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RESEARCH LETTER

Neurologic complications of influenza requiring pediatric intensive care: a multicenter study

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INTRODUCTION

Influenza is a common viral infection associated primarily with respiratory symptoms; however, neurologic complications may occur in a subset of pediatric patients and can lead to severe morbidity and mortality. Reported neurologic manifestations include febrile seizures, status epilepticus, encephalopathy, encephalitis, acute necrotizing encephalopathy, acute disseminated encephalomyelitis, stroke, and other neuroinflammatory syndromes.[1,2]

Although most children with influenza recover uneventfully, severe neurologic involvement may require admission to pediatric intensive care units (ICUs). Recent reports have highlighted increasing recognition of influenza-associated encephalopathy and acute necrotizing encephalopathy in children, particularly during the post-COVID-19 period.[3,4] However, multicenter data describing critically ill pediatric patients with influenza-associated neurologic complications remain limited.

In this multicenter study, we aimed to describe the clinical characteristics, organ dysfunction patterns, management strategies, and short-term outcomes of children admitted to pediatric ICUs with influenza-associated neurologic complications and to explore potential differences between influenza A and influenza B infections.

METHODS

This multicenter retrospective study included children aged 1 month to 18 years with laboratory-confirmed influenza and neurologic complications admitted to nine pediatric ICUs in Istanbul, Turkey, between July 2022 and April 2025. We confirmed influenza infection by polymerase chain reaction testing. We defined neurologic complications as seizures, encephalopathy, or encephalitis occurring within 5 days of influenza-like illness onset without an alternative etiology. We defined encephalopathy as altered mental status lasting ≥ 24 hours, and encephalitis as encephalopathy accompanied by at least two of the following: fever, focal neurologic findings, cerebrospinal fluid pleocytosis, electroencephalographic abnormalities, or neuroimaging findings suggestive of inflammation or infection. We included only children with influenza-associated neurologic complications aged 1 month to 18 years. Therefore, we excluded patients without neurologic involvement and neonates.

We retrospectively collected clinical, laboratory, treatment, and outcome data from medical records using standardized case report forms. Organ dysfunctions were defined according to standardized pediatric critical care criteria, including

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Kidney Disease: Improving Global Outcomes (KDIGO) criteria for renal failure and vasoactive support requirement for hemodynamic failure.[5] Illness severity was assessed using the Pediatric Risk of Mortality III (PRISM III) score[6] and Pediatric Glasgow Coma Scale (pGCS)[7] within the first 24 hours of pediatric ICU admission.

Categorical variables were compared using Pearson's Chi-squared or Fisher's exact test, while continuous variables were analyzed using the independent samples t-test or Mann-Whitney U test, as appropriate. A two-sided p value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 30.0 (IBM Corp., Armonk, NY, USA).

The local Ethics Committee approved the study (KAEK/2025.02.35), and the study was conducted in accordance with the Declaration of Helsinki. Because this was a retrospective study, the Ethics Committee waived the requirement for informed consent.

RESULTS

A total of 44 children with laboratory-confirmed influenza-associated neurologic complications were included, including 32 influenza A and 12 influenza B cases. Median age was 4.13 years (interquartile range [IQR] 1.62 - 7.82), and 65.9% were male. Influenza vaccination rates were low in both groups (6.8% overall).

Seizures (86.4%) and altered consciousness (70.5%) were the most common neurologic manifestations. Reasons for pediatric ICU admission differed between groups (p = 0.014): encephalopathy and encephalitis were more frequent among influenza A patients, whereas sepsis/multiorgan dysfunction syndrome and pneumonia/acute respiratory distress syndrome were more common in Influenza B cases. Mortality was 4.5% overall.

All patients received oseltamivir. Influenza B patients more frequently received corticosteroids, therapeutic plasma exchange, and inotropic support. Renal failure (41.7% *versus* 3.1%; p < 0.001) and hemodynamic failure (41.7% *versus* 12.9%; p = 0.038) were also more common in Influenza B cases.

Magnetic resonance imaging abnormalities were detected in 43.2% of patients, including restricted diffusion, hemorrhagic lesions, and necrotic changes. Acute necrotizing encephalopathy and acute disseminated encephalomyelitis were observed only in Influenza A patients. Electroencephalographic abnormalities were present in 29.5% of cases (Table 1).

Table 1 - Clinical characteristics, organ dysfunction, and outcomes of children with influenza-associated neurologic complications

Parameter	Influenza A (n = 32)	Influenza B (n = 12)	Total (n = 44)	p value
Age (years)	3.77 (1.65 - 8.56)	5.36 (1.46 - 7.57)	4.13 (1.62 - 7.82)	0.990
Male sex	19 (59.4)	10 (83.3)	29 (65.9)	0.127
Influenza vaccination	2 (6.3)	1 (8.3)	3 (6.8)	0.807
Convulsions	29 (90.6)	9 (75.0)	38 (86.4)	0.179
Altered consciousness	20 (62.5)	11 (91.7)	31 (70.5)	0.059
Primary reason for pediatric ICU admission				
Encephalopathy	11 (34.4)	0 (0.0)	11 (25.0)	0.014*
Status epilepticus	7 (21.9)	3 (25.0)	10 (22.7)	
Sepsis/MODS	1 (3.1)	4 (33.3)	5 (11.4)	
Others	13 (40.6)	5 (41.7)	18 (40.9)	
Renal failure	1 (3.1)	5 (41.7)	6 (13.6)	< 0.001*
Hemodynamic failure	4 (12.9)	5 (41.7)	9 (20.9)	0.038*
MRI abnormalities	14 (43.8)	5 (41.7)	19 (43.2)	0.897
EEG abnormalities	11 (34.4)	2 (16.7)	13 (29.5)	0.187
Neurologic/behavioral sequelae at discharge	13 (40.6)	6 (50.0)	19 (43.2)	0.113
Mortality	1 (3.1)	1 (8.3)	2 (4.5)	0.460

ICU - intensive care unit; MODS - multiorgan dysfunction syndrome; MRI - magnetic resonance imaging; EEG - electroencephalography. We used the Mann-Whitney U test and Pearson Chi-squared test as appropriate. * Statistical significance. Results expressed as mean (interquartile range) or n (%).

DISCUSSION

In this multicenter cohort of children admitted to pediatric intensive care units with influenza-associated neurologic complications, seizures, encephalopathy, and altered consciousness were the predominant clinical manifestations. Despite relatively low overall mortality (4.5%), nearly one-third of survivors experienced neurologic or behavioral sequelae at hospital discharge, underscoring the substantial morbidity associated with severe neuroinfluenza. Similar rates of persistent neurologic impairment have been reported in previous multicenter pediatric studies of influenza-associated encephalopathy.[8]

Recent surveillance reports from the Centers for Disease Control and Prevention have highlighted increasing recognition of influenza-associated encephalopathy and acute necrotizing encephalopathy in children during recent influenza seasons.[9,10] In our cohort, acute necrotizing encephalopathy was observed exclusively in influenza A patients, whereas influenza B cases more commonly demonstrated systemic and multiorgan involvement, including renal and hemodynamic dysfunction. However, these findings should be interpreted cautiously given the limited number of influenza B cases and the descriptive nature of the analysis.

Our findings are consistent with previous reports demonstrating that severe neurologic involvement in pediatric influenza is frequently associated with critical illness and organ dysfunction.[11-13] The high frequency of neurologic sequelae observed in our study further emphasizes the need for early recognition and close neurologic follow-up in affected children.

Comparisons between influenza A and influenza B subgroups should be considered exploratory and hypothesis-generating because of the limited sample size and multiple comparisons.

Several limitations should be acknowledged, including the retrospective design, relatively small sample size, lack of standardized long-term neurologic follow-up, and potential heterogeneity in treatment approaches across participating centers. In addition, the absence of a control group precludes causal inference and limits interpretation of differences between influenza A and B infections.

Despite these limitations, this study represents one of the largest multicenter pediatric ICU cohorts of pediatric influenza-associated neurologic complications reported from Turkey. Larger prospective studies are needed to better define prognostic factors and long-term neurologic outcomes in critically ill children with neuroinfluenza.

ETHICS APPROVAL

This multicenter retrospective study was approved by the Ethics Committee of the University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul, Turkey (approval No: KAEK/2025.02.35). We obtained institutional permissions for data use from all participating centers. Because of the study's retrospective design, the Ethics Committee waived the requirement for written informed consent. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

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AUTHORS' CONTRIBUTIONS

N. Akçay: conceptualization, study design, data collection, writing - original draft, writing - review & editing; I. Bingöl and D. Tosun: conceptualization, study design, data collection; M. Duyu, L. Telhan, O. Umur, G. Şık, M. E. Menentoğlu, C. Bilgün and E. Aygüler: data collection, data curation, writing - review & editing; A. Özel and S. Yüce: formal analysis, statistical analysis, writing - review & editing. All authors reviewed and approved the final version of the manuscript.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

The authors declare that no Artificial Intelligence tools were used in the preparation of this manuscript.

Publisher's note

Conflicts of interest: None.

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REFERENCES

1. Nayak J, Hoy G, Gordon A. Influenza in children. Cold Spring Harb Perspect Med. 2021;11(1):a038430.
2. Ekstrand JJ. Neurologic complications of influenza. Semin Pediatr Neurol. 2012;19(3):96-100.
3. Uyeki TM, Hui DS, Zambon M, Wentworth DE, Monto AS. Influenza. Lancet. 2022;400(10353):693-706.
4. Cleuziou P, Renaldo F, Renolleau S, Javouhey E, Tissieres P, Léger PL, et al.; Groupe Francophone de Réanimation et Urgences Pédiatriques (GFRUP). Mortality and neurologic sequelae in influenza-associated encephalopathy: retrospective multicenter PICU cohort in France. Pediatr Crit Care Med. 2021;22(11):e582-7.
5. Kellum JA, Lameire N, Aspelin P, Barsoum RS, Burdmann EA, Goldstein SL, et al. Kidney disease: improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012;2(1):1-138.
6. Pollack MM, Patel KM, Ruttimann UE. PRISM III: an updated Pediatric Risk of Mortality score. Crit Care Med. 1996;24(5):743-52.
7. Reilly PL, Simpson DA, Sprod R, Thomas L. Assessing the conscious level in infants and young children: a paediatric version of the Glasgow Coma Scale. Childs Nerv Syst. 1988;4(1):30-3.
8. Fazal A, Reinhart K, Huang S, Kniss K, Olson SM, Dugan VG, et al. Reports of encephalopathy among children with influenza-associated mortality - United States, 2010-11 through 2024-25 influenza seasons. MMWR Morb Mortal Wkly Rep. 2025;74(6):91-5.
9. Fazal A, Harker EJ, Neelam V, Olson SM, Rolfes MA, Reinhart K, et al.; CDC Influenza-Associated Encephalopathy Collaborators. Pediatric influenza-associated encephalopathy and acute necrotizing encephalopathy - United States, 2024-25 influenza season. MMWR Morb Mortal Wkly Rep. 2025;74(36):556-64.
10. Frankl S, Coffin SE, Harrison JB, Swami SK, McGuire JL. Influenza-associated neurologic complications in hospitalized children. J Pediatr. 2021;239:24-31.e1.
11. Yu MK, Leung CP, Wong WH, Ho AC, Chiu AT, Zhi HH, et al. Clinical spectrum and burden of influenza-associated neurological complications in hospitalised paediatric patients. Front Pediatr. 2022;9:752816.
12. Lin CH, Chen CH, Hong SY, Lin SS, Chou IC, Lin HC, et al. Comparison of severe pediatric complicated influenza patients with and without neurological involvement. Medicine (Baltimore). 2021;100(17):e25716.
13. Bi J, Wu X, Deng J. Mortality risk factors in children with influenza-associated encephalopathy admitted to the paediatric intensive care unit between 2009 and 2021. J Paediatr Child Health. 2024;60(9):456-61.