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THE IMPACT OF THE SARS-COV-2 (COVID-19) PANDEMIC ON THE NOSOMORPHOSIS OF PAEDIATRIC NEUROPATHOLOGY

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Summary.

The SARS-CoV-2 (COVID-19) pandemic continues to pose a substantial global challenge, impacting economic, demographic, cultural, scientific, and medical domains. A review of the contemporary medical literature on SARS-CoV-2 infection, sourced from the Web of Science and PubMed databases, suggests that current scientific efforts should focus on a comprehensive evaluation of the pandemic's scope and consequences. Moreover, ongoing research into the effects of the COVID-19 pandemic on children is required to optimise preventive strategies, identify high-risk populations, and ensure the provision of appropriate care. A further significant aspect of the pandemic's impact relates to its influence on the overall structure of population morbidity– referred to as nosomorphosis – including disorders of the nervous system. Characterisation of the nosomorphosis in neuropathology is essential to enable public health and medical systems to respond effectively to the challenges presented by the COVID-19 pandemic. Such characterisation should include institutional-level changes, such as modification and adaptation of healthcare infrastructure, resource reallocation, introduction of innovative technologies, and revision of medical education and training programmes, as well as individual-level developments, including enhancement of professional competencies, engagement in educational outreach, and promotion of vaccination.

***Aim.** To assess the impact of the SARS-CoV-2 (COVID-19) pandemic on the pattern of paediatric neuropathology through analysis hospital morbidity in children with acute nervous system lesions during the pre-pandemic period compared with the pandemic period.*

***Materials and methods.** A retrospective analysis was performed on medical records of paediatric patients hospitalised with acute lesions of the central and peripheral nervous system between 1 January 2017 and 1 January 2024 at the Communal Non-Commercial Enterprise «Regional Medical Centre for Family Health» of the Dnipropetrovsk Regional Council. A total of 32 children who met the predefined inclusion criteria were included: 17 patients were allocated to the pre-pandemic group and 15 patients to the pandemic group. Comparative statistical analyses were conducted on demographic variables (age, sex), duration of hospitalisation, and the distribution of neuropathological diagnoses before and during the pandemic. The study protocol was approved by the Local Ethics Committee of the institutions involved. The research was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all participants or their legal representatives prior to inclusion in the study. Descriptive and analytical statistical methods were employed for data analysis. The normality of distribution was assessed using the Shapiro–Wilk test. Normally distributed data were expressed as mean (M) with the 95% confidence interval (95% CI). Non-normally distributed data were presented as median (Me) with the interquartile range (25%–75%). Comparisons between two independent samples were performed using the Student t-test or the Mann–Whitney U test, depending data distribution. Relative values were compared using Pearson's chi-squared (χ^2) test with Yates' continuity correction. Statistical analyses were performed using Microsoft Excel and TIBCO Statistica™ 14.0.0 (trial version). Differences were considered statistically significant at $p < 0.05$, and trends were defined as $0.05 \leq p < 0.5$. The work was carried out as part of a research project: «Determination of epigenetic factors affecting the formation of acquired immunity in acute and chronic infectious diseases in children and adults»; Research Topic Code: IN.01.22; State Registration No. 0122U001998; Execution period: 2022-2026.*

***Results.** During the pre-pandemic period, bacterial meningitis was the predominant form of neuroinfection (41.2%), contributing to the overall predominance of bacterial aetiology (52.9%). Among viral encephalitides in this group, herpetic encephalitis (B00.4) was the most frequently diagnosed, accounting for 17.6% of cases. In the post-pandemic period, a redistribution in the pattern of neuropathological lesions was observed: viral forms accounted for 40.0% of cases and unspecified forms for 46.7%, whereas bacterial forms declined markedly to 13.3%. In both groups, the majority of cases occurred in children younger than two years of age (59% in Group I and 40% in Group II).*

***Conclusions.** A comparative clinical analysis of neuroinfections in the pre-pandemic and post-pandemic periods demonstrated that post-viral encephalitis became the predominant form of paediatric neuroinfection morbidity during the post-pandemic period, whereas the incidence of bacterial meningoencephalitis decreased significantly compared with the pre-pandemic period. Analysis of the aetiological profile revealed a between-group difference at the trend level, suggesting a potential post-pandemic shift in the aetiology of paediatric neuroinfections that warrants further investigation. Furthermore, the impact of the SARS-CoV-2 pandemic on infants and preschool-aged children – who experienced severe disease with neurological complications and potential subsequent development of post-COVID syndrome (PCS)—requires continued study.*

***Keywords:** Child; COVID-19 Pandemic; Nosomorphosis; Structure of Neuropathology.*

Introduction

The SARS-CoV-2 (COVID-19) pandemic continues to pose a major global challenge, impacting economic, demographic, cultural, scientific, and medical aspects of society. Analysis of current medical literature on SARS-CoV-2 infection, sourced from databases such as Web of Science and PubMed, confirms the ongoing need for research to delineate the full scope and consequences of this pandemic [2-4,12,13,15,24]. Continued investigation into the effects of the COVID-19 pandemic on children is required to identify high-risk populations, ensure the provision of optimal care, and optimise preventive strategies.

The primary burden of the pandemic stems from the direct pathological effects of SARS-CoV-2 on the human body, leading to the development of the «post-COVID-19 condition» or «post-COVID syndrome» (PCS). PCS is defined as a constellation of signs and symptoms that emerge during or after acute SARS-CoV-2 infection, persist for more than 12 weeks, and cannot be attributed to an alternative diagnosis [8,17]. A German study involving 525 participants reported that PCS was associated with increased rates of depression, post-traumatic stress, and fatigue, as well as diminished physical and mental health-related quality of life. An average of 69.1% of patients were classified as having PCS between 9 and 26 months after SARS-CoV-2 infection [5,12]. This syndrome has been incorporated into the International Classification of Diseases, 10th Revision (ICD-10) under code (U09.9) and is retained in the new ICD-11 under code (RA02) (Figure 1) [5, 21].

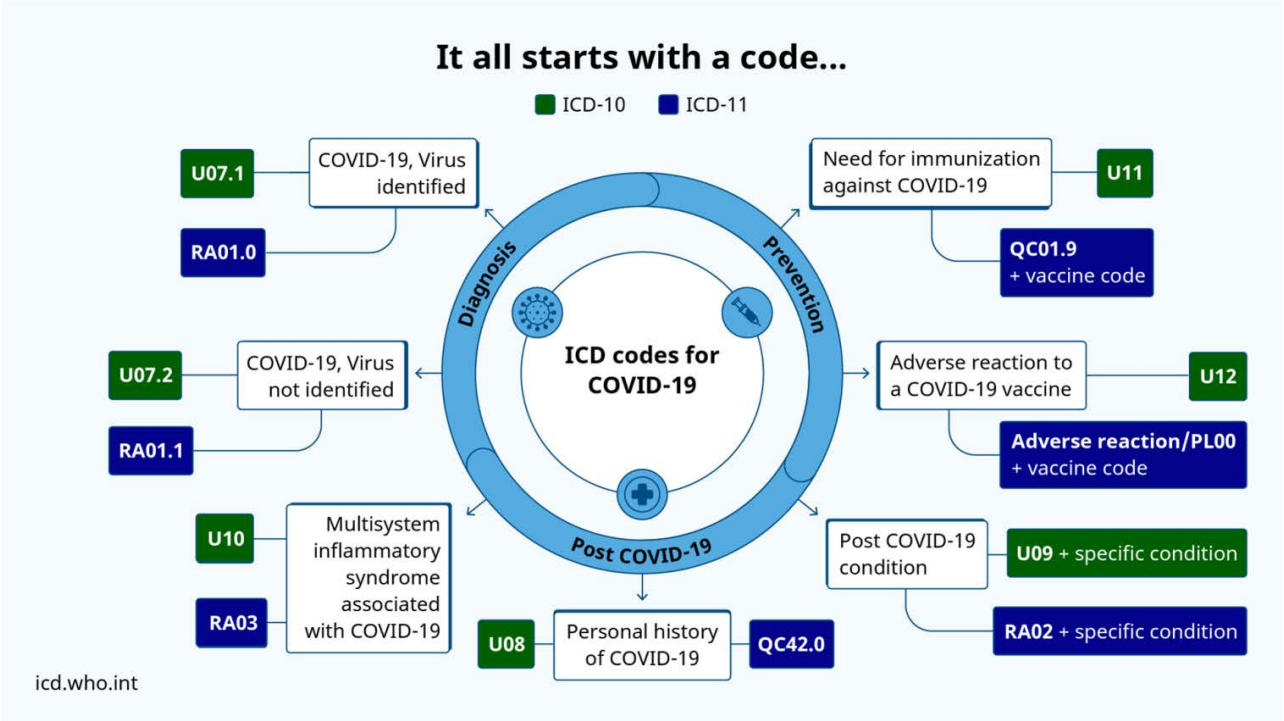

Figure 1. Post-COVID syndrome according to ICD-10 and ICD-11 classifications according to WHO recommendations. https://www.who.int/standards/classifications/classification-of-diseases/emergency-use-icd-codes-for-covid-19-disease-outbreak

Post-COVID syndrome (PCS) may follow any clinical manifestation of SARS-CoV-2 infection. However, it is observed predominantly in adults and may occur in adolescents, whereas it is less frequently reported in younger children and pre-adolescents. This disparity may be attributable to fundamental age-related differences in the functional characteristics of the immune and endocrine systems [9,13].

A second dimension of the pandemic's burden involves the influence of SARS-CoV-2 infection on the structure of population pathology – referred to as nosomorphosis – including disorders of the nervous system (NS) [4,9,17]. Characterisation of the nosomorphosis of neuropathology (NN) is essential to enable public health and medical systems to mount an effective response to the challenges posed by the COVID-19 pandemic. Such a response must encompass transformations at the institutional level – including adaptation of healthcare facility infrastructure, reallocation of investment priorities, implementation of innovations, and revision of medical education curricula – as well as at the individual level, such as enhancement of professional competencies, public health education initiatives, and advocacy for vaccination [21].

The objective of this study was to assess the impact of the SARS-CoV-2 (COVID-19) pandemic on the nosomorphosis of paediatric neuropathology by analyzing hospital admissions for acute central and peripheral nervous system lesions during the pre-pandemic and pandemic periods.

Materials and methods. A retrospective analysis was performed of medical records of children hospitalised with acute central and peripheral nervous system lesions between 1 January 2017 and 1 January 2024 at the Communal Non-Commercial Enterprise «Regional

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Medical Centre for Family Health» of the Dnipropetrovsk Regional Council in Dnipro (CNE «RMCFH» DRC). Two groups were established: Group I (pre-pandemic) included children with acute nervous system pathology hospitalized from 1 January 2017 to 31 December 2020 (n = 17); Group II (pandemic) comprised children with acute nervous system pathology hospitalized from 1 January 2021 to 1 January 2024 (n = 15). This time interval was selected because the first officially documented cases of SARS-CoV-2 infection among children in the Dnipropetrovsk region occurred in November 2020, despite the first national case in Ukraine having been officially registered in March 2020 [Resolution of the Cabinet of Ministers of Ukraine No. 215 of 16 March 2020 on the Introduction of Quarantine].

Patient evaluation included assessment of clinical complaints, medical and disease history, epidemiological data, general physical examination, and laboratory and instrumental diagnostic procedures. Case classification was performed according to ICD-10 codes within the categories G00–G99 (Diseases of the nervous system) and A80–A89 (Viral infections of the central nervous system). Inclusion criteria were immunocompetent children aged 28 days to 17 years, 11 months, and 29 days with acute, newly diagnosed nervous system pathology, in the absence of neurotrauma (including injuries sustained during military aggression, domestic incidents, or road traffic accidents) or congenital nervous system malformations.

Statistical analysis was conducted using descriptive and analytical statistical methods. Normality of data distribution was assessed using the Shapiro–Wilk test. Normally distributed variables were expressed as mean (M) with 95% confidence interval (95% CI); non-normally distributed variables were reported as median (Me) with interquartile range (25%–75%). Comparisons between two independent groups were performed using the Student t-test for normally distributed data or the Mann–Whitney U test for non-normally distributed data. Relative values were compared using Pearson's chi-squared (χ^2) test with Yates' continuity correction.

Statistical processing was conducted using Microsoft Excel and the trial version of TIBCO Statistica™ 14.0.0. Differences were considered statistically significant at $p < 0.05$, and trends were defined at $0.05 \leq p < 0.5$.

The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee. Informed consent was obtained from the parents or legal guardians and, where appropriate, from the children themselves.

Results

A total of 32 children who met the inclusion criteria were included in the study: 17 in the pre-pandemic Group I and 15 in the pandemic Group II. The characteristics of the participants with respect to age, sex, and clinical outcome are presented in Table 1 and Figure 2.

Table 1

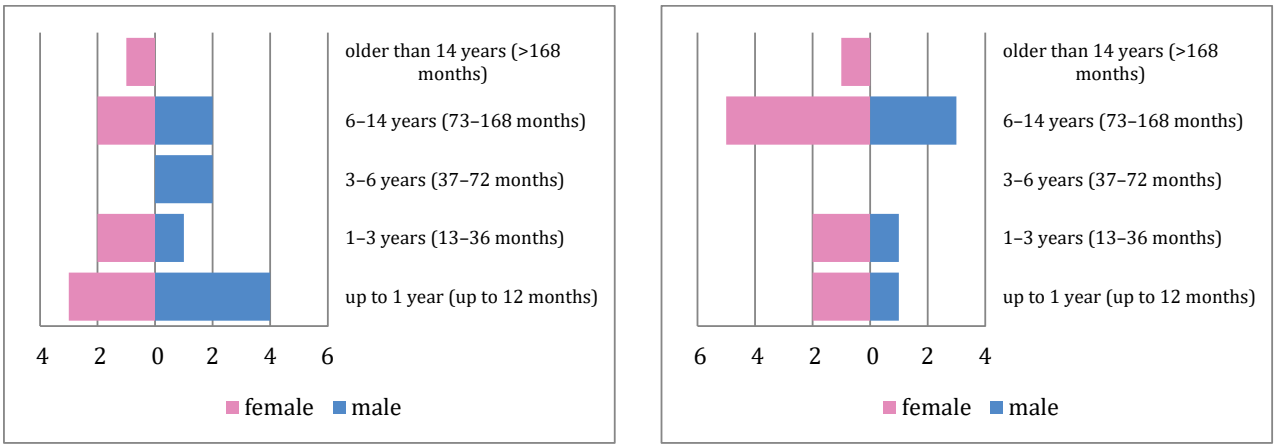
Comparative characteristics of children in the study groups

Indicator	Group I (n=17)	Group II (n=15)	p-value
Minimum age (months)	4 months	2 months	-
Maximum Age (years, months)	16 years 9 months	17 years	-
Mean age, M and 95% CI (years, months)	4 years 6 months (54.5 months, 95% CI (23.3-85.7) months)	6 years 11 months (82.8 months, 95% CI (48.5-117.1) months)	0.202
Sex ratio, m/f abs. / %	9 (52.9%) / 8 (47.1%)	5 (33.3%) / 10 (66.7%)	0.265
Complete recovery, abs. / %	14/82.4%	14/93.3%	0.349
Partial Recovery, abs. / %	3/17.6%	1/6.7%	
Complications, abs. / %	10/58.8%	9/60.0%	0.770
Mortality rate, abs. / %	0	0	-

Notes: *p – differences between groups using Pearson's χ^2 (including Yates' correction) for qualitative variables, and Student's t-test for quantitative variables.*

As shown in Table 1, a trend toward an increase in the median age of children was observed between the groups, rising from 4 years and 6 months in Group I to 6 years and 11 months in Group II by median values). Complete recovery was defined as a favourable clinical outcome followed by discharge for outpatient follow-up, whereas partial recovery was defined as transfer to another medical facility for continued care.

During the pre-pandemic period the sex distribution among children with acute neuroinfections was approximately balanced (52.9% boys and 47.1% girls). In contrast, during the post-pandemic period, an increased proportion of girls was observed (66.7% girls versus 33.3% boys; $p = 0.265$). Although this difference did not reach statistical significance, the trend was most pronounced in the subgroup of children older than 6 years, where a statistical trend was noted ($p = 0.064$), potentially reflecting age-dependent alterations in immune reactivity in the aftermath of the SARS-CoV-2 pandemic.



Group I Group II

Figure 2. Distribution of the examined children by age and sex (absolute number of patients in the respective group by sex)

Analysis of hospital morbidity data revealed an impact of the SARS-CoV-2 (COVID-19) pandemic on the nosomorphosis – i.e., the structural distribution – of nervous system pathology among children in the study groups (Table 2).

Table 2

Comparison of the structure (nosomorphosis) of paediatric neuropathology in the study groups (n=32)

ICD-10 Code	Pathology	Group I (n=17), %	Group II (n=15), %	p-value
A86	Unspecified viral encephalitis	0	20.0	0.184
B00.4	Herpetic encephalitis	17.6	0	0.184
B01.1	Varicella with encephalitis	0	6.7	0.541
G00.1	Pneumococcal meningitis	5.9	0	0.541
G00.2	Streptococcal meningitis	5.9	0	0.541
G00.9	Unspecified bacterial meningitis	29.4	13.3	0.641
G03.9	Meningitis, unspecified	0	26.6	0.044
G04.8	Other encephalitis, myelitis and encephalomyelitis	11.8	6.7	0.965
G04.9	Encephalitis, myelitis and encephalomyelitis, unspecified	0	6.7	0.541
G05.0	Meningoencephalitis and meningomyelitis in bacterial diseases classified elsewhere	11.8	0	0.541
G61.0	Inflammatory polyneuropathy	5.9	6.7	1.00
G96.9	CNS disorder, unspecified	0	13.3	0.329
Other[1] A39.8	Other meningococcal infections: meningococcal encephalitis	11.7	0	0.541

Notes:[1] *Meningococcal encephalitis, myelitis or encephalomyelitis (A39.8).*
[2] *G61.0 Guillain-Barré syndrome; acute (post) infectious polyneuritis; Miller Fisher syndrome.*
p – differences between groups using Pearson's χ^2 (including Yates' correction)

Table 2 demonstrates a general trend toward an increased incidence of NS lesions, encephalitis, and meningitis of undetermined etiology during the pandemic period. Specifically, the proportion of cases coded as unspecified meningitis (G03.9) increased significantly from 0% in the pre-pandemic period to 26.6% during the pandemic ($p = 0.0437$), indicating a statistically significant shift in the nosomorphosis of paediatric neuropathology.

Notable observations included an increased incidence of encephalitis caused by varicella-zoster virus (B01.1) and unspecified viral encephalitis (A86), concomitant with the absence of herpetic encephalitis (B00.4) and NS lesions attributed to other causes or localisations during the pandemic period. Although only a statistical trend was observed for unspecified viral encephalitis (A86) and herpetic encephalitis (B00.4) ($p = 0.18$), their opposing temporal dynamics may suggest an etiological shift in viral central nervous system (CNS) lesions during the pandemic. Furthermore, no increase in inflammatory polyneuropathies, such as Guillain–Barré syndrome, was observed.

The median duration of hospital stay during the pre-pandemic period (Figure 3) was 16.0 days (interquartile range: 10.75-24.75), whereas in the post-pandemic period, this duration was significantly shorter ($p = 0.011$), at 8.0 days (interquartile range: 6.25-11.0).

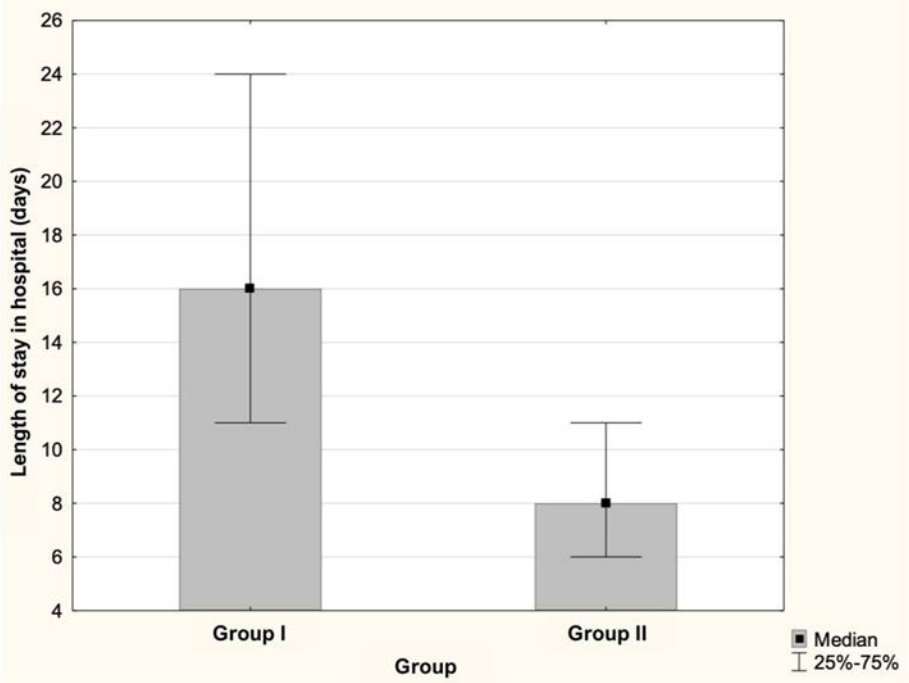


Figure 3. Mean length of hospital stay for children across the evaluated groups (median and interquartile range)

Figure 4 illustrates the nosological structure of Group I (pre-COVID).

In the pre-pandemic group, the most frequently recorded diagnoses were unspecified bacterial meningitis (G03.9)—present in 29.4% of cases – and acute herpetic viral encephalitis (B00.4)—recorded in 17.6% of cases. Overall, cases of bacterial meningitis (G00.1, G00.2, G03.9) accounted for 41.2% of all diagnoses, reflecting the predominance of bacterial NS pathology in the pre-pandemic period.

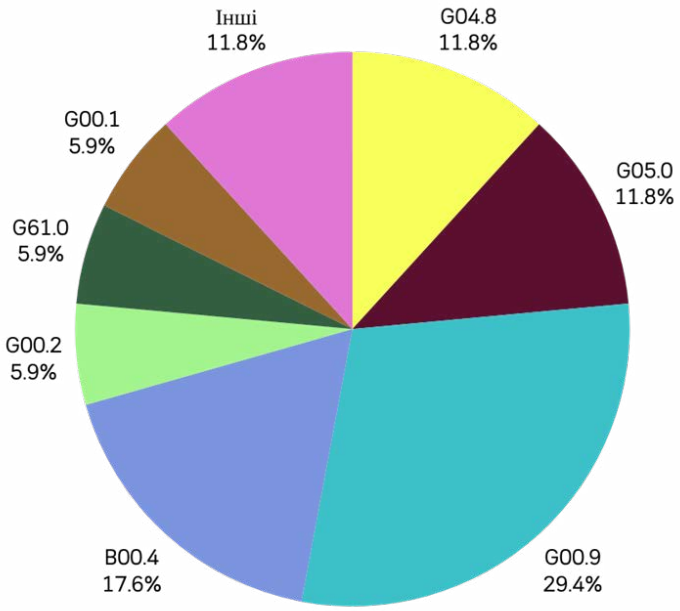


Figure 4. Nosological structure of Group I (pre-COVID) according to ICD-10.

Meningoencephalitis and meningomyelitis in bacterial diseases classified elsewhere (G05.0) and other encephalitis, myelitis, and encephalomyelitis (G04.8) each represented 11.8% of cases.

Among confirmed bacterial meningitis cases, *Streptococcus pneumoniae* (G00.1) and *Streptococcus species* (G00.2) were equally represented, each accounting for 5.9% of the total.

Inflammatory polyneuropathies constituted 5.9% of all diagnoses in Group I.

Among viral aetiologies, herpetic encephalitis (B00.4) was predominant; cases associated with varicella-zoster virus (B01.1) or unspecified viral encephalitis (A86) were not observed.

Figure 5 presents the distribution of patients in Group II (pandemic) by ICD-10 diagnosis.

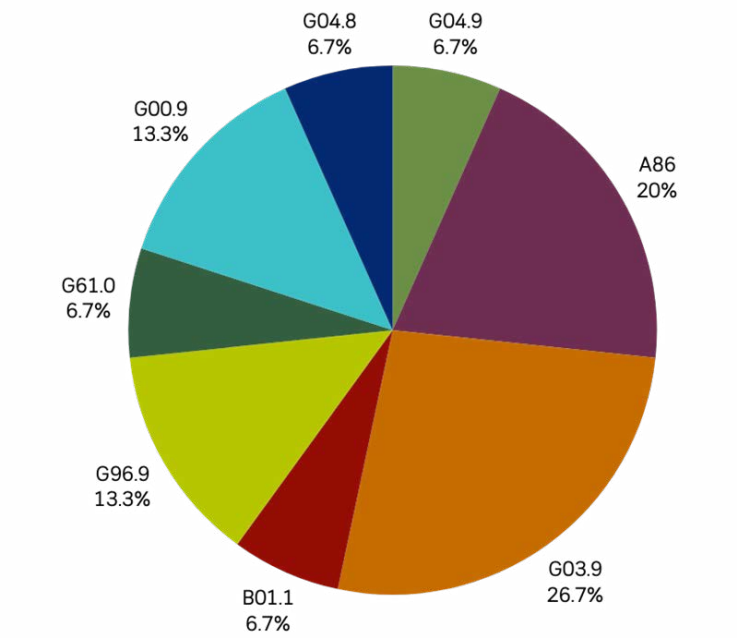


Figure 5. Nosological structure of Group II (pandemic) according to ICD-10.

The proportion of patients diagnosed with unspecified viral encephalitis was slightly higher in Group II (20.0%) than in Group I, where acute viral encephalitis accounted for 17.6% of cases, and unspecified encephalitides were not recorded. These differences, however, did not reach statistical significance (p = 0.180).

In Group II, an increase was observed in the frequency of unspecified bacterial meningitis (G03.9) and unspecified CNS disorders (G96.9), each representing 13.3% of cases. Overall, Group II was characterized by a dynamic shift in the aetiological structure of neuroinfections toward unspecified viral and mixed forms ($p = 0.073$) (Table 3).

Table 3

Structure of Nervous System Lesion Types by Aetiology in Children in the Study Groups, abs. (%)

Type of Lesion and Aetiology	Group I (n=17)	Група 2 (n=15)	*p*-value
Encephalitis, total including:	7 (41.2%)	6 (40.0%)	0.956
Bacterial	2 (11.8%)	0 (0%)	0.178
Viral	4 (23.5%)	5 (33.3%)	0.566
Unspecified / Other	1 (5.9%)	1 (6.7%)	0.934
Meningitis, total including:	8 (47.1%)	6 (40.0%)	0.700
Bacterial	7 (41.2%)	2 (13.3%)	0.057
Viral	0 (0%)	1 (6.7%)	0.983
Unspecified / Other	1 (5.9%)	3 (20.0%)	0.327
Other CNS Lesions	2 (11.7%)	3 (20.0%)	0.550

Note. p – differences between groups using Pearson's χ^2 (including Yates' correction)

Discussion

An accumulating body of evidence indicates that SARS-CoV-2 may impair both the central nervous system (CNS) and the peripheral nervous system (PNS), resulting in a heterogeneous spectrum of neurological manifestations [19]. Clinical features reported in children include, but are not limited to, encephalopathy, peripheral nervous system involvement, behavioral alterations, and hallucinations [20].

Although the precise pathogenesis of neurological manifestations in COVID-19 remains incompletely understood, several studies have identified a potential association between neural tissue injury and SARS-CoV-2 infection within the CNS, frequently accompanied by immune dysregulation [16]. The marked heterogeneity observed in clinical, radiological, and pathological descriptions of COVID-19-associated neurological disorders strongly suggests the involvement of multiple pathogenic mechanisms [18]. Current evidence indicates that SARS-CoV-2-induced neurological dysfunction may arise through several interrelated pathways. First, SARS-CoV-2 may gain access to the brain via retrograde neuronal transport or haematogenous dissemination, thereby disrupting brain structure and function. This process may either precipitate de novo neurological disorders or exacerbate pre-existing neurological conditions. Second,

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the systemic cytokine storm triggered by SARS-CoV-2 infection intensifies neuroinflammation and contributes to neuronal damage, potentially leading to impaired cerebral perfusion and reduced oxygen delivery to the brain. Third, SARS-CoV-2-associated cerebral ischaemia and hypoxaemia are considered plausible contributors to the development of neurological complications in the context of COVID-19 [6,10,19,25].

Comparative clinical and epidemiological analyses across study groups revealed a notable shift in the nosomorphosis of paediatric neuroinfections between the pre-pandemic and post-pandemic periods. During the pre-pandemic period, bacterial meningitis predominated (41.2%), resulting in an overall predominance of bacterial aetiology among neuroinfections (52.9%). Among viral encephalitides in this group, herpes simplex encephalitis (B00.4) was the most frequently diagnosed, accounting for 17.6% of cases. As noted by Tyler KL, herpes simplex encephalitis in children is a rare but life-threatening CNS infection that may also present as monophasic or recurrent aseptic meningitis, myelitis, or radiculitis, with a mortality rate of up to 70% in the absence of appropriate antiviral therapy [23]. Taba P et al., in a review of the European consensus, underscore the severity of post-viral encephalitis, particularly in children older than 1 year residing in regions with high endemicity for tick-borne encephalitis (≥5 cases per 100,000 population per year), where it may result in severe and persistent neurological sequelae [22].

The present study demonstrates that the post-pandemic period is characterised by a structural redistribution of neuroinfections, with viral forms accounting for 40.0% and unspecified forms for 46.7% of cases, concomitant with a marked decline in bacterial aetiologies (13.3%). Of particular note is the increased incidence of encephalitis caused by varicella-zoster virus (B01.1) and unspecified viral encephalitis (A86), alongside the complete absence of herpes simplex encephalitis (B00.4) or other non–SARS-CoV-2-related or anatomically localised nervous system lesions during the pandemic period.

A statistical difference in the aetiological structure of neuroinfections between the study groups was observed at the level of a trend ($p = 0.073$), suggesting a potential post-pandemic transformation in the aetiology of paediatric neuroinfections that warrants further investigation. This observation is supported by the findings of Krawczuk K et al., who reported that the epidemiology of CNS infections has been continually evolving due to the widespread implementation of vaccination programmes and the increasing use of sensitive, rapid molecular diagnostic methods [14].

The most pronounced differences in the present study were evident in the nosomorphosis of meningitis, wherein the proportion of cases of bacterial aetiology was lower during the post-pandemic period compared with the pre-pandemic period, reaching the level of a statistical trend ($p = 0.057$). Notably, the incidence of inflammatory polyneuropathies, such as Guillain–Barré syndrome, remained stable in the post-pandemic period relative to the pre-pandemic era.

The study revealed a trend toward a higher median age in the second (post-pandemic) group (6 years and 11 months); however, this observation could not be statistically attributed to the influence of the SARS-CoV-2 pandemic. The median duration of hospitalisation was significantly longer in the pre-pandemic group ($p = 0.011$), measuring 16.0 days (interquartile range: 10.75-24.75), compared with 8.0 days (interquartile range: 6.25-11.0) in the post-pandemic period.

A notable observation was that the majority of children in both groups were younger than two years of age (59% in Group I and 40% in Group II). A meta-analysis by Choi JH et al., based on a comprehensive search of the PubMed, EMBASE, Scopus, and KoreaMed databases, reported that neonates were at increased risk of severe COVID-19 compared with older paediatric populations (hazard ratio [HR] 2.69; 95% CI 1.83-3.97) [4]. Similarly, Woodruff RC et al. identified age under two years as a critical risk factor for neurological complications and severe disease in children with SARS-CoV-2 infection, with a reported risk of 95% [24]. Furthermore, a prospective Canadian study by Farrar DS et al. found that among hospitalised children with COVID-19, the most severe outcomes occurred in those younger than one year (37.9 hospitalisations and 5.4 severe cases per 100,000 population), whereas the mildest clinical course was observed in children aged 5 to 11 years (1.0 hospitalization and 0.4 severe cases per 100,000 population) [7].

Kompaniyets L et al. conducted a statistical analysis of 43,465 patients younger than 18 years with SARS-CoV-2 infection to evaluate the adjusted risk of severe disease. They reported that 3.9% had pre-existing CNS disorders, 3.2% had anxiety disorders, and 2.8% had depressive disorders. Among hospitalised patients aged 12 to 18 years, pre-existing epilepsy and/or seizure disorders were identified as a risk factor for severe COVID-19 in 95% of cases [13]. Similarly, Choi JH et al. noted in their systematic review that children with underlying neurological conditions, particularly seizure disorders, experienced a more severe clinical course of COVID-19 in 95% of cases [4].

Data from the Centers for Disease Control and Prevention (CDC) COVID Data Tracker indicate that 15.2% of children hospitalised between March 2020 and February 2023 with laboratory-confirmed SARS-CoV-2 infection had underlying neurological conditions [15]. Additionally, Ahmed IS et al. observed an increased burden of neurological disorders among paediatric patients affected by COVID-19 in their study [2].

In the present cohort, the youngest patient in the post-pandemic period was 2 months of age – a factor that should be considered a potential risk for the subsequent development of PCS in this vulnerable paediatric subgroup. This warrants heightened clinical vigilance during outpatient follow-up.

Conclusions

Comparative clinical analysis of neuroinfection characteristics in patients from the pre-pandemic and post-pandemic periods demonstrated a significant shift in the

nosomorphosis of paediatric neuropathology. During the post-pandemic period, post-viral encephalitis emerged as the predominant form of neuroinfection in children, whereas the incidence of bacterial meningoencephalitis declined substantially compared with the pre-pandemic period.

A distinctive feature of the post-pandemic period was the redistribution of the aetiological profile of neuroinfections, characterized by an increased proportion of unspecified viral and mixed forms. The intergroup difference in aetiological structure approached statistical significance ($p = 0.073$), suggesting a potential post-pandemic transformation in the aetiology of paediatric neuroinfections that warrants further investigation.

The impact of the SARS-CoV-2 pandemic on infants and preschool-aged children – who experienced severe disease courses with neurological complications and may therefore constitute a high-risk group for post-COVID syndrome – also necessitates continued, detailed, and longitudinal assessment.

Conflict of Interest: the authors declare no conflict of interest.

References:

1. Abbott A, Lusby H, Islam SP. A Protracted Course of Herpes Simplex Virus Type 1 Encephalitis With Persistent Cerebrospinal Fluid Polymerase Chain Reaction Positivity Post Treatment. Cureus. 2021;13(9): e18107. DOI: https://doi.org/10.7759/cureus.18107. PMID: 34692318; PMCID: PMC8525692.

2. Ahmed IS, Tapponi SL, Widatallah ME, Alakkad YM, Haider M. Unmasking the enigma: An in-depth analysis of COVID-19 impact on the pediatric population. J Infect Public Health. 2023;16(9):1346-60. DOI: https://doi.org/10.1016/j.jiph.2023.06.017. PMID: 37433256; PMCID: PMC10299956.

3. Chi H, Chang L, Chao YC, Lin DS, Yang HW, Fang LC, et al. Pathogenesis and Preventive Tactics of Immune-Mediated Non-Pulmonary COVID-19 in Children and Beyond. Int J Mol Sci. 2022;23(22):14157. DOI: https://doi.org/10.3390/ijms232214157. PMID: 36430629; PMCID: PMC9696849.

4. Choi JH, Choi SH, Yun KW. Risk Factors for Severe COVID-19 in Children: A Systematic Review and Meta-Analysis. J Korean Med Sci. 2022;37(5): e35. DOI: https://doi.org/10.3346/jkms.2022.37.e35. PMID: 35132841; PMCID: PMC8822112.

5. Dejenu Kibret G, Thomas J, Post JJ, et al. Concordance between ICD-10-AM clinical coding and SARS-CoV-2 PCR testing for COVID-19 in Australian hospitals. Health Information Management Journal[Internet]. 2025[cited 2025 Sep 16];0(0). Available from: https://journals.sagepub.com/doi/10.1177/18333583251370486?url_ver=Z39.88-2003&rfr_id=ori: rid: crossref.org&rfr_dat=cr_pub%20%200pubmed DOI: https://doi.org/10.1177/18333583251370486

6. Dewanjee S, Vallamkondu J, Kalra RS, Puvvada N, Kandimalla R, Reddy PH. Emerging COVID-19 Neurological Manifestations: Present Outlook and Potential Neurological Challenges in COVID-19 Pandemic. Mol Neurobiol. 2021;58(9):4694-715. DOI: https://doi.org/10.1007/s12035-021-02450-6. PMID: 34169443; PMCID: PMC8224263.

7. Farrar DS, Drouin O, Moore Hepburn C, Baerg K, Chan K, Cyr C, et al. Risk factors for severe COVID-19 in hospitalized children in Canada: A national prospective study from March 2020-May 2021. Lancet Reg Health Am. 2022;15:100337. DOI: https://doi.org/10.1016/j.lana.2022.100337. PMID: 35936225; PMCID: PMC9342862.

8. Filippatos F, Tatsi EB, Michos A. Post-COVID-19 syndrome in children (Review). Exp Ther Med. 2022;24(4):609. DOI: https://doi.org/10.3892/etm.2022.11547. PMID: 36160884; PMCID: PMC9468832.

9. Jimeno-Almazan A, Pallares JG, Buendia-Romero A, Martinez-Cava A, Franco-Lopez F, Sánchez-Alcaraz Martínez BJ, et al. Post-COVID-19 Syndrome and the Potential Benefits of Exercise. Int J Environ Res Public Health. 2021;18(10):5329. DOI: https://doi.org/10.3390/ijerph18105329. PMID: 34067776; PMCID: PMC8156194.

10. Jha NK, Ojha S, Jha SK, Dureja H, Singh SK, Shukla SD, et al. Evidence of Coronavirus (CoV) Pathogenesis and Emerging Pathogen SARS-CoV-2 in the Nervous System: A Review on Neurological Impairments and Manifestations. J Mol Neurosci. 2021;71(11):2192-209. DOI: https://doi.org/10.1007/s12031-020-01767-6. PMID: 33464535; PMCID: PMC7814864.

11. Kim MM, Murthy S, Goldman RD. Post-COVID-19 multisystem inflammatory syndrome in children. Can Fam Physician. 2021;67(8):594-6. DOI: https://doi.org/10.46747/cfp.6708594. PMID: 34385205; PMCID: PMC9683428.

12. Kirchberger I, Meisinger C, Warm TD, Hyhlik-Dürr A, Linseisen J, Goblau Y. Post-COVID-19 Syndrome in Non-Hospitalized Individuals: Healthcare Situation 2 Years after SARS-CoV-2 Infection. Viruses. 2023;15(6):1326. DOI: https://doi.org/10.3390/v15061326. PMID: 37376625; PMCID: PMC10303962.

13. Kompaniyets L, Agathis NT, Nelson JM, Preston LE, Ko JY, Belay B, et al. Underlying Medical Conditions Associated With Severe COVID-19 Illness Among Children. JAMA Netw Open. 2021;4(6): e2111182. DOI: https://doi.org/10.1001/jamanetworkopen.2021.11182. PMID: 34097050; PMCID: PMC8185607.

14. Krawczuk K, Czupryna P, Pancewicz S, Oldak E, Moniuszko-Malinowska A. Selected viral neuroinfections in children. Pol Merkur Lekarski. 2019;46(272):88-93. PMID: 30830896.

15. Lacinel Gurlevik S, Gunbey C, Ozsurekci Y, Oygar PD, Kesici S, Gocmen R, et al. Neurologic manifestations in children with COVID-19 from a tertiary center in Turkey and literature review. Eur J Paediatr Neurol. 2022;37:139-54. DOI: https://doi.org/10.1016/j.ejpn.2022.02.003. PMID: 35287009; PMCID: PMC8853984.

16. Lopes TRR, Sitton BS, Pillat MM, Mello CF, Weiblen R, Flores EF, et al. SARS-CoV-2 and neurotropism: evidence, gaps and reflections. J Med Microbiol. 2025;74(6):002016. DOI: https://doi.org/10.1099/jmm.0.002016. PMID: 40522851; PMCID: PMC12171017.

17. Lechner-Scott J, Levy M, Hawkes C, Yeh A, Giovannoni G. Long COVID or post COVID-19 syndrome. Mult Scler Relat Disord. 2021;55:103268. DOI: https://doi.org/10.1016/j.msard.2021.103268. PMID: 34601388; PMCID: PMC8447548.

18. Maury A, Lyoubi A, Peiffer-Smadja N, de Broucker T, Meppiel E. Neurological manifestations associated with SARS-CoV-2 and other coronaviruses: A narrative review for clinicians. Rev Neurol (Paris). 2021;177(1-2):51-64. DOI: https://doi.org/10.1016/j.neurol.2020.10.001. PMID: 33446327; PMCID: PMC7832485.

19. Pang Z, Tang A, He Y, Fan J, Yang Q, Tong Y, Fan H. Neurological complications caused by SARS-CoV-2. Clin Microbiol Rev. 2024;37(4): e0013124. DOI: https://doi.org/10.1128/cmr.00131-24. PMID: 39291997; PMCID: PMC11629622.

20. Ray STJ, Abdel-Mannan O, Sa M, Fuller C, Wood GK, Pysden K, et al. Neurological manifestations of SARS-CoV-2 infection in hospitalised children and adolescents in the UK: a prospective national cohort study. Lancet Child Adolesc Health. 2021;5:631-41. DOI: https://doi.org/10.1016/s2352-4642(21)00193-0. PMID: 34273304; PMCID: PMC8279959.

21. Soriano JB, Ancochea J. On the new post COVID-19 condition. Arch Bronconeumol. 2021;57(12):735-6. DOI: https://doi.org/10.1016/j.arbres.2021.04.001. PMID: 34703072; PMCID: PMC8531201.

22. Taba P, Schmutzhard E, Forsberg P, Lutsar I, Ljostad U, Mygland A, et al. EAN consensus review on prevention, diagnosis and management of tick-borne encephalitis. Eur J Neurol. 2017;24(10):1214-e61. DOI: https://doi.org/10.1111/ene.13356. PMID: 28762591.

23. Tyler KL. Herpes simplex virus infections of the central nervous system: encephalitis and meningitis, including Mollaret's. Herpes. 2004;11(2):57A-64A. PMID: 15319091.

24. Woodruff RC, Campbell AP, Taylor CA, Chai SJ, Kawasaki B, Meek J, et al. Risk Factors for Severe COVID-19 in Children. Pediatrics. 2022;149(1): e2021053418. DOI: https://doi.org/10.1542/peds.2021-053418. PMID: 34935038; PMCID: PMC9213563.

25. Zhang Y, Chen X, Jia L, Zhang Y. Potential mechanism of SARS-CoV-2-associated central and peripheral nervous system impairment. Acta Neurol Scand. 2022;146(3):225-36. DOI: https://doi.org/10.1111/ane.13657. PMID: 35699161; PMCID: PMC9349396.

ВПЛИВ ПАНДЕМІЇ ІНФЕКЦІЇ SARS-COV-2 (COVID-19) НА СТРУКТУРУ (НОЗОМОРФОЗ) НЕВРОПАТОЛОГІЇ У ДІТЕЙ

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Резюме.

Пандемія інфекції SARS-CoV-2 (COVID-19) залишається глобальною проблемою, яка впливає на економічні, демографічні, культурологічні, наукові та медичні аспекти сучасного життя. Аналіз актуальної медичної літератури, що присвячена питанням інфекції SARS-CoV-2, баз Web of Science, PubMed доводить, що сучасні наукові дослідження повинні бути спрямовані на визначення тягаря цієї пандемії. Вивчення наслідків пандемії інфекції COVID-19 у дітей повинне продовжуватись для вдосконалення профілактичних стратегій, визначення груп високого ризику та забезпечення оптимального лікування. Характеристика нозоморфозу в невропатології є необхідною для того, щоб системи охорони здоров'я та медицини могли ефективно реагувати на виклики, пов'язані з пандемією COVID-19. Визначення нозоморфозу нейропатології має важливе значення в реагуванні системи громадського здоров'я і медицини на виклики, що поставила пандемія COVID-19 і повинне включати зміни на інституціональному (адаптація структур закладів охорони здоров'я, спрямування інвестицій, втілення інновацій, зміни в освітньо-професійних програмах навчальних медичних закладах тощо) та персональному (підвищення професійної кваліфікації, просвітницька діяльність, адвокація вакцинації тощо) рівнях.

Мета: Визначити вплив пандемії інфекції SARS-CoV-2 (COVID-19) на структуру (нозоморфоз) нейропатології у дітей, шляхом аналізу госпітальної захворюваності дітей з гострими ураженнями нервової системи у «допандемійний час» та на сучасному етапі.

Матеріали і методи дослідження. Дослідження проведено методом ретроспективного аналізу історій хвороб дітей, яких було госпіталізовано з гострими ураженнями центральної та периферійної нервової систем за період з 01.01.2017 по 01.01.2024 роки в Комунальному некомерційному товаристві «Регіональний медичний центр родинного здоров'я» Дніпропетровської обласної Ради» м. Дніпро. Всього для вивчення було відібрано 32 дітей, що підпадали під вище вказані критерії включення, з яких в І-у групу, «допандемійну», потрапило 17 випадків, а у ІІ-у групу, «пандемійну» – 15 випадків. Проводився статистичний аналіз вікових, гендерних співвідношень, тривалості перебування в стаціонарі та структури невропатології у дітей у «допандемійний час» та на сучасному етапі. Протокол дослідження ухвалено Локальним етичним комітетом зазначених установ. Дослідження виконано відповідно до принципів Гельсінської декларації. На проведення дослідження отримано інформовану згоду. Для статистичного аналізу результатів застосовувалися методи описової та аналітичної статистики. Нормальність розподілу перевіряли за критеріям Шапіро-Уілка. При нормальному розподілі дані подано як M та 95% довірчий інтервал (95% ДІ), при відмінному від нормального – як Me (25%–75%). Для порівняння двох незалежних вибірок використовувався t-тест (Ст'юдента) або U-тест Манна-Уїтні залежно від типу розподілу. Порівняння відносних величин здійснювали за допомогою χ^2-тесту (Пірсона) з поправкою Йейтса. Статистична обробка проводилася за допомогою Microsoft Excel Microsoft Excel та програмного забезпечення trial software TIBCO Statistica™ 14.0.0. Статистично значущими вважали відмінності при $p<0,05$, а тенденції фіксувалися при $0,05\leq p<0,5$. Робота виконана в рамках НДР «Визначення епігенетичних факторів, що впливають на формування набутого імунітету при гострих та хронічних інфекційних захворюваннях у дітей та дорослих», Шифр НДР: ІН.01.22, № держ. реєстрації 0122U001998 Термін виконання: 2022-2026 рр.

Результати досліджень. В проведеному дослідженні у допандемічний період домінували бактеріальні менінгіти (41,2%) і це зумовлювало переважання бактеріальної етіології нейроінфекцій (52,9%). Серед збудників вірусного енцефаліту в даній групі переважали герпетичні енцефаліти (B00.4), які реєструвались у 17,6%. У постковідний період, згідно наших досліджень, простежується зсув структури уражень у бік вірусних (40,0%) та неуточнених (46,7%) форм при суттєвому зниженні частки бактеріальних (13,3%). Переважну кількість дітей в обох групах складали діти віком до двох років (59% та 40% в І та ІІ групах відповідно).

Висновки. При клінічному порівнянні особливостей перебігу нейроінфекцій у пацієнтів в доковідний та постковідний час виявлено, що в структурі захворюваності на нейроінфекції у дітей в постковідний період стали переважати поствірусні енцефаліти, а кількість бактеріальних менінгоенцефалітів значно знизилась у порівнянні з доковідним періодом. За етіологічною структурою відмічається статистична відмінність між групами на рівні тенденції, що свідчить про можливу постковідну трансформацію етіології нейроінфекцій у дітей, та потребує подальших досліджень. Потребує також подальшого вивчення вплив пандемії SARS-CoV-2 на дітей, особливо грудного та переддошкільного віку, які перенесли захворювання з важким перебігом та з ускладненнями з боку нервової системи й можливим подальшим розвитком постковідного синдрому.

Ключові слова: пандемія COVID-19; структура невропатології; нозоморфоз; діти.

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