Journal of Infection 90 (2025) 106424

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Letter to the Editor

Is the pathogen spectrum of encephalitis/meningitis changing in China?

We have thoroughly read several recent reports in this journal addressing the spectrum of pathogens identified in the cerebrospinal fluid of patients with encephalitis or meningitis.[1–3] The findings presented in these studies offer critical insights into the etiological underpinnings of these conditions. In 2020, the World Health Organization (WHO) released the "Defeating Meningitis by 2030" initiative. Through the efforts of scientists worldwide, the incidence and mortality of meningitis have significantly decreased. Timely understanding of the dynamic spectrum of encephalitis/meningitis pathogens within one's country is crucial for epidemic control. Considering that the last large-scale study of encephalitis/meningitis pathogens in China was conducted from 2009 to 2018,[4] we performed pathogen detection analysis using targeted next-generation sequencing (tNGS) on cerebrospinal fluid samples from 229 patients with encephalitis/meningitis from 18 provinces between 2018 and 2021 (Fig. 1 and Supplementary Table 1).

The detailed methodology can be found in the Supplementary Method. In essence, samples were subjected to a five-in-one mixture, followed by the utilization of tNGS to detect putative pathogenic reads. Subsequently, qPCR assays were performed on the five original samples of tNGS-positive library, and we included the results consistent between the two methods in the outcome. Ultimately, at least one pathogen was found positive in 34 samples (14.85%) (Supplementary Table 2). Among them, 2 samples tested positive for 2 pathogens simultaneously. A total of 23 samples (23/34, 67.65%) tested positive for viruses, with the main viruses detected being Enterovirus (EV) and Herpes simplex virus 1 (HSV1) (Table 1). 12 samples (12/34, 35.29%) tested positive for bacteria, with the detection rates ranking as *Streptococcus pneumoniae*, *Listeria monocytogenes*, *Brucella*, *Pseudomonas aeruginosa*, *Escherichia coli* (Table 1).

There were some differences between the pathogen spectrum of meningitis from 2018 to 2021 and the results of previous studies. In the study from 2009 to 2018, the detection rates of viruses were EV > Japanese encephalitis virus (JEV) > Herpes simplex virus (HSV) > Mumps Virus (MuV), and the detection rates of bacteria were *Neisseria meningitidis* > *Streptococcus pneumoniae* > *Staphylococcus aureus* > *Escherichia coli* > *Streptococcus suis* > *Haemophilus influenzae type b* > *Mycobacterium tuberculosis*.[4] Among these, the detection rate of EV was the highest in children aged 5–17. Compared to previous studies, HSV1 and EV remained the main sources of virus positivity from 2018 to 2021; however, JEV and MuV were not detected in this sample. Moreover, recent studies on meningitis cases in China sporadically showed positivity for JEV or MuV.[5–9] Nine cases (9/11, 81.91%) positive for EV were all in children aged 5–17 years old. In addition, tNGS determined the types of EV, including Echovirus 30 (6/11, 54.54%), Echovirus 7 (2/11, 18.18%), Coxsackie B5 (2/11, 18.18%), Echovirus 18 (2/11, 9.09%). A recent serological study on enterovirus-related meningitis patients also indicated Echovirus 30 as the dominant type.[10] The overall positivity rate of bacteria was relatively low, and *N. meningitidis* was not found. However, thanks to tNGS technology, some pathogens not included in routine testing were revealed, such as Varicella-zoster virus (VZV), Human adenovirus type 41 (HAdV-41), Herpes simplex virus 2, Epstein-Barr virus (EB), Hepatitis B virus (HBV), *L. monocytogenes*, *Brucella*, *P. aeruginosa*.

In conclusion, we provided data on the pathogen spectrum of encephalitis/meningitis in China from 2018 to 2021. HSV1 and EV remained the main positive viruses. However, there are also some significant changes compared to previous data, such as the absence of JEV, MuV, or *N. meningitidis* traces in these samples. This phenomenon can be attributed to the widespread vaccination against such pathogens in recent years, resulting in a significant decrease in incidence. This data can provide a reference for clinical testing and vaccine development in the global encephalitis/meningitis prevention and control process.

https://doi.org/10.1016/j.jinf.2025.106424

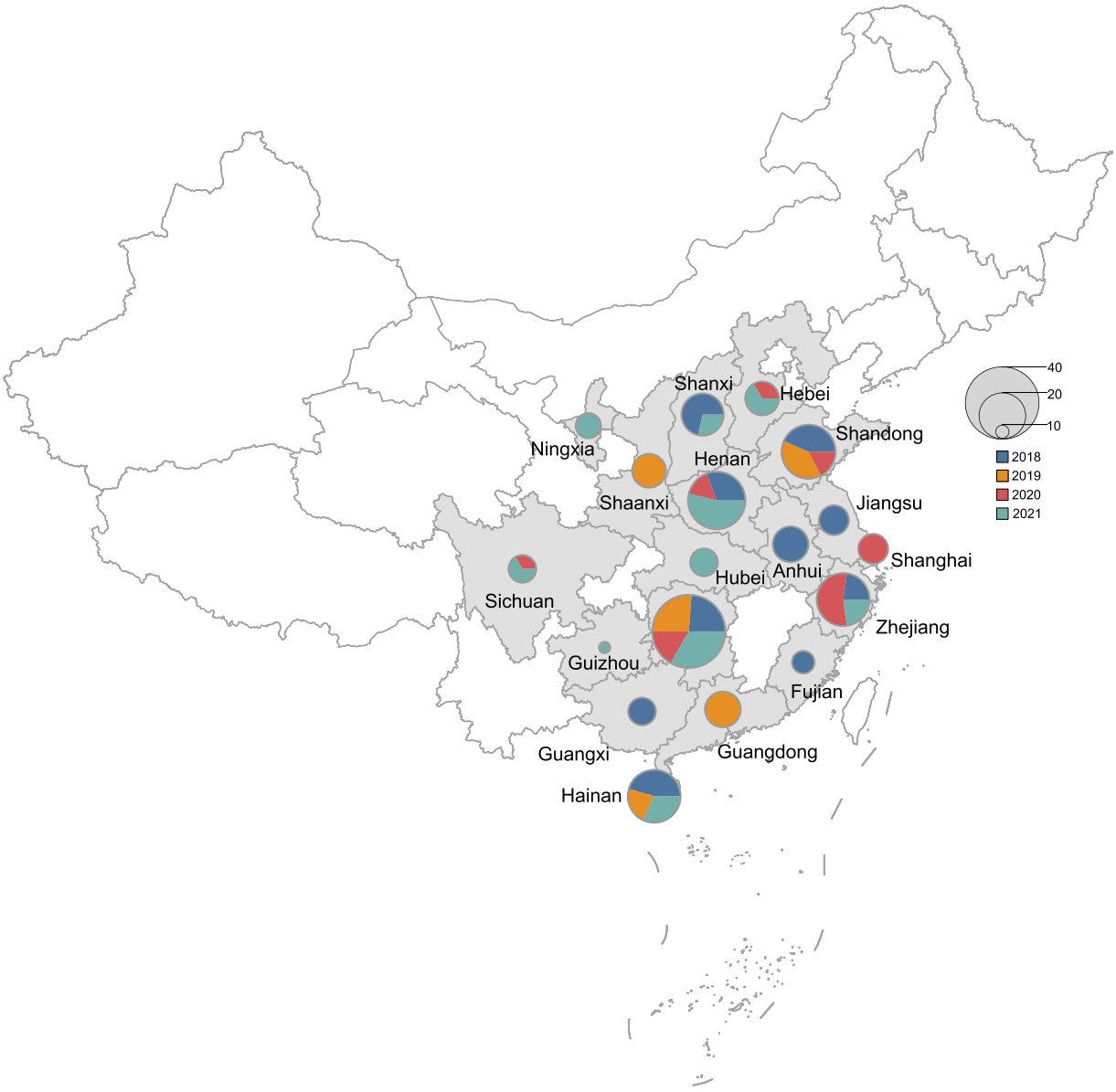

Fig. 1. Overview of sampling information. Dark background blocks indicate that sample collection was performed. The size of the pie chart indicates the number of samples, and the color indicates the year information. The map resource is from https://datav.aliyun.com/portal/school/atlas/area_selector (accessed on 12 April 2023), map approval number is GS jing(2022)1061.

Table 1
Positive pathogen -detection results.

Pathogen	Number of Cases (Proportion)
Virus	**23**
Enterovirus	11 (47.83%)
Herpes simplex virus 1	6 (26.09%)
Varicella-zoster virus	2 (8.70%)
Human adenovirus type 41	2 (8.70%)
Herpes simplex virus 2	1 (4.35%)
Epstein-Barr virus	1 (4.35%)
Hepatitis B virus	1 (4.35%)
Bacterium	**12**
Streptococcus pneumoniae	4 (33.33%)
Listeria monocytogenes	3 (25.00%)
Brucella	3 (25.00%)
Pseudomonas aeruginosa	1 (8.33%)
Escherichia coli	1 (8.33%)

The total positive counts were larger than the number of positive patients because of the coinfection.

Ethics approval

Not required.

Funding

This research was funded by the National Key R&D Program of China, grant numbers 2024YFC2311502 and 2022YFC2302700.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We greatly appreciate the contributions of the CDC staff from various provinces and cities in sample collection.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2025.106424.

References

1. Zhou H, Ren X, Li Y, Ji C, Wei X, Huang X, et al. *Microbial landscape in cerebrospinal fluid of suspected intracranial infections based on clinical metagenomics, a multicentre retrospective study. J Infect* 2024:106385.
2. Kadambari S, Abdullahi F, Celma C, Ladhani S. *Epidemiological trends in viral meningitis in England: prospective national surveillance, 2013–2023. J Infect* 2024;**89**(3):106223.
3. Chen W, Liu G, Cui L, Tian F, Zhang J, Zhao J, et al. *Evaluation of metagenomic and pathogen-targeted next-generation sequencing for diagnosis of meningitis and encephalitis in adults: a multicenter prospective observational cohort study in China. J Infect* 2024;**88**(5):106143.
4. Wang LP, Yuan Y, Liu YL, Lu QB, Shi LS, Ren X, et al. *Etiological and epidemiological features of acute meningitis or encephalitis in China: a nationwide active surveillance study. Lancet Reg Health West Pac* 2022;**20**:100361.
5. Xing XW, Zhang JT, Ma YB, He MW, Yao GE, Wang W, et al. *Metagenomic next-generation sequencing for diagnosis of infectious encephalitis and meningitis: a large, prospective case series of 213 patients. Front Cell Infect Microbiol* 2020;**10**:88.
6. Fan G, Li S, Tian F, Yang L, Yi S, Chen S, et al. *RNA-sequencing-based detection of human viral pathogens in cerebrospinal fluid and serum samples from children with meningitis and encephalitis. Microb Genom* 2023;**9**(8).
7. Guo J, Wang Y, Zhang M, Zheng H, Zang Q, Huang P, et al. *Human parvovirus B19 infection in hospitalized patients suspected of infection with pathogenic microorganism. Front Cell Infect Microbiol* 2022;**12**:1083839.
8. Wang YL, Guo XT, Zhu MY, Mao YC, Xu XB, Hua Y, et al. *Metagenomic next-generation sequencing and proteomics analysis in pediatric viral encephalitis and meningitis. Front Cell Infect Microbiol* 2023;**13**:1104858.
9. Liu JJ, Teng LP, Hua CZ, Xie YP, Pan YX, Hu BF, et al. *Etiological analysis of viral encephalitis in children in Zhejiang Province from 2018 to 2019. Diagnostics* 2022;**12**(8):1964.
10. Sun Y, Miao Z, Yan J, Gong L, Chen Y, Chen Y, et al. *Sero-molecular epidemiology of enterovirus-associated encephalitis in Zhejiang Province, China, from 2014 to 2017. Int J Infect Dis* 2019;**79**:58–64.

Ruichen Wang, Qikai Yin, Kai Nie, Fan Li, Shihong Fu, Qianqian Cui, Han Chen, Songtao Xu *, Huanyu Wang *

National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases, NHC Key Laboratory of Biosafety, National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing 102206, China

*Corresponding authors.

E-mail addresses: wangrc96@163.com (R. Wang), yinqk@ivdc.chinacdc.cn (Q. Yin), niekai@ivdc.chinacdc.cn (K. Nie), lifan@ivdc.chinacdc.cn (F. Li), fush@ivdc.chinacdc.cn (S. Fu), cuiqq@ivdc.chinacdc.cn (Q. Cui), zaven1205@163.com (H. Chen), xust@ivdc.chinacdc.cn (S. Xu), wanghy@ivdc.chinacdc.cn (H. Wang).