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CHARACTERISTICS OF POST-COVID SYNDROME IN CHILDREN

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Abstract: This article presents information on the neurological features of children in the post-COVID period. Post-COVID syndrome (PCS) is a symptom complex that occurs during and after COVID-19, lasting more than 12 weeks, and is not the result of another disease. Clinical manifestations of PCS are diverse, and under their mask, either the debut or exacerbation of chronic organic pathology triggered by the virus may be hidden. PCS is a diagnosis of exclusion. The main manifestations of PCS include: autonomic dysregulation, cognitive and psycho-emotional disorders, and impairments of the respiratory, cardiovascular, and digestive systems. The direct pathogenetic factors of the main neurological manifestations of PCS are persistent cerebral hypoperfusion, hypoxia, and hypoxemia, which lead to energy deficits in neuronal structures, metabolic disturbances, as well as virus-induced structural damage to cortical neurons and subcortical structures of the brain.

Keywords: COVID-19, SARS-CoV-2, PCS, hypoxia, neuron

БАЛАЛАРДАҒЫ ПОСТКОВИДТІК СИНДРОМНЫҢ СИПАТТАМАСЫ

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Аңдатпа: Осы мақалада балалардағы постковидтік кезеңнің неврологиялық ерекшеліктері туралы мәліметтер ұсынылады. Постковидтік синдром (ПКС) – COVID-19 індеті кезінде немесе одан кейін пайда болып, 12 аптадан астам уақытқа созылатын, басқа аурулармен түсіндірілмейтін симптомдар кешені. ПКС-тің клиникалық көріністері алуан түрлі, олардың астарында вирустың триггерлік әсерінен туындаған созылмалы органикалық патологияның дебюті немесе өршуі жасырынуы мүмкін. ПКС – бұл басқа патологияны жоққа шығару арқылы қойылатын диагноз. ПКС-тің негізгі көріністеріне вегетативтік дисрегуляция, когнитивтік және психоэмоционалдық бұзылыстар, тыныс алу, жүрек-қантамыр және ас қорыту жүйелері тарапынан болатын өзгерістер жатады. ПКС-тің негізгі неврологиялық симптомдарының патогенетикалық факторларының бірі – ұзақ сақталатын ми гипоперфузиясы, гипоксия және гипоксемия. Бұл өзгерістер нейрондық құрылымдардың энергия тапшылығына, метаболизмнің бұзылыстарына, сондай-ақ вирус туындатқан ми қыртысы мен қыртысасты құрылымдарындағы нейрондардың құрылымдық зақымдануына әкеледі.

Түйін сөздер: COVID-19, SARS-CoV-2, постковидтік синдром, гипоксия, нейрон.

ХАРАКТЕРИСТИКА ПОСТКОВИДНОГО СИНДРОМА У ДЕТЕЙ

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Аннотация: В данной статье представлены сведения о неврологических особенностях в постковидном периоде у детей. Постковидный синдром (ПКС) – симптомокомплекс, имеющий место во время и после COVID-19 продолжительностью более 12 нед, не являющийся результатом другого заболевания. Клинические проявления ПКС многолики, и под их маской могут быть скрыты дебют либо обострение хронической органической патологии, триггером которой явился вирус. ПКС – диагноз исключения. Основные проявления ПКС: вегетативная дисрегуляция, когнитивные и психоэмоциональные расстройства, нарушения со стороны респираторной, сердечно-сосудистой, пищеварительной систем. Непосредственными патогенетическими факторами основных неврологических проявлений ПКС являются сохраняющиеся гипоперфузия мозга, гипоксия и гипоксемия, влекущие за собой энергодефицит нейрональных структур, нарушения метаболизма, а также индуцированное вирусом структурное повреждение нейронов коры и подкорковых структур головного мозга.

Ключевые слова: COVID-19, SARS-CoV-2, постковидный синдром, гипоксия, нейрон.

Introduction

Currently, the entire global community is focused on one common problem—the spread of the novel coronavirus infection, COVID-19. The coronavirus has affected not only adults but also children, showing high aggressiveness and causing serious neurological complications [1]. In severe acute respiratory syndrome caused by SARS-CoV-2, neurological and psychiatric complaints are widespread and often occur both during the acute phase of the disease and in the recovery period [2]. Post-COVID syndrome (PCS) is a set of symptoms that arise during COVID-19 and after it, persist for more than 12 weeks, and are not associated with other diseases. The clinical manifestations of post-COVID syndrome are diverse; under their influence, the development or exacerbation of chronic organic pathology triggered by the virus is possible. The main manifestations of post-COVID syndrome include autonomic dysregulation, cognitive and psycho-emotional disorders, as well as dysfunctions of the respiratory, cardiovascular, and digestive systems [3]. The key pathogenetic factors of the neurological manifestations of post-COVID syndrome are persistent cerebral hypoperfusion, hypoxia, and hypoxemia, which lead to an energy deficit in neuronal structures, metabolic disturbances, and virus-induced structural damage to cortical neurons and subcortical brain structures [4].

Despite the relatively low prevalence of acute COVID-19 in children, it has been established that SARS-CoV-2 infection primarily causes two long-term effects. The first is multisystem inflammatory syndrome in children (MIS-C), temporarily associated with SARS-CoV-2, which is an immune-mediated condition. It occurs in a small percentage of children (approximately 0.1%) and develops 2–6 weeks after a SARS-CoV-2 infection [5].

The second is the so-called “long COVID,” also known as post-COVID syndrome or the long-term consequences of SARS-CoV-2 infection. These terms refer to symptoms that persist after recovering from COVID-19. However, it has been found that they mainly affect the emotional, neurological, and cardiopulmonary systems, as well as the mental health of patients. In addition to respiratory illnesses, COVID-19 in children is associated with various neurological

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disorders, including headache, encephalopathy, and multisystem inflammatory syndrome [6]. Furthermore, severe neurological conditions have been observed in children, such as encephalitis, epilepsy, dysgeusia or ageusia, aseptic meningitis, stroke, dysarthria, dysphagia, cerebellar ataxia, hypotonia, drowsiness, coma, and peripheral neuropathy [7].

Objective of the study: To investigate the characteristics of post-COVID syndrome in children.

Materials and Methods: The study included 100 children aged 8 to 17 years who received treatment at the Specialized Multidisciplinary Infectious Diseases Hospital in the Zangiata District of Tashkent Region during the period from 2021 to 2023. Clinical-neurological examinations, neuropsychological tests, biochemical analyses, and statistical research methods were used in the study.

To identify post-COVID conditions among children, a survey was conducted involving 100 patients. It was found that the novel coronavirus infection occurred significantly more often in children aged 8 to 17 years (55%). The average age of the patients was 8.7 ± 4.6 years (95% CI: 7.8–9.7). A comparison of age groups showed that the highest number of hospitalizations occurred in children aged 4–7 years (31%) and 8–12 years (29%) ($p < 0.01$).

Among the respondents, 69% reported complaints related to various organs and systems. The most frequent were disorders of the central nervous system — in 71.9% of children — and gastrointestinal disturbances — in 37.7%. Nearly one-quarter of patients exhibited cardiovascular and respiratory system disorders, 30.4% experienced thermoregulation issues, and 8.7% had skin pathologies (Fig. 1).

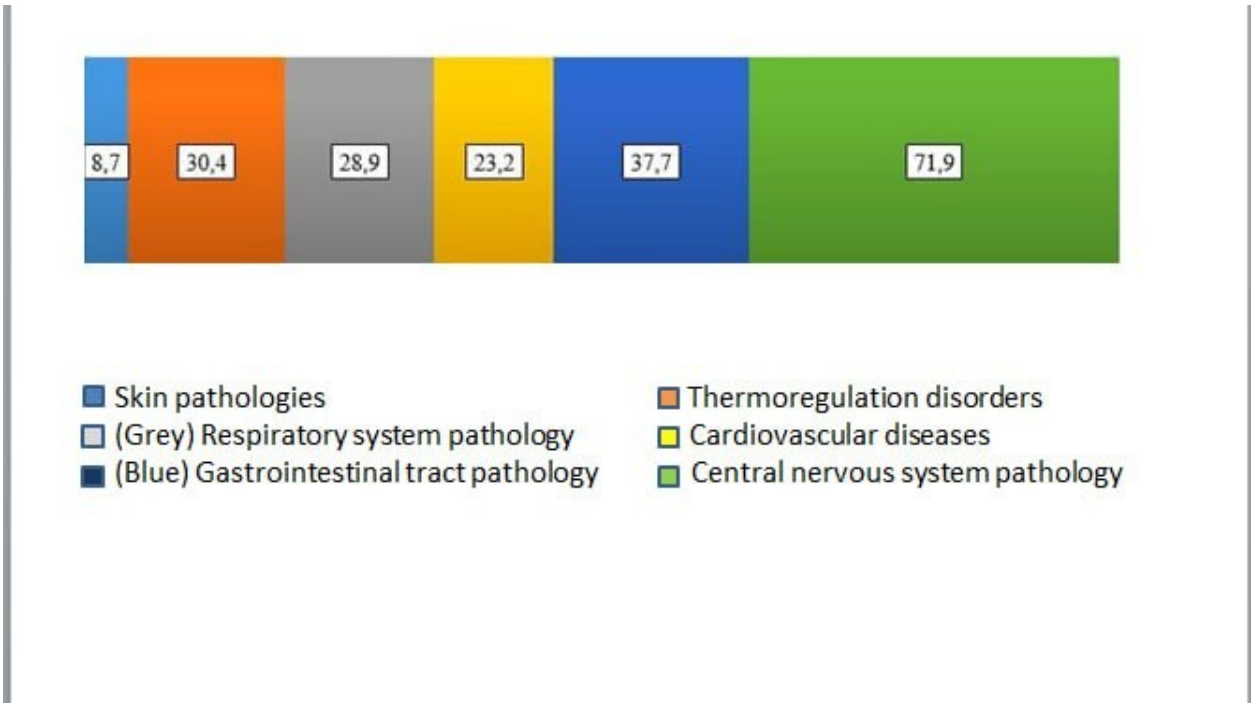

Figure 1. Post-COVID diseases of various organs and systems

In the post-COVID period, children experienced psycho-emotional disorders such as general fatigue, weakness, drowsiness, increasing anxiety, and lowered mood. Some children after recovering from COVID-19 also showed impairments in smell and taste, as well as complaints of headaches (Table 1).

Age-related complaints in children who had COVID-19

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Symptoms:	Up to 12 months	1–3 years	4–7 years	8–12 years	13–18 years	p
Weakness	4 (100,0)	10(100,0)	31(100,0)	28 (96,6)	25 (96,2)	0,794
Cough	0 (0,0)	0 (0,0)	12 (38,7)	21 (72,4)	20 (76,9)	<0,001
Headache	0 (0,0)	1 (10,0)	1 (3,2)	3 (10,3)	3 (11,5)	0.732
Anosmia (loss of smell)	3 (0,0)	2 (20,0)	6 (19,4)	8 (27,6)	6 (23,1)	0,188
Abdominal pain	0 (0,0)	2 (20,0)	0 (0,0)	3 (10,3)	2 (7,7)	0.219
Diarrhea	0 (0,0)	2 (20,0)	3 (9,7)	4 (13,8)	3 (11,5)	0,844
Runny nose	0 (0,0)	2 (20,0)	6 (19,4)	8 (27,6)	5 (19,2)	0,749
Sore throat	0 (0,0)	0 (0,0)	2 (6,5)	0 (0,0)	1 (3,8)	0,616
Shortness of breath	0 (0,0)	2 (20,0)	1 (3,2)	3 (10,3)	4 (15,4)	0,409
Nausea / vomiting	0 (0,0)	0 (0,0)	2 (6,5)	4 (13,8)	2 (7,7)	0,619
Dizziness	0 (0,0)	0 (0,0)	0 (0,0)	2 (6,9)	2 (7,7)	0.488
Myalgia (muscle pain)	0 (0,0)	0 (0,0)	0 (0,0)	1 (3,4)	0 (0,0)	0,649
Ageusia (loss of taste)	0 (0,0)	0 (0,0)	0 (0,0)	1 (3,4)	2 (7,7)	0,497
Increased sweating	0 (0,0)	2 (20,0)	6 (19,4)	2 (6,9)	3 (11,5)	0,534
Loss of appetite	2 (50,0)	7 (70,0)	26 (83,9)	23 (79,3)	19 (73,1)	0,547
Anxiety	1 (25,0)	2 (20,0)	5 (16,1)	4 (13,8)	4 (15,4)	0,976
Fever	3 (75,0)	9 (90,0)	26 (83,9)	26 (89,7)	23 (88,5)	0,896

As shown in the figure, in children after COVID-19, abnormalities of the central nervous system most often manifested as general fatigue (39.1%), drowsiness (29%), cognitive impairments (27.5%), as well as psycho-emotional changes — irritability (23.2%) and decreased mood (15.9%).

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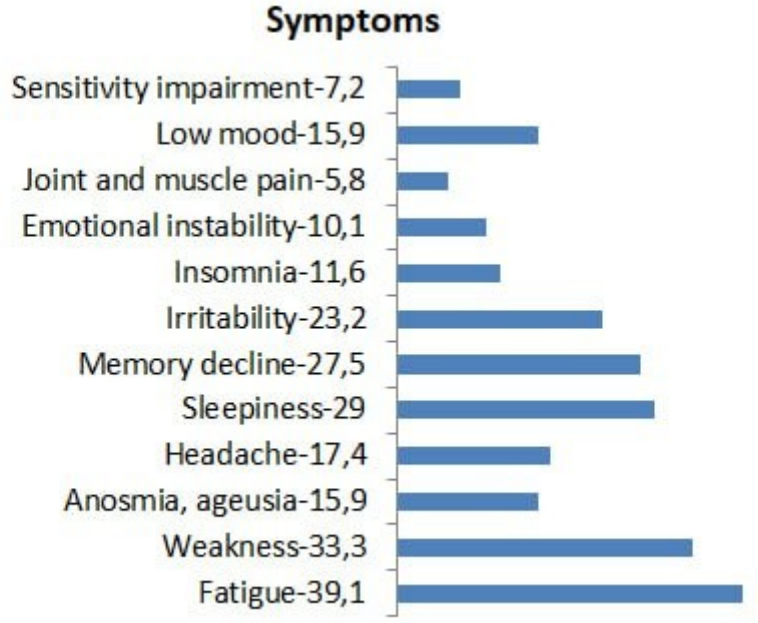

Fig. 2. Major neurological disorders in children with post-COVID complications.

In some children after recovering from COVID-19, disturbances of smell and taste perception persisted (15.9%), and 17.4% complained of headaches (see Fig. 2).

To determine whether the SARS-CoV-2 pathogen has a direct impact on the psycho-emotional and cognitive state of children, we analyzed the data using the Spielberger–Khanin Anxiety Inventory and the Montreal Cognitive Assessment (MoCA).

To assess the cognitive domain, the Montreal Cognitive Assessment (MoCA) was used - a screening method for mild cognitive impairment. Using this method, various cognitive abilities of children were evaluated during the study. This assessment covers such important aspects as attention, executive functions, memory, speech, visuospatial perception, logical thinking, calculation, and orientation.

The methodology includes 10 separate sections, with points calculated depending on the successful completion of the proposed tasks. The maximum possible score is 30. A score of 26 and above is considered sufficient to indicate the absence of cognitive impairments.

To assess the psycho-emotional state of school-aged children, the Spielberger–Hanin method was used. This method is widely applied in clinical practice and has proven its effectiveness. It allows the study of anxiety in two dimensions:

- as a stable personality trait,
- and as a temporary, situational (reactive) state.

The questionnaire consists of two parts, each containing 20 questions. For each question, four response options are offered:

1 - No, this is not true
2 - Possibly yes
3 - True
4 - Completely true

Scoring was carried out using a key by summing the points corresponding to the selected responses. Data interpretation was performed according to the established anxiety scale:

Low level - up to 30 points
Medium level - 31–44 points
High level - above 45 points

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To identify the characteristics of the psycho-emotional and cognitive spheres in the structure of post-COVID syndrome, two groups of children over 8 years old were formed:

- Group I-A — children with central nervous system (CNS) disorders
- Group I-B — children without CNS disorders in the post-COVID period

Results of anxiety assessment revealed significant differences depending on the presence of post-COVID manifestations ($p<0.001$ for both; Mann–Whitney test).

When comparing the indicators between Groups I-A and I-B, a statistically significant difference in anxiety levels was observed:

In Group I-A, children had a high level of anxiety — 48.0 (43.5; 50.0), exceeding the upper limit of the norm.

In Group I-B, situational anxiety averaged 43.0 (40.8; 44.0) points.

At the same time, according to the Montreal Cognitive Assessment (MoCA), adolescents in Group I-A showed lower cognitive function scores, allowing for the diagnosis of cognitive deficit — 26.0 (25.0; 26.0) ($p_1<0.001$).

Even considering the older age category of patients in Group I-B, the average MoCA score was 28.0 (27.0; 29.0).

Conclusions

1. Post-COVID syndrome in children and adolescents occurs quite frequently. According to the results of this study, its signs were observed in 69% of the examined participants, indicating a high prevalence of post-infectious neurological and psycho-emotional disorders in the pediatric population after COVID-19.

2. The main clinical manifestations of the post-COVID period in children were: central nervous system dysfunctions, increased fatigue, general weakness, drowsiness, decreased memory and attention, heightened anxiety, irritability, and headaches. These symptoms typically persisted for several months after recovering from COVID-19.

3. According to neuropsychological assessment using the Montreal Cognitive Assessment (MoCA), adolescents in Group I-A (children with CNS disorders) exhibited significant cognitive impairments, with scores reduced to 26.0 (25.0; 26.0) points ($p_1<0.001$). In contrast, children in Group I-B (without CNS disorders) had an average score of 28.0 (27.0; 29.0), which corresponds to the normal range.

4. Analysis of the psycho-emotional state using the Spielberger–Hanin method revealed significant differences between the groups. Adolescents in Group I-A showed a high level of anxiety -- 48.0 (43.5; 50.0), significantly exceeding normative values, whereas in Group I-B, anxiety was at a medium level - 43.0 (40.8; 44.0) ($p<0.001$).

5. The obtained data indicate complex involvement of the neuro-psychological sphere in children who have recovered from COVID-19, encompassing both psycho-emotional disorders and cognitive deficits, as confirmed by psychometric scale results ($p<0.001$ for both methods).

6. The development of cognitive and emotional impairments is likely associated with the neurotropic effects of the SARS-CoV-2 virus, as well as secondary metabolic and hypoxic disorders that occur during the acute and subacute phases of the disease.

7. Therefore, post-COVID syndrome in children and adolescents requires a multidisciplinary approach, involving a neurologist, psychoneurologist, psychologist, and pediatrician. Long-term dynamic assessment of cognitive functions and implementation of rehabilitation programs aimed at restoring memory, attention, emotional stability, and the child’s adaptive abilities are necessary.

8. Early detection and correction of post-COVID impairments allow for the prevention of persistent neurological and psycho-emotional consequences, improving the quality of life and social adaptation of children.

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Conflicts of Interest: The authors declare no conflicts of interest.

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