik və endokrin xəstəliklər; neonatal skrininq; kritik vəziyyət.

ВРОЖДЕННЫЕ МЕТАБОЛИЧЕСКИЕ И ЭНДОКРИННЫЕ НАРУШЕНИЯ У ДЕТЕЙ, ГОСПИТАЛИЗИРОВАННЫХ В КРИТИЧЕСКОМ СОСТОЯНИИ

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Резюме

Врожденные метаболические и эндокринные нарушения, многие из которых имеют наследственную природу, характеризуются нарушениями биохимических путей и при отсутствии ранней диагностики могут приводить к жизнеугрожающей метаболической декомпенсации. Ограниченное внедрение программ неонатального скрининга может способствовать поздней диагностике данных состояний и развитию критических состояний.

Целью настоящего исследования явился анализ структуры и клинических характеристик метаболических и эндокринных нарушений, выявленных у детей в возрасте до одного года, госпитализированных в отделение интенсивной терапии в критическом состоянии.

Проведен ретроспективный и проспективный анализ данных 1256 пациентов в возрасте до одного года, госпитализированных в отделение интенсивной терапии в критическом состоянии с диагнозом врожденной аномалии в период 2019–2022 гг. У 90 пациентов (7,2%) были подтверждены врожденные метаболические и эндокринные нарушения. Наиболее часто данные нарушения выявлялись в возрастной группе от 29 дней до 6 месяцев (52,2%). Мальчики составили 65,6% пациентов. В 80% случаев диагноз был установлен в отделении интенсивной терапии. Среди метаболических и эндокринных нарушений преобладали муковисцидоз (31,1%), дефицит глюкозо-6-фосфатдегидрогеназы (25,5%), врожденный гипотиреоз (14,4%) и врожденная гиперплазия надпочечников (6,7%). Показатель летальности составил 15,6%.

Метаболические и эндокринные нарушения при отсутствии ранней диагностики могут приводить к развитию критических состояний в грудном возрасте и ассоциированы с высоким риском летального исхода. Расширение программ неонатального скрининга и совершенствование возможностей ранней лабораторной диагностики могут сыграть ключевую роль в снижении частоты госпитализаций, обусловленных метаболической декомпенсацией, и уменьшении уровня летальности.

Ключевые слова: врожденные метаболические и эндокринные заболевания; неонатальный скрининг; критическое состояние.