

Features of Clinical and Neurological Manifestations and Biochemical Aspects of the New Coronavirus Infection (COVID-19) in Children

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Abstract The article reveals the relevance of the problem of coronavirus infection in children, examines the risks of the disease, neurological manifestations, laboratory data, and considers options for the severe course of the disease.

Keywords COVID-19, New coronavirus infection, Pediatric multisystem inflammatory syndrome, Meningitis, Encephalitis, Encephalopathy

1. Introduction

At the end of December 2019, an outbreak of a new coronavirus infection (COVID-19) caused by the SARS-CoV-2 coronavirus, leading to severe acute respiratory syndrome, was recorded in Wuhan (Hubei Province, China). [1] In almost all published original studies of COVID-19 cases, it is noted that, in addition to impaired respiratory system function, one third of patients (30%-35%) show signs of damage to the nervous system. [2-3] When infected with the SARS-CoV-2 virus, patients experience headache, nausea, vomiting, dizziness, myalgia, weakness, fatigue. Nausea and vomiting can be the result of disorders of both the digestive and nervous systems, if these symptoms manifest themselves along with headache, high intracranial pressure. Obviously, SARS-CoV-2 can infect the nervous system. The presence of viral particles directly in neurons is shown using electron microscopy on brain slices of patients who died from COVID-19. [4] According to recent publications, this virus causes a range of neurological complications: viral encephalitis, meningoencephalitis, ischemic and hemorrhagic strokes. [5]

2. Objective

To study the clinical, neurological and biochemical (Substance P) features in children with coronavirus infection.

3. Materials and Methods

The research work is based on the results of an examination

and study of 80 children who received inpatient treatment in the departments of the Specialized Hospital Zangiota №1 for the treatment of patients with coronavirus infection of the hospital, as well as an outpatient examination in the period 2021-2022.

4. The Results of the Study

80 children with coronavirus infection were under our supervision. The main group consisted of 49 (61.3%) patients, of which 33 (67.3%) boys and 16 (23.7%) girls with confirmed COVID-19 (based on PCR testing of the upper respiratory tract, serological examination for antibodies to SARS-CoV-2, and clinical outcomes) and neurological disorders. The comparison group consisted of 16 (20%) children, of which 7 (43.8%) boys and 9 (56.2%) girls with established COVID-19 infection (based on PCR testing of the upper respiratory tract, serological examination for antibodies to SARS-CoV-2, and clinical outcomes) without neurological disorders.

The control group consisted of 15 (18.7%) healthy children, of which 6 (40%) were boys and 9 (60%) were girls.

The main group of patients was divided into 2 additional groups: group I, 26 (53.1%) children with neurological disorders without systemic manifestations and group II, 23 (46.9%) children with neurological disorders on the background of systemic disorders (CD and MSVS).

A comparative study of the features of the unfavorable premorbid background of children with ITE and secondary encephalitis was conducted. We conducted an analysis of the antenatal period, obstetric and gynecological anamnesis, as well as an analysis of the age category of mothers. (Table 1)

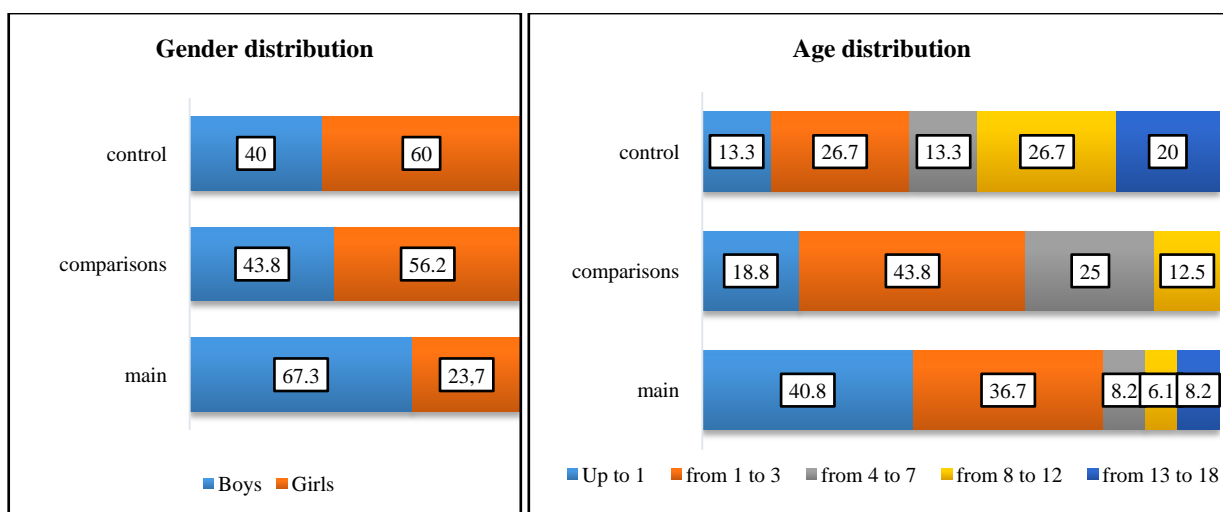


Figure 1. Sex and age characteristics of the examined patients

Table 1. Factors of unfavorable premorbid background of the examined children

ATTRIBUTE	Main group		Comparison group		P
	n=49	%	n=16	%	
Risk of miscarriage	20	40,8	6	37,5	>0,05
SARS	33	67,3	10	62,5	0,722
Anemia of the 1st degree	38	77,6	12	75	0,833
Anemia of the 2nd degree	6	12,2	2	12,5	>0,05
Anemia of the 3rd degree	5	10,2	0	0	0,322
Gestosis of 1 half	6	12,2	2	12,5	>0,05
Gestosis of 2 halves	7	14,3	2	12,5	>0,05
Kidney diseases	4	8,2	1	6,25	>0,05
Hypertensive syndrome	8	16,3	2	12,5	>0,05
Thyroid diseases	7	14,3	1	6,25	0,668
TORCH	32	65,3	8	50	0,376
Gastrointestinal diseases	8	16,3	2	12,5	>0,05
Lack of water	6	12,2	1	6,25	0,671
Polyhydramnios	15	30,6	3	18,75	0,357
Dirty amniotic fluid	8	16,3	2	12,5	>0,05
Inflammatory diseases of the genitals	4	8,2	1	6,25	>0,05
Toxicosis	37	75,5	10	62,5	0,313

Note: * - reliability of data between groups (P<0.05)

Table 2. Comorbid pathology of the examined children

ATTRIBUTE	Main group		Comparison group		P
	n=49	%	n=16	%	
Comorbid pathology	31	63,3	7	43,8	0,243
Respiratory disorders	10	20,4	3	18,8	>0,05
Diseases of the central nervous system	15	30,6	2	12,5	0,152
Cardiac disorders	5	10,2	1	6,3	>0,05
Allergic pathology	9	18,4	2	12,5	0,718
Endocrine pathology	3	6,1	0	0,0	0,569
Diseases of the ENT organs	2	4,1	2	12,5	0,252
Diseases of the genitourinary system	1	2,0	0	0,0	>0,05
Gastrointestinal diseases	1	2,0	0	0,0	>0,05

Note: * - reliability of data between groups (P<0.05)

As we can see from the above table, the frequency of the threat of spontaneous miscarriage in women of the main and comparative groups was approximately the same – 40.8% and 37.5%, respectively, the incidence of SARS in the antenatal period in the main group of patients was 67.3%, and in the comparative group – 62.5%. Anemia of severity 1 and 2 was observed equally in both groups, whereas in the main group 3 severity was observed in 10.2% of children, and it was not compared. Gestosis in both halves of pregnancy was observed in approximately the same ratio – 12%-14%. In other conditions, diseases were more common in the main group, but the significant difference was only in TORCH pathology, polyhydramnios and toxicosis.

Table 3. Diagnosis in children with COVID-19 and neurological disorders

DIAGNOSIS	The main group	
	N=49	%
Infectious and toxic encephalopathy	33	67,3
Damage to the peripheral nervous system	6	32,7
Convulsive syndrome	6	12,2
Secondary encephalitis	4	8,2

Note: * - reliability of data between groups (P<0.05)

In general, comorbid pathology was observed in both groups, but it was most common in patients of the main group (63.3% vs. 43.8%), especially neurological burden (30.6% in the main group vs. 12.5% in the comparison group). Allergic pathology was also slightly more common (18.4% vs. 12.5%). Otherwise, the difference between the groups was unreliable. It should be noted that there was no

endocrine pathology in the comparison group, and diseases of the ENT organs were observed more often than in the main group (12.5% vs. 4.1%). (Table 2)

Table 4. Neurostatus in children with COVID-19 and CNS damage

SYMPTOM	the main group	
	N=49	%
Oculomotor disorders	14	28,6
Ptosis	3	6,1
Strabismus	14	28,6
Nystagmus	27	55,1
Lesion of the facial nerve	8	16,3
Facial asymmetry	18	36,7
Smoothness of the nasolabial fold	19	38,8
Bulbar violations	10	20,4
Hypertension	22	44,9
Hypotension	19	38,8
Paresis and paralysis	11	22,4
Pathological reflexes	26	53,1
Increased tendon reflexes	21	42,9
Reduction of tendon reflexes	18	36,7
Meningeal symptoms	17	34,7
Hypesthesia	11	22,4
Hyperesthesia	28	57,1
Dysarthria	12	24,5
Syndrome of motor disorders	23	46,9

Note: * - reliability of data between groups (P<0.05)

Table 5. The main blood parameters in children with COVID-19 and neurological complications, depending on the involvement of systemic disorders

Indicator	Group	Me	Q ₁ – Q ₃	n	P
	General blood test				
Hemoglobin group	I-группа	109,5	104,2 – 115,0	26	0,423
	II-группа	102,0	93,0 – 118,5	23	
Erythrocytes	I-группа	4,14	3,76 – 4,44	26	0,802
	II-группа	4,14	3,23 – 4,49	23	
Leukocytes	I-группа	10,59	7,78 – 17,49	26	0,211
	II-группа	7,63	6,29 – 13,64	23	
SOE	I-группа	21,0	9,8 – 34,0	24	0,376
	II-группа	16,5	9,0 – 24,5	20	
Platelets	I-группа	374,5	291,0 – 470,0	24	0,039*
	II-группа	310,0	228,0 – 378,5	23	
Biochemical blood analysis					
D-dimer	I-группа	1006,3	614,3 – 1296,3	24	<0,001*
	II-группа	2200,0	1263,2 – 2700,3	19	
Ferritin	I-группа	75,2	44,4 – 117,6	14	0,396
	II-группа	86,6	68,1 – 128,6	10	
Procalcitonin	I-группа	0,19	0,14 – 0,26	21	0,185
	II-группа	0,21	0,20 – 0,30	16	
IL-6	I-группа	11,7	10,7 – 15,1	15	0,222
	II-группа	16,6	11,1 – 35,2	11	

Note: * - reliability of data between groups (P<0.05)

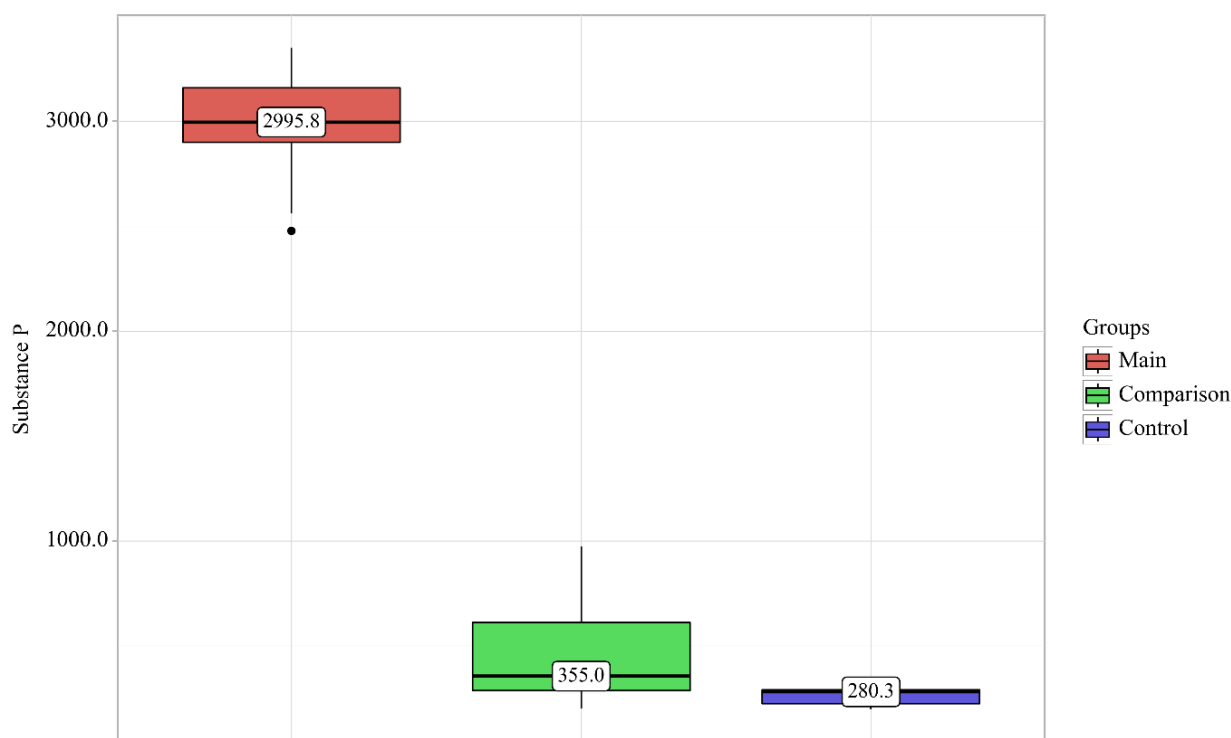


Figure 2. The level of Substance P depending on the patient group

The main diagnosis among patients with COVID-19 was infectious-toxic encephalopathy, which was diagnosed in 33 (67.3%) children, convulsive syndrome in 16 (32.7%), isolated damage to the peripheral system in 6 (12.2%), respectively, and in 4 - secondary encephalitis/ meningoencephalitis was observed. (Table 3)

When examining patients of the main group, 39 children (79.6%) showed symptoms of TBI damage, in the form of oculomotor disorders, facial nerve neuritis, as well as bulbar disorders. (Table 4)

Only in 8 children, the tone corresponded to normal, whereas in 41 (83.7%), it was impaired. A decrease in muscle strength was observed in 11 (22.4%) patients. Reflexes in patients were more often elevated (42.9%), and pathological reflexes were detected in more than half (53.1%) of children. Reflexes in patients were more often elevated (42.9%). Sensitive disorders were manifested mainly by hyperesthesia in 57.1% of patients. Meningeal symptoms occurred in 17 (34.7%) patients.

When evaluating proinflammatory markers, the average values in COVID-19 children significantly exceeded the reference values, and the difference between the average values in children with and without neurological disorders was significant (method used: Mann–Whitney U–test). (Table 5)

When conducting a comparative analysis of substance P in accordance with the group of patients, significant statistically significant differences ($p < 0.001$) were found (method used: The Kruskal–Wallis test).

As we can see, the level of substance P was significantly higher in the main group and amounted to 2995.8 (2900.1; 3158.8) on average, whereas in the comparison and control group these indicators were 355 (285.6; 611.2) and 280.3 (223.9; 290.1), respectively, while the difference between the comparison group and the control group was also it was statistically significant. (Fig. 2)

5. Conclusions

Neurological disorders in children with coronavirus infection can occur both in isolation and in the structure of a systemic lesion, which is manifested by multisystem inflammatory syndrome or Kawasaki disease. Neurological disorders in children with COVID-19 most often occur in infancy and in preschool age.

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