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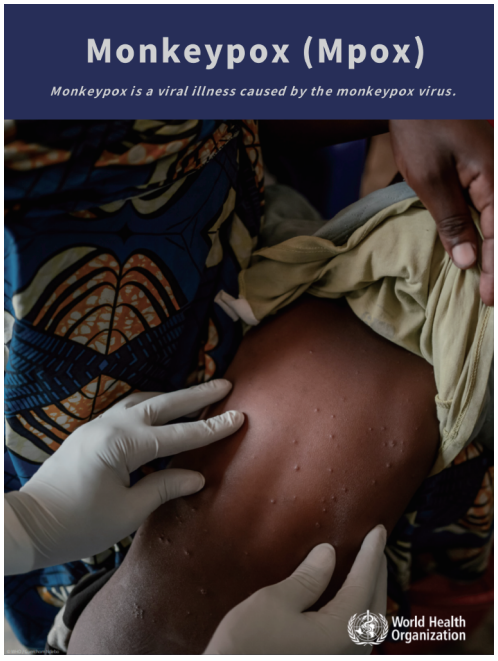

Vital Surveillances

Preplanned Studies

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Vital Surveillances

Comparative Analysis of Epidemiological and Clinical Characteristics Between Mpox Cases with and Without HIV — China, 2023

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ABSTRACT

Objective: This study aimed to analyze the epidemiological characteristics and clinical symptoms of mpox cases with and without human immunodeficiency virus (HIV) reported in China in 2023, providing evidence for coordinated prevention and control strategies for both infections.

Method: All confirmed mpox cases reported in 2023 were extracted from China's Information System for Disease Control and Prevention. Data were collected from the surveillance system and epidemiological investigations. Statistical analyses were performed using SPSS 24.0, with group comparisons conducted using *t*-tests and chi-square tests.

Results: Among 1,712 confirmed mpox cases in China during 2023, 802 (46.8%) were people with human immunodeficiency virus (PWH). Of the 1,702 male cases, 97.3% of PWH and 91.1% of those without HIV self-identified as men who have sex with men (MSM). Age distribution showed 79.4% of PWH and 87.6% of those without HIV were under 40 years old, while 64.2% of PWH and 71.3% of those without HIV were reported from eastern regions. Cardinal symptoms at diagnosis occurred at similar rates between those with and without HIV, including rash (90.9% *vs.* 93.4%), fever (52.5% *vs.* 53.8%), and lymphadenopathy (23.8% *vs.* 25.4%). Among coinfected cases, individuals diagnosed with HIV after mpox or within one year before mpox demonstrated higher rates of immunodeficiency and lower rates of HIV viral suppression.

Conclusion: Male mpox cases with HIV was more likely to be MSM, older, and reported from central and western regions compared to those without HIV. No significant differences were observed in cardinal symptom occurrence between groups. These findings emphasize the importance of implementing integrated prevention strategies targeting both HIV and mpox, particularly among key populations.

Mpox is a zoonotic viral infection transmitted through contact with bodily fluids, skin, or mucosal lesions, respiratory droplets, and contaminated objects (*1*). By the end of 2023, the 2022–2023 global mpox outbreak had resulted in 93,030 laboratory-confirmed cases (*2*). The first imported case in China was reported in Chongqing municipality in September 2022 (*3*). In response to emerging local transmission, the National Disease Control and Prevention published the Guideline on Mpox Prevention and Control in July 2023, and subsequently classified mpox as a category B notifiable communicable disease in September.

People with human immunodeficiency virus (PWH) have been disproportionately affected by mpox, with the World Health Organization (WHO) reports that 52.1% of mpox cases with known HIV status were PWH (*2*). This association stems from two key factors. First, sexual contact has been frequently implicated in mpox transmission (*4*). Men who have sex with men (MSM), who constitute the predominant affected population in the current global mpox outbreak (*5*), are also a key population in HIV transmission. Second, PWH may be more vulnerable to mpox infection and experience more severe symptoms and clinical outcomes due to immunological deficiency (*6*). Given these overlapping transmission routes and the potential for adverse prognosis, coordinated efforts to control HIV and mpox coinfection warrant particular attention. This study aimed to analyze the epidemiological characteristics and clinical symptoms of mpox cases reported in China during 2023, compare outcomes between those with and without

HIV, and provide evidence to support integrated prevention and control strategies for both infections.

METHODS

This study encompassed all laboratory-confirmed mpox cases reported in China during 2023. Data were collected from two primary sources: the internet-based National Infectious Diseases Reporting System and the National HIV/AIDS Case Reporting System. Cases were linked across systems a using unique identification numbers, with all personally identifiable information removed during data processing. The collected data included demographic characteristics (gender, occupation, age), residence code (categorized into eastern, central, and western regions based on geographical distribution and economic development), and reporting dates for both mpox and HIV diagnoses. For HIV-positive cases, additional clinical parameters were collected, including antiretroviral therapy (ART) status, recent HIV RNA copies/mL, and CD4+T lymphocytes (CD4) count within 6 months before or after mpox diagnosis, as recorded by the end of 2023. Clinical symptoms at diagnosis and behavioral information was extracted from epidemiological investigations. Participants who reported male homosexual behaviors in either mpox or HIV investigations were classified as MSM. Statistical analyses were performed using SPSS (version 24.0, IBM Corp., Armonk, NY, USA) and Excel 2019 (Microsoft Corp., WA, USA). Differences between HIV-positive and HIV-negative groups were assessed using *t*-test and chi-square test, with statistical significance set at $P<0.05$.

RESULTS

Among the 1,712 confirmed mpox cases reported in 2023, 802 (46.8%) were PWH. Of the 10 reported female cases, none were HIV positive. Among the 1,702 male cases, 94.0% self-identified as MSM. The mean age of male cases was 33.0±7.2 years, with 83.7% under 40 years old. PWH was significantly older than those without HIV (34.6±6.9 years *vs.* 31.7±7.2 years, $t=8.419$, $P<0.001$). The proportion of PWH among mpox cases was lower in the Eastern region compared Central and Western regions (Table 1).

Hospital-based detection accounted for 93.0% of male mpox cases, with no significant differences between HIV-positive and HIV-negative groups. Among 1,444 cases with available exposure history data, sexual contact with men within 21 days before symptom onset was reported by 98.7% of PWH and 98.1% of HIV-negative cases, though some participants also reported heterosexual contact. Of the 1,274 individuals who provided information about sexual partners, 69.7% reported one partner, 26.7% reported two to four partners and 3.6% reported five or more partners. HIV-negative individuals were more likely to report multiple sexual partners compared to PWH (32.9% *vs.* 27.1%, $\chi^2=4.925$, $P=0.026$).

The predominant clinical manifestations at diagnosis included rash (92.2%), fever (53.2%), lymphadenopathy (24.7%), headache (9.6%), and proctitis (8.3%). The Anogenital rash was reported in 53.1% of cases. No significant differences were observed in cardinal symptoms between individuals with and without HIV, including rash (90.9% *vs.* 93.4%, $\chi^2=3.845$, $P=0.050$), fever (52.5% *vs.* 53.8%, $\chi^2=0.281$, $P=0.596$), and lymphadenopathy (23.8% *vs.* 25.4%, $\chi^2=0.605$, $P=0.437$) (Figure 1).

Analysis of clinical characteristics among mpox and HIV coinfections were stratified by time from HIV to mpox diagnosis (Table 2). Among 802 coinfected cases, 673 (98.4%) were diagnosed with mpox more than one year after HIV diagnosis, 61 (7.6%) within one year following HIV diagnosis, and 57 (7.1%) were diagnosed with HIV after mpox. By the end of 2023, ART coverage reached 96.6% (775/802) among coinfected patients; however, the initiation rate was markedly lower (78.9%) among those diagnosed with HIV after mpox. Of those on ART, 606 (78.2%) had recent viral load results available, with 517 (85.3%) achieving viral suppression (VL<50 copies/mL). Notably, viral suppression rates were substantially lower among those diagnosed with HIV after mpox (24.3%) or within one year before mpox (65.4%). Among 652 cases with recent CD4 count data, 77 (11.8%) exhibited severe immunodeficiency (CD4 count <200 cells/μL). The proportion of severe immunodeficiency was notably higher in cases where HIV was diagnosed after mpox or within one year before mpox.

DISCUSSION

MSM represent the predominant demographic affected by mpox in China, aligning with global epidemiological patterns (*7*). National representative studies conducted in 2022 revealed significant knowledge gaps regarding mpox among both HIV-

TABLE 1. Demographics and epidemiological characteristics of male mpox cases with and without HIV in China.

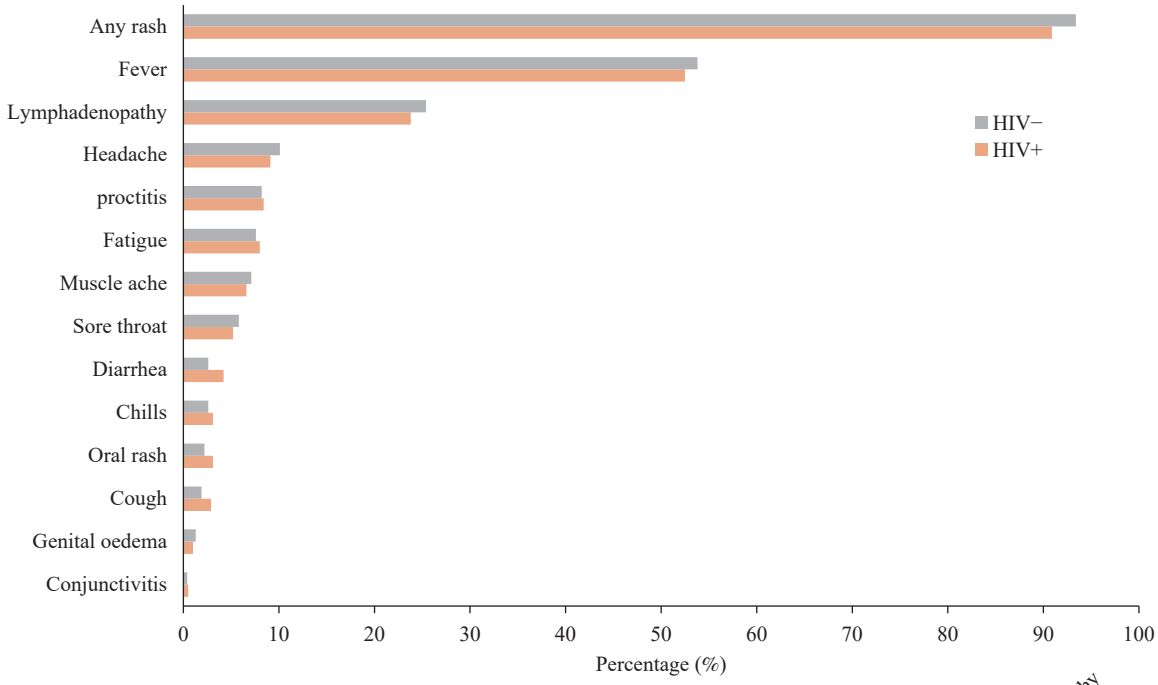
Variable	Total (*N*=1,702)	With HIV (*N*=802)	Without HIV (*N*=900)	Comparisons between those with and without HIV	
				Chi-square	*P*
MSM, *n* (%)					
Yes	1,600 (94.0)	780 (97.3)	820 (91.1)	28.432	<0.001
No	102 (6.0)	22 (2.7)	80 (8.9)		
Age group, *n* (%)					
15–29	652 (38.3)	226 (28.2)	426 (47.3)	69.542	<0.001
30–39	774 (45.5)	411 (51.2)	363 (40.3)		
40–49	238 (14.0)	143 (17.8)	95 (10.6)		
≥50	38 (2.2)	22 (2.7)	16 (1.8)		
Geographical, *n* (%)					
Eastern	1,157 (68.0)	515 (64.2)	642 (71.3)	14.025	<0.001
Central	268 (15.7)	153 (19.1)	115 (12.8)		
Western	277 (16.3)	134 (16.7)	143 (15.9)		
Detection routes, *n* (%)					
Hospital visits	1,528 (89.8)	718 (89.5)	810 (90.0)	0.705	0.703
Close contacts	84 (4.9)	38 (4.7)	46 (5.1)		
Other	90 (5.4)	46 (5.6)	44 (4.9)		
Risk behaviors most likely to cause infection during 21 days preceding symptom onset, *n* (%)					
Sex activities with men	1,421 (83.5)	658 (82.0)	763 (84.8)	5.209	0.157
Sex activities with women	19 (1.1)	7 (0.9)	12 (1.3)		
Non-sexual close contacts	4 (0.2)	1 (0.1)	3 (0.3)		
Declined to disclose	258 (15.2)	136 (17.0)	122 (13.5)		

Abbreviation: HIV=human immunodeficiency virus; MSM=men who have sex with men.

TABLE 2. Clinical characteristics of HIV and mpox coinfected cases by time of HIV diagnosis.

Variable	Total (*n*=802)	Time from HIV diagnosis to mpox diagnosis		
		>1 year (*n*=684)	≤1 year (*n*=61)	HIV after mpox (*n*=57)
Antiretroviral therapy				
Yes	775 (96.6)	673 (98.4)	57 (93.4)	45 (78.9)
No	27 (3.4)	11 (1.6)	4 (6.6)	12 (21.1)
Recent HIV load (copies/mL)				
1–50	517 (85.3)	474 (91.7)	34 (65.4)	9 (24.3)
50–1,000	32 (5.3)	20 (3.9)	6 (11.5)	6 (16.2)
>1,000	57 (9.4)	23 (4.4)	12 (23.1)	22 (59.5)
Recent CD4 count (cells/μL)				
0–199	77 (11.8)	43 (7.9)	20 (36.4)	14 (28.0)
200–349	92 (14.1)	63 (11.5)	15 (27.3)	14 (28.0)
350–500	141 (21.6)	121 (22.1)	8 (14.5)	12 (24.0)
>500	342 (52.5)	320 (58.5)	12 (21.8)	10 (20.0)

Note: Data on HIV viral load and CD4 count were not available for all cases.
Abbreviation: HIV=human immunodeficiency virus.



	Conjunctivitis	Genitaloedema	Cough	Ora rash	Chills	Diarrhea	Sore throat	Muscle ache	Fatigue	Proctitis	Headache	Lymphadenopathy	Fever	Any rash
HIV−	0.4	1.3	1.9	2.2	2.6	2.6	5.8	7.1	7.6	8.2	10.1	25.4	53.8	93.4
HIV+	0.5	1.0	2.9	3.1	3.1	4.2	5.2	6.6	8.0	8.4	9.1	23.8	52.5	90.9

FIGURE 1. Clinical symptoms at diagnosis among male mpox cases with and without HIV. (*n*=1,702)
Abbreviation: HIV=human immunodeficiency virus.

positive and general MSM populations, particularly concerning transmission routes, susceptible populations, and preventive measures (*8*–*9*). This combination of limited awareness and frequent high-risk behaviors have rendered MSM particularly vulnerable to mpox infections. However, the risk of mpox infection is not exclusive to males, as evidenced by ten confirmed female cases and reports of heterosexual transmission among male cases.

The 15–39 age group bears the highest burden of mpox infections, attributable to both their sexual activity patterns and lack of smallpox vaccination following its global eradication.

The absence of significant differences in cardinal symptoms at diagnosis between individuals with and without HIV is likely attributed to China's high ART coverage among PWH. This finding parallels the research from Poland, where no significant clinical differences or complication rates were observed between mpox cases with and without HIV, with 97.7% of HIV-coinfected cases receiving ART (*10*). Previous research indicates that PWH is experiencing severe disease typically were either not receiving ART or presented with late-stage HIV (*5*,*11*). However, symptom analysis in this study was limited to the initial patient complaints at diagnosis, lacking comprehensive follow-up data on disease progression and detailed clinical examinations. Analysis of hospitalized mpox patients in Beijing revealed that some PWH developed severe complications, including pneumonia, bacterial peritonitis, and intestinal obstruction (*12*). Additionally, Nigerian reports indicate that PWH typically experience longer disease duration compared to HIV-negative individuals (*13*).

The epidemiological analysis yields several critical implications for mpox epidemic control. First, targeted knowledge dissemination regarding mpox prevention among key populations, particularly MSM, is essential. This can be achieved through expanded educational initiatives utilizing social media platforms and innovative communication channels to enhance understanding of self-prevention measures. Additionally, given that mpox transmission occurs through close contact, broader public health awareness campaigns are equally crucial. Second, surveillance and case detection capabilities require further

strengthening. While this study found that most mpox cases were identified through hospital visits, research indicates that only 49.3% of cases are diagnosed during initial hospital presentation (*14*). Therefore, focused training for healthcare professionals in dermatology, anorectal medicine, and genitourinary departments could significantly improve case identification and diagnosis rates.

The coinfected cases reveal concerning patterns of late HIV diagnosis and ongoing transmission risk. The finding that approximately 3% of coinfected patients were unaware of their HIV status at mpox diagnosis, combined with low CD4 counts indicating late presentation, suggests persistent gaps in HIV testing awareness and utilization among sexually active MSM. Current HIV sentinel surveillance data shows that only 61.2% of MSM in China had undergone HIV testing and knew their status in the past year (*15*). These findings underscore the urgent need to expand HIV testing coverage and improve early detection strategies among MSM populations in China. For mpox cases with HIV coinfection, prioritizing ART initiation and adherence is crucial, particularly for those who have not yet achieved viral suppression.

The findings underscore the necessity of integrating HIV and mpox surveillance and prevention efforts among high-risk populations, particularly MSM. This integration should occur across three key domains: First, health promotion and behavioral interventions for both mpox and HIV should be combined to enhance risk perception among key populations. Mpox education and intervention strategies can be effectively incorporated into existing HIV services, including voluntary counseling and testing, follow-up care, and ART for PWH. Second, HIV screening should be prioritized for individuals being evaluated for mpox with unknown HIV status, with appropriate follow-up testing to exclude window period infections when initial results are negative. Third, when PWH is diagnosed with mpox, comprehensive consultations should address ongoing HIV transmission risk through strategies such as promoting consistent condom use, ensuring ART adherence, and facilitating timely HIV screening or post-exposure prophylaxis for sexual partners.

This research presents the first national epidemiological profile of mpox and HIV coinfection in China, documenting both epidemiological characteristics and clinical symptoms. However, several limitations warrant consideration. First, the analysis relies on surveillance system data, and mpox cases may be underreported due to its typically self-limiting nature and mild symptomatology. Second, exposure history and symptom data were collected through self-reporting at diagnosis, introducing potential information bias. Despite these limitations, this research provides valuable insights for developing integrated approaches to prevent and control both infections.

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Vital Surveillances

Epidemiological Characteristics of Human Respiratory Syncytial Virus in Children with Acute Respiratory Infection — Shijiazhuang City, Hebei Province, China, 2021–2023

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ABSTRACT

Introduction: Human respiratory syncytial virus (HRSV) is the predominant respiratory pathogen causing acute respiratory tract infection (ARTI). Globally, HRSV infection represents the leading cause of acute respiratory morbidity and hospitalization in children under 2 years of age. HRSV infection continues to pose a significant public health challenge worldwide. Through epidemiological surveillance of HRSV in children with ARTI, we can elucidate its incidence patterns and epidemic characteristics to inform evidence-based prevention and control strategies.

Methods: We collected upper and lower respiratory tract specimens and clinical data from children under 14 years of age with ARTI. HRSV was detected using Real-time Polymerase Chain Reaction to analyze its incidence and epidemic characteristics.

Results: Among 1,440 specimens, the overall HRSV detection rate was 7.8% (HRSVA and HRSVB detection rates were 4.0% and 3.8%, respectively). Detection rates peaked in spring (12.2%), followed by winter (10.3%), with the lowest rates in autumn (2.8%) (P<0.05). HRSVB was the dominant subtype throughout 2021, while HRSVA predominated during 2022 and the first half of 2023. Detection rates were significantly higher in children under 5 years compared to older children, with lower respiratory tract infections in the 0–2 years age group showing notably higher detection rates (18.1%) than upper respiratory tract infections (8.1%) (P<0.05).

Conclusions: HRSV exhibited consistent circulation among children with ARTI in the Shijiazhuang area from 2021 to 2023, characterized by winter and spring outbreaks and alternating predominance of subtypes A and B. Infections predominantly affected children under 5 years of age.

Acute respiratory tract infections (ARTIs), encompassing both the upper and lower respiratory tract infections (RTIs) (*1–3*), represent a significant cause of morbidity and mortality in children under five years of age, particularly in developing countries (*4*). Approximately 85% of children worldwide experience an ARTI annually. While multiple pathogens can cause ARTIs, viruses are responsible for nearly 90% of cases in children (*2*,*5*). Human respiratory syncytial virus (HRSV) stands as the primary etiologic agent of acute lower RTIs in pediatric patients, characterized by rapid onset, high transmissibility, early non-specific presentations, and a propensity for seasonal and regional epidemics. The severity of the clinical manifestations correlate directly with viral load. Furthermore, HRSV has garnered substantial attention due to its considerable disease burden, being associated with approximately three million hospitalizations and over 100,000 deaths annually in children younger than 5 years globally (*5*). Epidemiological surveillance of the HRSV in children with ARTI enables understanding of its incidence and epidemic patterns, thereby providing an evidence base for prevention and control strategies. To this end, we analyzed HRSV distribution patterns in children with ARTI from 2021–2023.

METHODS

This study employed sentinel surveillance at four monitoring sites in Shijiazhuang City, Hebei Province, China: the Second and Fourth Hospitals of Hebei Medical University, Hebei Provincial Children's Hospital, and Lu Quan District People's Hospital. We collected throat swabs from 20 children with upper RTIs and alveolar lavage fluid samples from 20 children with lower RTIs monthly from 2021 to 2023,

yielding 1,440 total cases. All participants met the case definitions and underwent standardized epidemiological investigations with completed case investigation forms. Upper RTI samples were collected from all four sentinel hospitals, with 4–6 samples randomly obtained weekly per site. Lower RTI samples were exclusively collected from Hebei Children's Hospital, with 4–6 samples randomly collected weekly. Inclusion criteria required patients to be ≤14 years old and permanent residents of Shijiazhuang City. All samples were tested specimens were analyzed using a one-step respiratory multiple detection kit (Hangzhou Newrosimin Biotechnology Co., Ltd) to test for human parainfluenza virus (HPIV), influenza virus (IFV), adenovirus (ADV), HRSVA/B, rhinovirus (HRV), human enterovirus, human Boca virus (HBoV), human metapneumovirus, coronavirus OC43/HKU1/229E/NL63, and severe acute respiratory syndrome coronavirus-2.

RESULTS

A total of 112 HRSV-positive cases were detected out of the 1,440 specimens, with a detection rate of 7.8%. The detection rates of upper and lower respiratory tract specimens were 6.9% and 8.6%, respectively. There were 23 cases of coinfection (only detected in cases of lower RTIs), including 19 cases of double infection and 4 cases of triple infection. Coinfections with Human bocavirus and influenza virus were the most common (Table 1).

The detection rate of HRSV was the highest in the spring (12.2%), followed by the winter (10.3%), and was lowest in the autumn (2.8%) (P<0.05). Among the upper RTIs, HRSV infection was more common in the spring (14.4%). Lower RTIs were more common in the winter and spring (13.3% and 10.3%) (P<0.05). HRSV rates were the highest in the spring, summer and winter of 2021 (10.0%, 12.5%, and 10.8%), the winter and spring of 2022 (15.8%, 10.0%), and the spring of 2023 (16.7%) (Table 2 and Table 3) . Peak HRSV detection in the spring and summer of 2021 was mainly caused by HRSV-B infection (and was mainly lower RTI cases). Upper RTIs detected in the winter of 2021 were largely caused by HRSVA+HRSVB, and lower RTIs at this time were mainly caused by HRSVA. The spring 2022 peak was mainly caused by HRSVA+HRSVB (and was mainly upper RTIs). The winter 2022 peak and spring 2023 peak were mainly caused by HRSVA infections (Figure 1).

TABLE 1. Detection of HRSV coinfection in children with ARTI.

Coinfection	Mixed type	Number
Double infection	HRSV+ADV	1
	HRSV+IFV	4
	HRSV+HBoV	5
	HRSV+HPIV	3
	HRSV+HRV	3
	HRSV+EV	1
	HRSV+OC43	2
Triple infection	HRSV+HBoV+IFV	2
	HRSV+HPIV+HRV	1
	HRSV+HBoV+HRV	1

Abbreviation: HRSV=human respiratory syncytial virus; ARTI= acute respiratory tract infection; ADV=adenovirus; IFV=influenza virus; HBoV=human Boca virus; HPIV=human parainfluenza virus; HRV=rhinovirus; EV=human enterovirus; OC43=coronavirus OC43.

As age increased, the HRSV detection rate gradually decreased, with the highest detection rate in the 0 to 1 year group (13.9%), followed by the >1 to 2 years group (11.0%). The detection rate in the >2 to 5 years group is 9.5%, while the detection rate in the age group over 5 years old is the lowest (4.1%) (P<0.05). Additionally, the detection rate of lower RTIs in children in 0 to 2 years group (18.1%, 25/138) was much higher than the detection rate of upper RTIs in the same age group (8.1%, 18/223) (P<0.05). In patients who were in 0 to 2 years group, there was no significant difference in the detection rate of the HRSVA and HRSVB subtype in upper *vs.* lower (Table 4).

DISCUSSION

This study analyzed 1,440 specimens collected from children under 14 years of age with ARTI in Shijiazhuang City, Hebei Province, China, between 2021 and 2023. The overall HRSV detection rate was 7.8% (112 positive specimens). A clear pattern of subtype dominance emerged, with HRSVB predominating throughout 2021, followed by HRSVA dominance during 2022 and the first half of 2023, demonstrating alternating subtype prevalence. While HRSV typically exhibits winter and spring seasonality, we observed an unusual summer epidemic in 2021. This out-of-season outbreak aligns with a globally observed phenomenon where HRSV cases initially decreased during the coronavirus disease in 2019 (COVID-19) pandemic restrictions but subsequently

TABLE 2. Seasonal distribution of HRSV in children with ARTI in Shijiazhuang City, Hebei Province, China, 2021–2023.

Detection rate	Spring *n* (%)	Summer *n* (%)	Autumn *n* (%)	Winter *n* (%)	χ^2	*P*
Total detection rate (*N*=360)	44 (12.2)	21 (5.8)	10 (2.8)	37 (10.3)	27.496	<0.001
Detection rate of upper RTIs (*N*=180)	26 (14.4)	7 (3.9)	4 (2.2)	13 (7.2)	24.501	<0.001
Detection rate of lower RTIs (*N*=180)	18 (10.0)	14 (7.8)	6 (3.3)	24 (13.3)	12.072	0.007

Note: Spring includes March to May; Summer includes June to August; Autumn includes September to November; Winter includes December to February.
Abbreviation: ARTI=acute respiratory tract infection; RTI=respiratory tract infection; HRSV=Human respiratory syncytial virus.

TABLE 3. Seasonal distribution of HRSV and HRSVA/B in children with ARTI in Shijiazhuang City, Hebei Province, China, 2021–2023.

Season		Detection rate (*N*=120) *n* (%)	Upper RTIs (*N*=60) *n* (%)	Lower RTIs (*N*=60) *n* (%)	Upper RTIs (*N*=60)		Lower RTIs (*N*=60)	
					HRSVA *n* (%)	HRSVB *n* (%)	HRSVA *n* (%)	HRSVB *n* (%)
2021	Spring	12 (10.0)	4 (6.7)	8 (13.3)	2 (3.3)	2 (3.3)	1 (1.7)	7 (11.7)
	Summer	15 (12.5)	3 (5.0)	12 (20.0)	0 (0.0)	3 (5.0)	1 (1.7)	11 (18.3)
	Autumn	4 (3.3)	2 (3.3)	2 (3.3)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.3)
	Winter	13 (10.8)	6 (10.0)	7 (11.7)	2 (3.3)	4 (6.7)	6 (10.0)	1 (1.7)
2022	Spring	12 (10.0)	10 (16.7)	2 (3.3)	6 (10.0)	4 (6.7)	2 (3.3)	0 (0.0)
	Summer	2 (1.7)	2 (3.3)	0 (0.0)	2 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)
	Autumn	2 (1.7)	0 (0.0)	2 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.3)
	Winter	19 (15.8)	5 (8.3)	14 (23.3)	3 (5.0)	2 (3.3)	10 (16.7)	4 (6.7)
2023	Spring	20 (16.7)	12 (20.0)	8 (13.3)	9 (15.0)	3 (5.0)	8 (13.3)	0 (0.0)
	Summer	4 (3.3)	2 (3.3)	2 (3.3)	2 (3.3)	0 (0.0)	0 (0.0)	2 (3.3)
	Autumn	4 (3.3)	2 (3.3)	2 (3.3)	1 (1.7)	1 (1.7)	0 (0.0)	2 (3.3)
	Winter	5 (4.2)	2 (3.3)	3 (5.0)	1 (1.7)	1 (1.7)	0 (0.0)	3 (5.0)

Note: Spring includes March to May; Summer includes June to August; Autumn includes September to November; Winter includes December to February.
Abbreviation: ARTI= acute respiratory tract infection; RTI= respiratory tract infection; HRSV=Human respiratory syncytial virus;HRSVA/B=Human respiratory syncytial virus A/B.

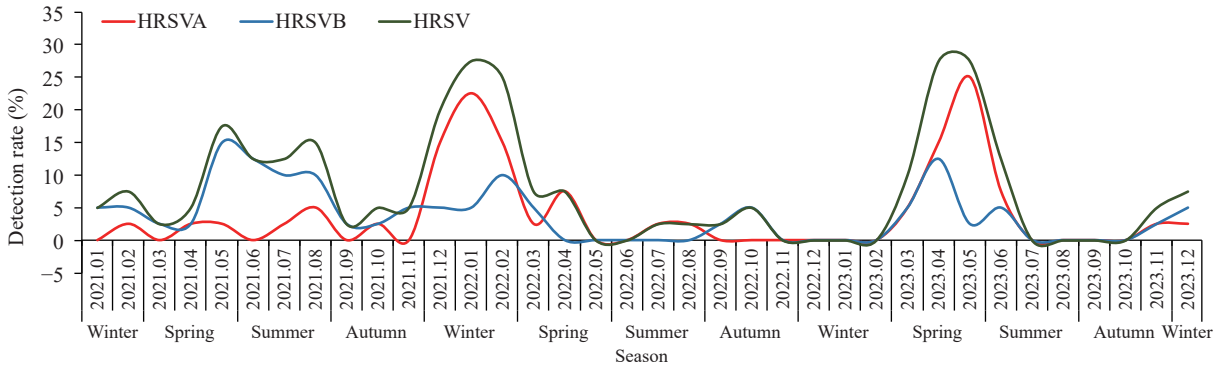

FIGURE 1. Seasonal distribution of human respiratory syncytial virus subtypes in children with acute respiratory tract infections in Shijiazhuang City, Hebei Province, China.
Abbreviation: HRSV=Human respiratory syncytial virus; HRSVA/B=Human respiratory syncytial virus A/B.

increased during non-typical seasons after the restriction relaxation (*6–9*). This pattern may be attributed to two key factors: the attenuation of pre-existing immunity to respiratory viruses during containment measures, and reduced maternal antibody transfer due to decreased maternal HRSV exposure, potentially increasing infant and young child susceptibility (*10–11*). Additionally, virus-virus interactions may influence HRSV's epidemic dynamics and seasonality, highlighting the critical importance of

TABLE 4. Age distribution of HRSV in children with ARTIs in Shijiazhuang City, Hebei Province, China, 2021–2023.

Age group (year)	Detection rate	Upper RTIs (%)	Lower RTIs (%)	HRSV-A		HRSV-B	
				Upper RTIs (%)	Lower RTIs (%)	Upper RTIs (%)	Lower RTIs (%)
0 to 1	13.9 (16/115)*	9.2 (6/65)†	20.0 (10/50)†	6.62 (4/65)§	12 (6/50)§	3.1 (2/65)¶	8 (4/50)¶
>1 to 2	11.0 (27/246)*	7.6 (12/158)†	17.5 (15/88)†	3.2 (5/158)**	6.8 (6/88)**	4.4 (7/158)††	10.2 (9/88)††
>2 to 5	9.5 (44/463)*	8.8 (25/284)	10.6 (19/179)	5.6 (16/284)	4.5 (8/179)	3,2 (9/284)	6.1 (11/179)
>5 to 14	4,1 (25/616)*	3.3 (7/213)	4.5 (18/403)	1.9 (4/213)	2.0 (8/403)	1.4 (3/213)	2.5 (10/403)

* χ^2=23.344, P<0.001;
† Total data for 0 to 1 year and >1 to 2 years groups: χ^2=8.196, P=0.004;
§ χ^2=0.592, P=0.442;
¶ χ^2=0.568, P=0.451.
** χ^2=1.015, P=0.314;
†† χ^2=3.123, P=0.077.

maintaining continuous surveillance and early warning systems for effective HRSV prevention and control.

Our results demonstrated that HRSV detection rates were significantly higher in children under 5 years old (10.6%, 87/824) compared to those over 5 years old (4.1%, 25/616). Notably, in the 0–2 years age group, the detection rate was markedly higher in lower RTIs (18.1%) than upper RTIs (8.1%), indicating that infants and young children represent the primary susceptible population for HRSV infection. No significant differences were observed in the detection rates between HRSVA and HRSVB subtypes across upper and lower RTIs. Following HRSV infection, infants and young children are particularly prone to developing severe complications such as bronchiolitis and pneumonia. Compared to single HRSV infections, children with poly-viral RTIs exhibited more severe clinical manifestations, including higher fever incidence, prolonged fever duration, and extended hospital stays. The observation that HRSV coinfections with other viruses were exclusively detected in lower RTI cases suggests that viral coinfections may significantly influence disease severity and progression, warranting careful monitoring of pediatric HRSV cases. Non-pharmacological interventions (NPIs) during HRSV seasons, including social distancing, mask-wearing, and hand hygiene, remain crucial strategies for preventing pediatric RTIs (*12*). The implementation of NPIs during the COVID-19 pandemic substantially altered HRSV epidemiological patterns in Hebei Province. Pre-pandemic HRSV detection rates of approximately 17% dropped to less than 1% following strict NPI implementation. The traditional autumn-winter prevalence pattern shifted, with an unusual summer outbreak occurring in 2021. Following the relaxation of NPIs in 2022, the epidemic peak showed significant temporal displacement, appearing during winter and spring, demonstrating the strong correlation between HRSV prevalence and NPI measures. This study revealed that HRSV predominantly affects children under 5 years old in the Shijiazhuang area, with peak prevalence during spring and winter. The 0–2 years age group showed higher detection rates in the lower respiratory tract specimens compared to upper respiratory specimens. For effective HRSV prevention, particularly in high-risk infants and young children, comprehensive measures are essential: maintaining proper hand hygiene, implementing respiratory isolation protocols, promoting breastfeeding, avoiding exposure to tobacco smoke, and improving living conditions. Additionally, children should avoid crowded spaces and wear masks in public settings. Healthcare providers should wear masks when exhibiting upper RTI symptoms, and strict adherence to hand hygiene protocols and personal protective equipment use in medical facilities is crucial to prevent nosocomial transmission. While vaccination represents a critical preventive strategy against HRSV, currently no approved vaccines exist in China for pediatric HRSV prevention. However, with vaccines becoming available internationally, active immunization against HRSV in children aged 0–2 years represents a promising future prevention strategy.

Conflicts of interest: No conflicts of interest.

Ethical statement: Received ethics approval from the Institutional Ethics Committee for Research of Institutional Review Board of the Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention (No.IVDC2018(012)).

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Vital Surveillances

Variations in Prevalence and Characteristics of Rotavirus Diarrhea Among Outpatients — Shanghai Municipality, China, 2017–2023

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ABSTRACT

Introduction: This study investigated temporal changes in rotavirus group A (RVA) prevalence, epidemiological characteristics, and genotype distribution patterns among diarrhea outpatients in Shanghai Municipality, China.

Methods: We conducted prospective active surveillance of diarrheal disease in pediatric and adult outpatients in Shanghai. Stool specimens were analyzed for five viral and twelve bacterial pathogens. Real-time reverse transcription polymerase chain reaction (rRT-PCR) was employed for RVA detection, followed by genotyping of RVA-positive specimens through partial amplification of VP7 and VP4 genes.

Results: The study analyzed 2,331 diarrhea cases in children aged 0–14 years and 8,418 cases in individuals aged ≥15 years between January 2017 and December 2023. Overall RVA positivity rates decreased significantly from 7.43% in 2017 to 1.19% in 2023 (P=0.024). The most pronounced decline occurred in children aged 2–5 years, where positivity rates fell from 13.08% to 1.72%. Adults aged ≥30 years also showed a substantial reduction. Among RVA-positive pediatric cases (≤14 years), the proportion of cases aged 6–14 years increased from 2.33% to 18.18%. While G9P[8] remained the predominant strain, its prevalence decreased from 77.78% to 31.25%, concurrent with the emergence of G8P[8] strains.

Conclusions: RVA prevalence has shown a marked decline since 2018–2019, accompanied by a shift in age distribution toward older children. The diminishing dominance of G9P[8] strains coincided with the emergence of G8P[8] strains. Continued epidemiological and genetic surveillance of rotavirus diarrhea, coupled with real-world effectiveness evaluations of domestic vaccines, remains crucial for optimizing rotavirus immunization strategies.

Diarrhea remains a significant global public health challenge, particularly among children under 10 years of age, where it ranks as the third leading cause of disability-adjusted life years (*1*). In China, rotavirus group A (RVA) has emerged as the predominant viral etiology of diarrhea, ranking first among children and second among adults in terms of frequency (*2*). Between 2005 and 2018, China experienced a fluctuating but generally increasing trend in rotavirus diarrhea incidence (*3*). In Shanghai specifically, rotavirus represents the third most prevalent pathogen in pediatric diarrheal cases and the second most common in adult cases, highlighting its substantial public health impact (*4*–*5*).

Given the absence of specific therapeutic interventions for rotavirus infection, vaccination stands as the most effective preventive strategy against rotavirus transmission (*6*). Prior to 2024, Shanghai offered two voluntary, self-funded oral rotavirus vaccines: the Lanzhou lamb rotavirus vaccine (LLR), licensed in 2001, and the oral human attenuated pentavalent rotavirus vaccine (RotaTeq), licensed in 2018.

Evidence indicates that LLR vaccination confers population-level health benefits through the prevention of rotavirus gastroenteritis (*7*). However, the impact of RotaTeq vaccination on rotavirus infection among both pediatric and adult populations in China remains to be fully elucidated. This study aims to investigate the temporal changes in rotavirus prevalence and characterize the epidemiological and genetic features among diarrheal outpatients from 2017 to 2023.

METHODS

Shanghai Diarrhea Comprehensive Surveillance

A comprehensive active prospective surveillance

system for diarrheal diseases in both adult and pediatric populations has been operational in Shanghai since 2012. The current surveillance network encompasses 28 sentinel hospitals strategically distributed across all 16 districts of Shanghai, including 6 dedicated pediatric sentinel facilities. The network integrates primary, secondary, and tertiary healthcare facilities to ensure comprehensive coverage. This study builds upon this established surveillance infrastructure. Detailed protocols regarding sentinel hospital selection criteria, case definitions, specimen collection and storage procedures, RNA extraction methodologies, and laboratory testing protocols have been previously documented (*4*–*5*).

Laboratory Tests

Comprehensive pathogenic screening was conducted on stool samples to detect five viral pathogens (rotavirus, norovirus, astrovirus, sapovirus, and adenovirus) and twelve bacterial agents (*Vibrio cholerae*, *Shigella* spp., *Salmonella* spp., *V. parahaemolyticus*, *Campylobacter jejuni*, *Yersinia enterocolitica*, *Campylobacter coli*, EPEC, ETEC, EHEC, EAggEC, EIEC).

RVA Genotyping

RVA detection employed a dual-screening approach using real-time reverse transcription polymerase chain reaction (rRT-PCR) with commercial kits from Shanghai Zhijiang Biotechnology Co. Ltd, and Jiangsu Shuoshi Biotechnology Co., Ltd, following manufacturer-specified protocols. For specimens yielding positive results with both rRT-PCR kits, VP4 and VP7 genomic regions were amplified through nested PCR using established reagents and primers as documented in the literature (*8*). Genotype identification was subsequently performed through capillary gel electrophoresis based on product size analysis, following previously described methodologies (*8*).

Statistical Analysis

Statistical analyses and data visualization were conducted using SAS software (version 9.4, SAS Institute Inc., Cary, USA) and R software (version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria). For continuous variables, analyses employed either the Wilcoxon rank-sum test or the Kruskal-Wallis test based on data distribution characteristics. Categorical variables were evaluated using the Pearson chi-square test, continuous corrected chi-square test, or Fisher's exact test as appropriate. Pathogen-specific positivity rates were calculated as the ratio of positive samples to total samples tested for each respective pathogen. Temporal trends in positivity rates were assessed using the Mann-Kendall trend test. All statistical analyses were conducted using two-sided tests with statistical significance defined at $P<0.05$.

RESULTS

Characteristics of Diarrhea Outpatients

Between January 1, 2017, and December 31, 2023, the study enrolled 10,749 outpatients presenting with diarrhea. Among 2,331 pediatric cases aged 0–14 years, 2,328 underwent RVA screening, yielding a positivity rate of 6.62%. The detection rates for other viral and bacterial pathogens were 20.96% and 21.73%, respectively. Age-stratified analysis revealed significantly higher RVA positivity rates in infants aged 0–1 year (7.9%) and children aged 2–5 years (7.08%) compared to those aged 6–14 years (3.59%) (P=0.045). Notable variations in RVA positivity were observed across residential status categories, with rates of 13.48% in migrant populations, 10.53% in temporary residents, and 6.18% in long-term residents (P=0.004). RVA-positive patients demonstrated significantly higher Vesikari scores compared to RVA-negative cases (P=0.023), with a greater proportion of moderate to severe cases in the positive group (P=0.001) (Table 1).

In the adult cohort (≥15 years, n=8,418), 8,093 specimens were tested for RVA, with a positivity rate of 5.10%, significantly lower than the pediatric cohort (P=0.005). Other viral and bacterial pathogens were detected at rates of 22.25% and 24.26%, respectively. Age-stratified analysis revealed significant variations in RVA positivity (P=0.028), with the highest rate observed in adults aged 30–59 years (5.98%) and the lowest in those aged 15–29 years (4.17%). Clinical presentation analysis showed that RVA-positive cases exhibited increased frequency of diarrhea and higher incidence of vomiting compared to RVA-negative cases (Table 1).

Changes in RVA Prevalence

The overall RVA positivity rate across all age groups from 2017 to 2023 was 5.44%. A significant declining trend was observed, from 7.43% in 2017 and 7.77% in 2018 to 5.76% in 2019, followed by further reductions

TABLE 1. Demographic and clinical characteristics of pediatric and adult diarrhea outpatients, stratified by RVA test results and temporal periods*.

Characteristics	All diarrhea patients	Diarrhea patients†			RVA positive			
		RVA negative	RVA positive	*P*	2017–2018	2019	2020–2023	*P*
Children								
No.	2,331	2,174	154		86	46	22	
Gender				0.603				0.002
Male	1,293 (55.47)	1,202 (55.29)	89 (57.79)		39 (45.35)	34 (73.91)	16 (72.73)	
Female	1038 (44.54)	972 (44.71)	65 (42.21)		47 (54.65)	12 (26.09)	6 (27.27)	
Age group (years)				0.045				0.031
0–1	1,407 (60.36)	1,303 (59.94)	103 (66.88)		57 (66.28)	33 (71.74)	13 (59.09)	
2–5	606 (26.00)	565 (25.99)	40 (25.97)		27 (31.40)	8 (17.39)	5 (22.73)	
6–14	318 (13.64)	306 (14.08)	11 (7.14)		2 (2.33)	5 (10.87)	4 (18.18)	
Census register				0.004				0.059
Long-term residents	1,894 (81.25)	1,781 (81.92)	110 (71.43)		54 (62.79)	37 (80.43)	19 (86.36)	
Temporary residents	336 (14.41)	304 (13.98)	32 (20.78)		21 (24.42)	8 (17.39)	3 (13.64)	
Migrant population	101 (4.33)	89 (4.09)	12 (7.79)		11 (12.79)	1 (2.17)	0 (0.00)	
Vesikari score	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	6.00 (4.00, 7.00)	0.023	5.00 (4.00, 6.00)	6.00 (5.00, 7.00)	6.00 (5.00, 6.75)	0.004
Vesikari severity				0.001				0.240
Mild	2,240 (96.10)	2,098 (96.50)	139 (90.26)		81 (94.19)	39 (84.78)	19 (86.36)	
Moderate	71 (3.05)	59 (2.71)	12 (7.79)		4 (4.65)	6 (13.04)	2 (9.09)	
Severe	20 (0.86)	17 (0.78)	3 (1.95)		1 (1.16)	1 (2.17)	1 (4.55)	
Frequency of diarrhea (times/day)	4.00 (3.00, 5.00)	4.00 (3.00, 5.00)	4.00 (3.00, 5.00)	0.598	4.00 (3.00, 5.00)	4.00 (3.00, 6.00)	4.50 (3.00, 6.00)	0.203
Frequency of diarrhea (times/day)				0.766				0.074
3–4	1,240 (59.62)	1,154 (59.48)	85 (61.15)		53 (69.74)	23 (51.11)	9 (50.00)	
≥5	840 (40.38)	786 (40.52)	54 (38.85)		23 (30.26)	22 (48.89)	9 (50.00)	
Fever				<0.001				0.523
Yes	205 (8.79)	179 (8.23)	26 (16.88)		12 (13.95)	9 (19.57)	5 (22.73)	
Vomiting				<0.001				0.538
Yes	177 (7.59)	148 (6.81)	28 (18.18)		13 (15.12)	10 (21.74)	5 (22.73)	
Adults								
No.	8,418	7,680	413		286	90	37	
Gender				0.3335				0.543
Male	4,447 (52.83)	4,065 (52.93)	208 (50.36)		149 (52.10)	41 (45.56)	18 (48.65)	
Female	3,971 (47.17)	3,615 (47.07)	205 (49.64)		137 (47.90)	49 (54.44)	19 (51.35)	
Age group (years)				0.028				0.496
15–29	1,956 (23.32)	1,800 (23.52)	75 (18.29)		55 (19.43)	12 (13.33)	8 (21.62)	
30–59	4,105 (48.94)	3,730 (48.73)	223 (54.39)		151 (53.36)	55 (61.11)	17 (45.95)	
≥60	2,326 (27.73)	2,124 (27.75)	112 (27.32)		77 (27.21)	23 (25.56)	12 (32.43)	
Census register				0.157				0.631
Long-term residents	6,862 (81.52)	6,252 (81.41)	351 (84.99)		244 (85.31)	78 (86.67)	29 (78.38)	
Temporary residents	1,007 (11.96)	909 (11.84)	42 (10.17)		29 (10.14)	7 (7.78)	6 (16.22)	
Migrant population	549 (6.52)	519 (6.76)	20 (4.84)		13 (4.55)	5 (5.56)	2 (5.41)	

Continued

Characteristics	All diarrhea patients	Diarrhea patients†			RVA positive			
		RVA negative	RVA positive	*P*	2017–2018	2019	2020–2023	*P*
Frequency of diarrhea (times/day)	5.00 (4.00, 8.00)	5.00 (4.00, 8.00)	6.00 (4.00, 10.00)	<0.001	6.00 (4.00, 10.00)	6.00 (4.00, 10.00)	8.00 (6.00, 10.00)	0.028
Frequency of diarrhea (times/day)				<0.001				0.062
3–4	2,878 (35.78)	2,644 (36.06)	110 (27.23)		81 (29.03)	25 (28.41)	4 (10.81)	
≥5	5,165 (64.22)	4,689 (63.94)	294 (72.77)		198 (70.97)	63 (71.59)	33 (89.19)	
Fever				0.262				0.863
Yes	1,184 (14.07)	1,084 (14.11)	67 (16.22)		48 (16.78)	14 (15.56)	5 (13.51)	
Vomiting				<0.001				0.447
Yes	1,941 (23.06)	1,737 (22.62)	136 (32.93)		97 (33.92)	25 (27.78)	14 (37.84)	

Abbreviation: RVA=Rotavirus group A; IQR=interquartile range.

* Values are presented as *N* (%) or Median (IQR).

† RVA testing was not conducted for 325 adult and 3 pediatric diarrhea cases.

to 2.2%, 1.93%, 3.24%, and 1.19% from 2020 to 2023, respectively (*P*=0.024). The most pronounced decline occurred in children aged 2–5 years, where rates decreased significantly from 13.08% in 2017 to 1.72% in 2023 (*P*=0.024). Among infants aged 0–1 year, although rates decreased from 6.74% to 3.77%, this reduction was not statistically significant. In the 30–59 year age group, RVA positivity rates showed a significant reduction from 8.36% in 2017 to 1.06% in 2023 (*P*=0.004). Similarly, cases aged 60 years and over demonstrated a significant decline from 6.88% in 2017 to 0.48% in 2023 (*P*=0.011). Notably, the overall positivity rates for bacterial and other viral pathogens did not exhibit a decreasing trend during the study period. Despite temporary reductions during periods of non-pharmacological interventions, by 2023, these rates had returned to or slightly exceeded their 2017 levels (Figure 1).

Seasonal Pattern of RVA Circulation

Seasonal patterns of RVA in diarrhea cases were analyzed across three distinct time periods (2017–2018, 2019, and 2020–2023) for two age cohorts: individuals aged 5 and under, and those aged 15 and above.

Among children aged 5 and under, RVA positivity rates in 2017–2018 reached their peak during January and February, with rates of 30.43% to 31.34%. The 2019 period exhibited a sharp, concentrated peak of 41.38% in February, followed by a precipitous decline. In contrast, during 2020–2023, the maximum rate occurred in January at just 7.41%, representing only 23.64% and 17.91% of the peak rates observed in the two preceding periods, respectively (Figure 2).

For individuals aged 15 and older, the 2017–2018 period demonstrated a pronounced peak of 30.74% in January, followed by a swift decline. The 2019 period exhibited a broader seasonal pattern, with elevated rates persisting from January through March (ranging from 14.41% to 16.5%), characterized by lower peak intensity but extended duration compared to the previous period. During 2020–2023, the January peak diminished to 7.55%, representing only 24.56% and 45.76% of the peak rates observed in the two preceding periods, respectively (Figure 2).

Characteristics of RVA Positive Diarrhea Cases

Analysis of diarrhea cases in children aged 5 and younger revealed significant age distribution variations across the three time periods (*P*=0.031). The proportion of cases aged 0–1 years and 6–14 years shifted markedly in 2020–2023, reaching 59.09% and 18.18% respectively, compared to 66.28% and 2.33% in 2017–2018. Vesikari scores also showed significant differences across the three periods (*P*=0.004), with the lowest scores observed in 2017–2018. However, when categorized by severity using the Vesikari scoring system, these differences did not reach statistical significance (Table 1).

Among diarrhea cases aged 15 and older, the frequency of diarrheal episodes differed significantly across the three time periods (*P*=0.028), with the highest frequency documented during 2020–2023. No other clinical or demographic parameters showed statistically significant differences across these periods (Table 1).

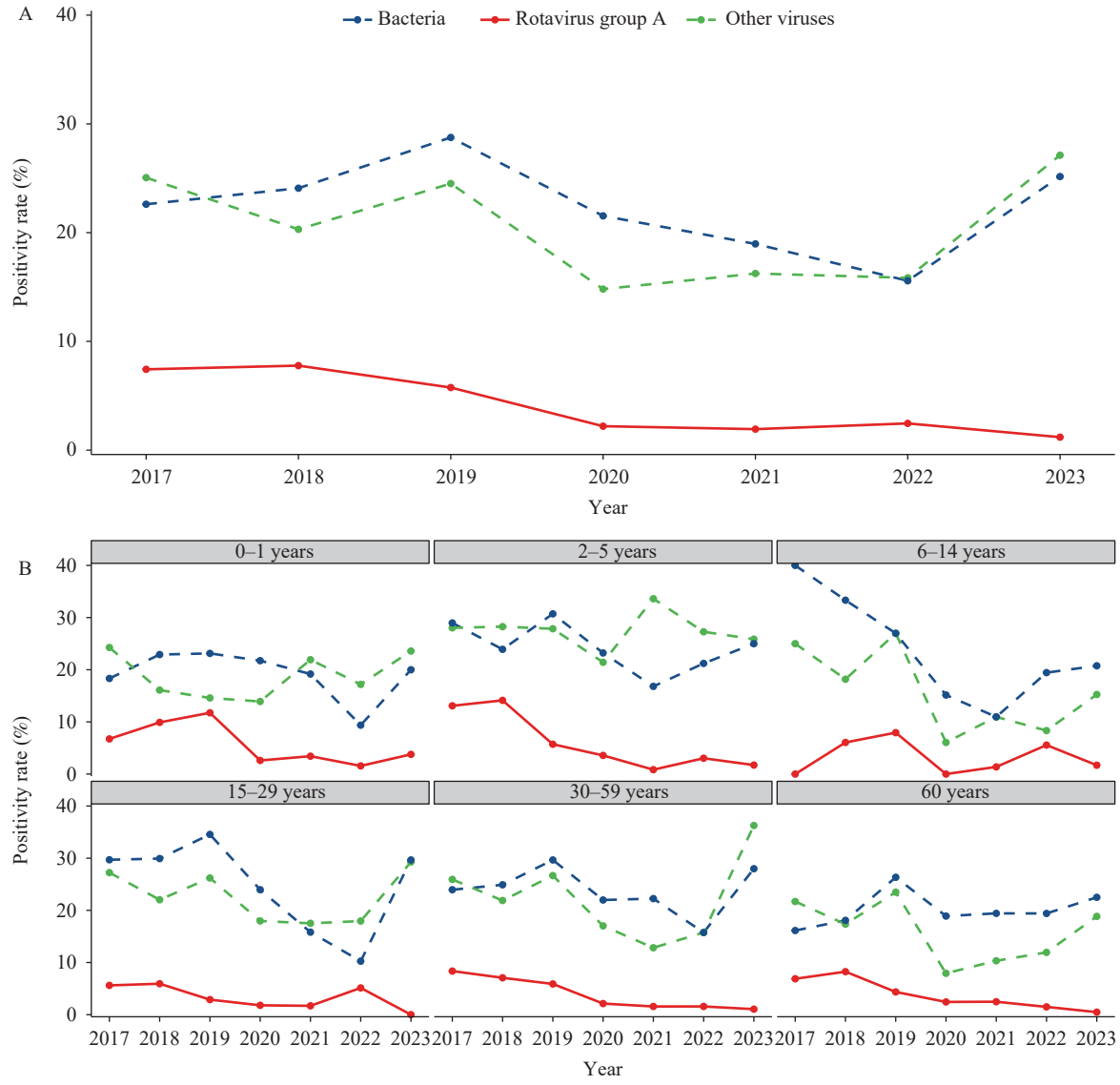

FIGURE 1. Variation in positivity rates over different years, both overall and within various age groups. (A) variation in overall positivity rates over different years. (B) variation in positivity rates over different years within various age groups.
Note: The total positivity rates for bacteria were 22.61% in 2017, 24.09% in 2018, 28.75% in 2019, 21.54% in 2020, 18.96% in 2021, 15.57% in 2022, and 25.16% in 2023. The total positivity rates for other viruses were 25.06% in 2017, 20.31% in 2018, 24.51% in 2019, 14.81% in 2020, 16.24% in 2021, 15.85% in 2022, and 27.12% in 2023.

RVA genotype diversity

Among 112 successfully genotyped RVA samples from children aged five and under, G9P[8] and G3P[8] emerged as the predominant strains, accounting for 75% and 12.5% of cases, respectively. The genotype composition underwent significant changes across the three time periods (P<0.001). From 2017–2018 to 2020–2023, the proportion of G9P[8] decreased markedly from 77.78% to 31.25%, while previously undetected strains G1P[8] and G8P[8] emerged in the population (Table 2, Figure 2).

Analysis of 330 successfully genotyped RVA samples from individuals aged 15 years and older revealed G9P[8], G2P[4], and G3P[8] as the dominant strains, representing 64.23%, 14.85%, and 13.33% of cases, respectively. The genotype distribution exhibited significant temporal variation across the three time periods (P<0.001). From 2017–2018 to 2020–2023, G9P[8] prevalence decreased from 65.3% to 48.65%, while G8P[8] emerged and increased to 16.22%. The proportion of G2P[4] remained relatively stable throughout this period (Table 2, Figure 2).

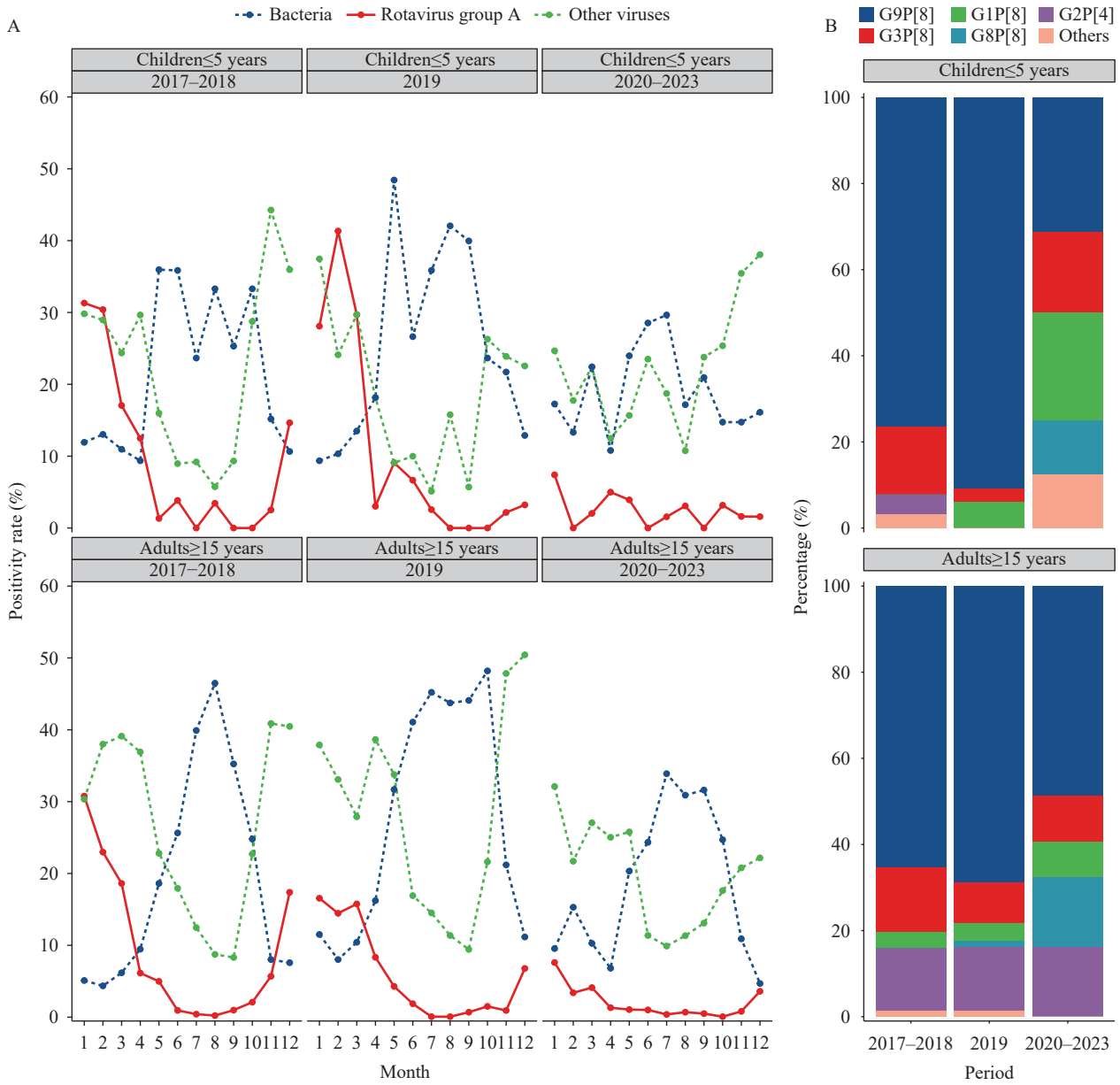

FIGURE 2. Variation of positivity rate and genotype spectrum across different (A) months and (B) periods in adults and children over three time periods, 2017–2023.

CONCLUSIONS

Clinical manifestations were significantly more severe in both adult and pediatric outpatients who tested positive for RVA compared to those who tested negative. The highest positivity rates were observed in children aged 5 years and younger, with particular vulnerability noted among infants under 1 year of age. These findings underscore the critical importance of implementing effective rotavirus prevention strategies, especially for these high-risk age groups.

Since 2018–2019, RVA positivity rates have shown differential declines across age groups, with the most pronounced reduction observed in children aged 2–5 years. By 2023, the RVA positivity rate in this group had decreased dramatically to 1.72% from 13.08% in 2017, representing an 11.36 percentage point reduction. Similar declining trends were documented in adult populations. These findings align with data reported from multiple Beijing hospitals (*9*). In Shanghai, the introduction of RotaTeq in 2018 coincided with a sharp decline in LLR coverage among infants born in 2020, dropping from 66% to 11.8%, while RotaTeq coverage rapidly exceeded 40% (*10*).

TABLE 2. Genotype constitution in children and adult RVA positive diarrhea outpatients over three time periods, 2017–2023.

RVA genotypes	2017–2018 *n* (%)	2019 *n* (%)	2020–2023 *n* (%)	Total (2017–2023) *n* (%)
Children ≤5 years				
G9P[8]	49 (77.78)	30 (90.91)	5 (31.25)	84 (75.00)
G3P[8]	10 (15.87)	1 (3.03)	3 (18.75)	14 (12.50)
G1P[8]	0 (0)	2 (6.06)	4 (25.00)	6 (5.36)
G8P[8]	0 (0)	0 (0)	2 (12.50)	2 (1.79)
G2P[4]	3 (4.76)	0 (0)	0 (0)	3 (2.68)
G1P[8]+G3P[8]	0 (0)	0 (0)	1 (6.25)	1 (0.89)
LLR vaccine strain	1 (1.59)	0 (0)	0 (0)	1 (0.89)
RotaTeq vaccine strain	0 (0)	0 (0)	1 (6.25)	1 (0.89)
Total	63 (100)	33 (100)	16 (100)	112 (100)
Adults ≥15 years				
G9P[8]	143 (65.30)	51 (68.92)	18 (48.65)	212 (64.24)
G3P[8]	33 (15.07)	7 (9.46)	4 (10.81)	44 (13.33)
G1P[8]	8 (3.65)	3 (4.05)	3 (8.11)	14 (4.24)
G8P[8]	0 (0)	1 (1.35)	6 (16.22)	7 (2.12)
G2P[4]	32 (14.61)	11 (14.86)	6 (16.22)	49 (14.85)
G9P[4]	2 (0.91)	0 (0)	0 (0)	2 (0.61)
G2P[4]+G9P[8]	1 (0.46)	0 (0)	0 (0)	1 (0.30)
G9P[8]+G2P[4]	0 (0)	1 (1.35)	0 (0)	1 (0.30)
Total	219 (100)	74 (100)	37 (100)	330 (100)

Comparable trends have been observed internationally; in Japan, the introduction of Rotarix and RotaTeq as optional immunizations led to a reduction in RVA positivity rates from 20% to 4% within two years (*11*). This pattern is consistent with global data showing decreased rotavirus prevalence among acute gastroenteritis cases following widespread vaccine implementation (*12*).

The stability of bacterial and other viral pathogen positivity rates from 2017 to 2023, returning to baseline levels by 2023, suggests that the decline in RVA positivity rates was not attributable to temporal variations in testing methodology or non-pharmacological interventions implemented during 2020–2022. Notably, transient populations exhibited approximately double the positivity rates of permanent residents. The limited effectiveness of improved hygiene measures in controlling rotavirus transmission (*6*), coupled with vaccination coverage among transient populations being less than half that of permanent residents (*10*), highlights the crucial relationship between vaccination coverage and infection rates. These findings strongly suggest that the introduction of RotaTeq as a voluntary vaccine has been instrumental in reducing RVA infections among children since 2018–2019.

A notable decline in RVA positivity rates among adult diarrhea outpatients suggests that pediatric rotavirus vaccination may confer indirect population-wide protection against infection. This observation aligns with studies from America demonstrating that childhood rotavirus immunization provides indirect protective effects for unvaccinated cohorts, including both pediatric and adult populations (*13–14*).

From 2017 to 2023, the age distribution of rotavirus diarrhea cases exhibited a significant shift toward older pediatric groups, a pattern consistent with observations in other countries (*12*). Specifically, the period from 2017–2018 to 2020–2023 saw a decrease in both the absolute number and proportion of cases among infants aged 0–1 years. Conversely, while the absolute number of cases in children aged 6–14 years remained relatively stable, their proportional representation increased. The typical seasonal epidemic pattern of rotavirus, characterized by January peaks, has shown diminishing peak intensity since 2018.

The surveillance period from 2017 to 2023 revealed a marked decline in G9P[8] strain predominance, concurrent with the emergence of G8P[8]. The most pronounced reduction in G9P[8] prevalence occurred

among children aged 5 years and younger, though it maintained its position as the dominant strain from 2020 to 2023. Studies from northern and central China have reported similar trends, noting a transition from G9P[8] to G8P[8] as the predominant strain during 2021–2022 (*9*,*15*). Genetic analyses identified G9P[8], G1P[8], G3P[8], and G8P[8] as the prevalent RVA strains in Shanghai, indicating substantial genetic diversity. The emergence of G8P[8] strains may be associated with rotavirus vaccine implementation (*11*,*15*). Continued surveillance is essential to monitor the potential persistence of this G8P[8] strain shift in Shanghai.

This study presents several limitations. First, its focus on outpatient cases reflects the healthcare practices in Shanghai, where prompt treatment of pediatric diarrhea typically prevents hospitalization, resulting in limited inpatient data. Second, the use of positivity rates without community disease burden assessment provides only a measure of infection prevalence intensity. Third, non-pharmacological interventions, including reduced population mobility and enhanced infectious disease prevention awareness, led to decreased medical consultations for diarrhea and reduced surveillance cases. Consequently, the lower number of diarrhea cases and RVA-positive samples during this period constrains the ability to conduct comprehensive annual analyses of seasonal patterns and genotype distribution.

Given the recent licensing and completion of phase III clinical trials for multiple domestically produced vaccines, maintaining vigilant surveillance of rotavirus diarrhea epidemiological trends and genotypes, coupled with real-world vaccine effectiveness evaluations, is crucial. These efforts will generate essential scientific evidence to optimize rotavirus immunization strategies.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

Evaluation of the Factors Influencing the Survival Times of Chinese Patients with Probable Creutzfeldt-Jacob Disease — China, 2020–2022

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Summary

What is already known about this topic?

The clinical durations of sporadic Creutzfeldt-Jacob disease (sCJD) patients typically do not exceed 2 years, though considerable variation exists. The factors influencing survival among Chinese sCJD patients remain incompletely characterized.

What is added by this report?

A comprehensive evaluation of 31 factors across 7 categories was conducted in a retrospective cohort of 300 probable Chinese sCJD patients. The analysis revealed that patients over 65 years of age at onset, those presenting with pyramidal or extrapyramidal dysfunction, those showing high signal intensity in caudate/putamen on magnetic resonance imaging, and those not receiving nasal feeding demonstrated significantly shorter survival times.

What are the implications for public health practice?

This study provides the first systematic documentation of potential risk factors affecting survival times in Chinese sCJD patients, establishing an evidence base for developing and implementing targeted intervention strategies.

ABSTRACT

Introduction: The clinical durations of sporadic Creutzfeldt-Jacob disease (sCJD) patients typically do not exceed 2 years, though considerable variation exists. The factors influencing survival among Chinese sCJD patients remain incompletely characterized.

Methods: We analyzed the potential elements associated with survival using the data of 300 probable sCJD cases from 2020 to 2022 by China National Surveillance for CJD. The associations of 31 factors in 7 categories with survival were estimated by univariate analysis of Kaplan-Meier and multivariate regression analysis of Cox proportional hazard model.

Results: Statistical assays figured out that the patients >65 year-old at onset, having pyramidal or extrapyramidal dysfunction, recording high signal in caudate/putamen on magnetic resonance imaging (MRI), and not receiving nasal feeding were closely associated with short survival. In the subgroup analysis of ≤65 years and >65 years at onsetage, nasal feeding was the contributor to prolonged survival for both groups. MRI high signal of caudate/putamen in the younger group and pyramidal or extrapyramidal dysfunction in older group seemed to be more associated with poor survival separately.

Conclusions: The data indicate the onsetage and nasal feeding are the most crucial factors influencing the prognosis for Chinese sCJD patients, establishing an evidence base for developing and implementing targeted intervention strategies.

Human prion diseases encompass Creutzfeldt-Jacob disease (CJD), Kuru, Gerstmann-Sträussler-Scheinker syndrome (GSS), and fatal familial insomnia (FFI). Globally, sporadic CJD (sCJD) accounts for approximately 85% of human prion diseases, while 10%–15% are genetic forms associated with mutations in the *PRNP* gene — including genetic CJD (gCJD), GSS, and FFI. The remaining 1% are acquired forms, such as Kuru, iatrogenic CJD (iCJD), and variant CJD (vCJD) (*1*). While sCJD predominantly affects individuals aged 60–70 years, onset can occur between 20–90 years. Clinical presentations vary substantially among sCJD patients, with disease durations ranging from several months to 2 years (*2*). Despite numerous clinical trials over recent decades (*3*–*4*), effective prophylactic and therapeutic interventions remain elusive. Therefore, prompt and appropriate symptomatic management, along with proper nursing

care, are crucial for improving patient outcomes.

Previous evaluations of Chinese sCJD patients revealed a median clinical duration of approximately 5.3 months (*5*). However, factors influencing survival time remain incompletely understood. In this retrospective cohort study, we analyzed 300 probable sCJD cases diagnosed through the China National Surveillance for CJD (CNS-CJD) from January 1, 2020, to December 31, 2022. Diagnoses were established according to the Chinese National Health Commission's CJD diagnostic criteria as previously described. The study incorporated comprehensive medical records, epidemiological information, clinical data, laboratory findings, and follow-up documentation. We examined the relationship between survival time and 31 factors across 7 categories, including demographic characteristics, clinical features, laboratory results, and post-diagnosis medical care. To ensure data integrity, cases were selected based on criteria outlined in Figure 1, with standardized questionnaires administered by trained investigators to minimize information bias. Follow-up concluded on December 31, 2023, with surviving cases classified as censored. Survival time was calculated from disease onset to death.

Statistical analysis was performed using SPSS 21.0 statistical software (IBM, Armonk, NY, USA). Survival times with 95% confidence intervals (*CI*) were calculated using the Kaplan-Meier estimator. Between-group differences in survival time were assessed using the log-rank test. Factors showing statistical significance ($P<0.05$) in univariate analysis were subsequently evaluated through multivariate analysis using the Cox proportional hazard model to determine hazard ratios (*HR*) with corresponding 95% *CI*. The complete workflow for data collection and statistical evaluation is detailed in Supplementary Figure S1 (available at https://weekly.chinacdc.cn/).

Of the 300 sCJD cases documented in CNS-CJD, 285 cases had confirmed death dates prior to the follow-up endpoint, while 15 cases were censored. The median survival time was 5 months (95% *CI*: 4.165, 5.835). The cohort demonstrated a male-to-female ratio of 1:1.14, with an average onset age of 65 years (range: 39–84 years). The majority of cases (187 cases, 62.3%) occurred in patients aged 60–74 years.

Analysis of 31 factors across 7 categories using Kaplan-Meier methodology revealed several significant associations with survival time (Table 1). Among demographic factors, onset age showed statistical significance ($P=0.035$), with patients >65 years demonstrating shorter survival times (median: 5 months, 95% *CI*: 3.644, 6.356) (Supplementary Figure S2A, available at https://weekly.chinacdc.cn/). Regarding clinical manifestations, patients without pyramidal or extrapyramidal dysfunction exhibited significantly longer survival times (median: 7 months, 95% *CI*: 2.962, 11.038, $P=0.003$) (Supplementary

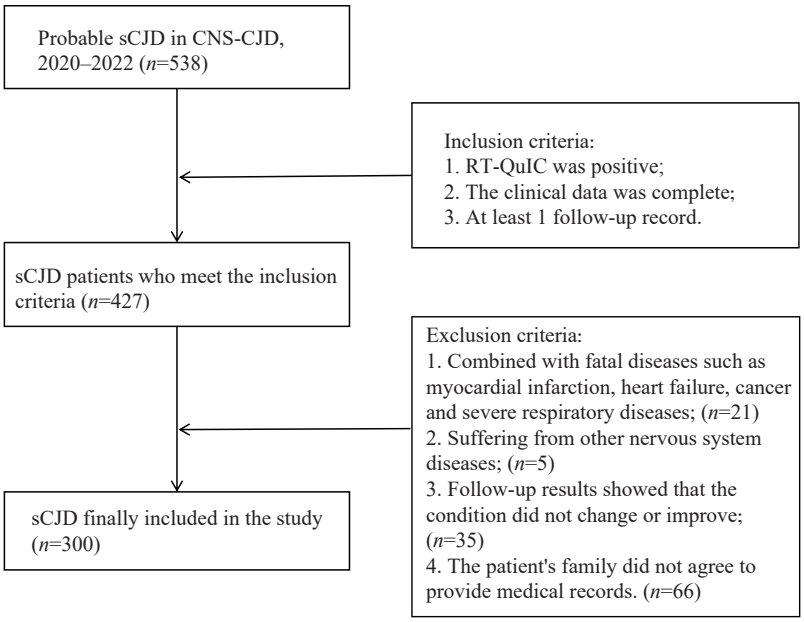

FIGURE 1. Flow chart of case selection.
Abbreviation: sCJD=sporadic Creutzfeldt-Jacob disease; CNS-CJD=China National Surveillance for CJD; RT-QuIC=Real-time Quaking-Induced Conversion.

TABLE 1. Univariate analysis of factors associated with survival in sCJD patients.

Factor	Cases (%)	Median (m) (95% *CI*)	χ^2	*P*
Demographics				
Onsetage (years)			4.441	0.035*
35–65	166 (55.3)	6 (4.356, 7.644)		
≥66	134 (44.7)	5 (3.644, 6.356)		
Gender			0.127	0.721
Male	140 (46.7)	5 (3.762, 6.238)		
Female	160 (53.3)	6 (4.229, 7.771)		
Geographic area			4.543	0.604
Northeastern	21 (7.0)	6 (1.514, 10.486)		
Eastern	86 (28.7)	6 (4.403, 7.597)		
Northern	43 (14.3)	4 (2.847, 5.153)		
Central	56 (18.7)	7 (4.340, 9.660)		
Southern	10 (3.3)	3 (1.482, 4.518)		
Southwestern	66 (22.0)	5 (3.508, 6.492)		
Northwestern	18 (6.0)	5 (0, 11.237)		
Residence			0.821	0.365
Urban	121 (40.3)	5 (4.600, 7.400)		
Rural	179 (59.7)	6 (3.690, 6.310)		
Initial symptom				
Rapid dementia			0.001	0.971
Yes	236 (78.7)	5 (3.950, 6.050)		
No	64 (21.3)	6 (3.060, 8.940)		
Slow dementia			1.833	0.176
Yes	17 (5.7)	10 (3.277, 16.723)		
No	283 (94.3)	5 (4.162, 5.838)		
Mental problems			0.210	0.647
Yes	109 (36.3)	6 (4.198, 7.802)		
No	191 (63.7)	5 (4.010, 5.990)		
Cortical blindness			1.297	0.255
Yes	31 (10.3)	4 (2.205, 5.795)		
No	269 (89.7)	6 (4.934, 7.066)		
Cerebellar disturbance			2.821	0.093
Yes	105 (35.0)	4 (3.163, 4.837)		
No	195 (65.0)	6 (4.632, 7.368)		
Pyramidal or extrapyramidal dysfunction			3.318	0.069
Yes	100 (33.3)	5 (3.726, 6.274)		
No	200 (66.7)	6 (4.570, 7.430)		
Clinical manifestation				
Myoclonus			1.073	0.300
Yes	200 (66.7)	5 (4.012, 5.988)		
No	100 (33.3)	6 (4.272, 7.728)		
Visual or cerebellar disturbance			2.162	0.141

Continued

Factor	Cases (%)	Median (m) (95% *CI*)	χ^2	*P*
Yes	222 (74.0)	5 (4.071, 5.929)		
No	78 (26.0)	7 (5.569, 8.431)		
Pyramidal or extrapyramidal dysfunction			9.043	0.003**
Yes	248 (82.7)	5 (4.095, 5.905)		
No	52 (17.3)	7 (2.962, 11.038)		
Akinetic mutism			2.316	0.128
Yes	238 (79.3)	6 (4.839, 7.161)		
No	62 (20.7)	4 (2.980, 5.020)		
Clinical examination				
EEG (PSWC)			<0.001	0.985
Yes	82 (27.3)	5 (2.953, 7.047)		
No	218 (72.7)	5 (3.842, 6.158)		
MRI				
High signal in caudate/putamen			8.084	0.004**
Yes	101 (33.7)	5 (3.972, 6.028)		
No	199 (66.3)	6 (4.467, 7.533)		
‘‘Ribbon’’ signs			0.233	0.629
Yes	233 (77.7)	5 (4.103, 5.897)		
No	67 (22.3)	7 (4.824, 9.176)		
High signal in posterior tuberosity of thalamus			0.007	0.935
Yes	29 (9.7)	6 (4.688, 7.312)		
No	271 (90.3)	5 (4.121, 5.879)		
Laboratory test				
CSF 14-3-3			1.903	0.168
pos	213 (71.0)	5 (4.022, 5.998)		
neg	87 (29.0)	6 (4.481, 7.519)		
PRNP seq				
Codon 129			0.611	0.737
MM	295 (98.3)	5 (4.172, 5.828)		
MV	4 (1.3)	2		
VV	1 (0.3)	9		
Codon 219			–	–
EE	300 (100)	5 (4.165, 5.835)		
EK	0 (0.0)	–		
Nursing and care				
Place			3.739	0.154
Professional unit	150 (50.0)	6 (4.588, 7.412)		
At home	106 (35.3)	4 (2.739, 5.261)		
Both	44 (14.7)	4 (2.561, 5.439)		
Personnel			1.362	0.506
Registered nurse	63 (21.0)	6 (2.667, 9.333)		
Care worker	182 (60.7)	5 (4.009, 5.991)		
Both	55 (18.3)	6 (3.587, 8.413)		

Continued

Factor	Cases (%)	Median (m) (95% *CI*)	χ^2	*P*
Symptomatic care			0.741	0.389
Yes	280 (93.3)	6 (4.913, 7.087)		
No	20 (6.7)	4 (0.000, 8.361)		
Medical supporting and therapeutics				
Nasal feeding			20.795	<0.001***
Yes	146 (48.7)	8 (6.137, 9.863)		
No	154 (51.3)	4 (3.330, 4.670)		
Nutrition injection i.v.			1.620	0.203
Yes	114 (38.0)	5 (3.573, 6.427)		
No	186 (62.0)	5 (3.972, 6.028)		
Nutrition oral			0.044	0.833
Yes	29 (9.7)	7 (4.890, 9.110)		
No	271 (90.3)	5 (4.136, 5.864)		
Respiratory support			0.105	0.746
Yes	95 (31.7)	5 (3.322, 6.678)		
No	205 (68.3)	6 (4.885, 7.115)		
Symptomatic treatment			1.952	0.162
Yes	88 (29.3)	6 (4.471, 7.529)		
No	212 (70.7)	5 (3.876, 6.124)		
Antibiotic therapy			0.896	0.344
Yes	35 (11.7)	7 (3.688, 10.312)		
No	265 (88.3)	5 (4.097, 5.903)		
Antiviral therapy			0.243	0.622
Yes	53 (17.7)	5 (3.714, 6.286)		
No	247 (82.3)	6 (4.941, 7.059)		

Abbreviation: sCJD=sporadic Creutzfeldt-Jakob disease; m=months; *CI*=confidence intervals; PSWC=periodic sharp wave complexes; EEG=electroencephalogram; MRI=magnetic resonance imaging; CSF=cerebrospinal fluid; seq=sequence; i.v.=intravenous.
* $P<0.05$;
** $P<0.01$;
*** $P<0.001$.

Figure S2B). Clinical examinations revealed that cases with high signal intensity in caudate/putamen on magnetic resonance imaging (MRI) had shorter survival times (median: 4 months, 95% *CI*: 3.972, 6.028, $P=0.004$) (Supplementary Figure S2C). In the category of medical support and therapeutics, nasal feeding demonstrated significant impact on survival ($P<0.001$), with patients receiving nasal feeding showing longer duration (median: 8 months, 95% *CI*: 6.137, 9.863) (Supplementary Figure S2D). Further analysis of survival based on the frequency of four sCJD-associated symptoms (visual or cerebellar disturbance, myoclonus, pyramidal and extrapyramidal symptoms, mutism) or three MRI abnormalities (symmetrical or asymmetrical cortical "ribbon" signs on diffusion weighted imaging (DWI), high signal in caudate/putamen, or high signal in bilateral posterior thalamic tuberosity in the proton density phase) showed no statistical significance, although patients with more symptoms or MRI abnormalities tended toward shorter survival durations (Supplementary Table S1, available at https://weekly.chinacdc.cn/).

The factors demonstrating statistical significance in the univariate analysis were further evaluated using multivariate regression with Cox proportional hazard modeling. As shown in Table 2, all four factors maintained statistical significance. Analysis of *HR* values revealed significantly elevated hazard risks in patients who were >65 years at onset (*HR*: 1.379, 95% *CI*: 1.088, 1.748), presented with pyramidal or extrapyramidal dysfunction (*HR*: 1.476, 95% *CI*: 1.060, 2.054), demonstrated high signal intensity in

TABLE 2. Multivariate regression analysis of the factors associated with survival in sCJD.

Factor	β	SE	Wald χ^2	*P*	*HR* (95% *CI*)
Onset age (years)					
35–65					1.000
≥66	0.321	0.121	7.039	0.008**	1.379 (1.088, 1.748)
Pyramidal or extrapyramidal dysfunction					
No					1.000
Yes	0.389	0.169	5.319	0.021*	1.476 (1.060, 2.054)
High signal in caudate/putamen					
No					1.000
Yes	0.297	0.129	5.278	0.022*	1.346 (1.045, 1.733)
Nasal feeding					
Yes					1.000
No	0.537	0.121	19.642	<0.001***	1.711 (1.349, 2.169)

Abbreviation: sCJD=sporadic Creutzfeldt-Jacob disease; *HR*=hazard ratio; *CI*=confidence intervals.
* *P*<0.05;
** *P*<0.01;
*** *P*<0.001.

caudate/putamen on MRI (*HR*: 1.346, 95% *CI*: 1.045, 1.733), or did not receive nasal feeding (*HR*: 1.711, 95% *CI*: 1.349, 2.169).

Further stratified analyses were conducted by dividing cases into age groups (≤65 years and >65 years) for both univariate and multivariate regression analyses (Table 3). In the ≤65 years group, univariate analysis identified five significant factors associated with survival time: cortical blindness as an initial symptom (*P*=0.037), cerebellar disturbance (*P*=0.032), pyramidal or extrapyramidal dysfunction (*P*=0.028), high signal in caudate/putamen on MRI (*P*=0.004), and nasal feeding (*P*=0.019). Subsequent multivariate Cox regression analysis revealed two significant factors: high signal in caudate/putamen (*HR*: 1.556, 95% *CI*: 1.111, 2.178, *P*=0.010) and absence of nasal feeding (*HR*: 1.476, 95% *CI*: 1.072, 2.033, *P*=0.017) In the group of >65 years group, four factors showed statistical significances in the univariate assay, including care place (*P*=0.022), akinetic mutism (*P*=0.016), pyramidal or extrapyramidal dysfunction (*P*=0.027), nasal feeding (*P*=0.019). Multivariate Cox regression analysis indicated 1.695-fold increased death risk (95% *CI*: 1.056, 2.721, *P*=0.025) in the patients with pyramidal or extrapyramidal dysfunction, and 2.386-fold increased death risk (95% *CI*: 1.605, 3.548, *P*<0.001).

DISCUSSION

Human prion diseases, including sCJD, remain universally fatal with significantly shorter clinical durations compared to other neurodegenerative disorders such as Alzheimer disease (AD) and Parkinson disease (PD) (*1*). Through analysis of 300 probable sCJD cases reported to the China National Surveillance for CJD between January 2020 and December 2022, we identified four key factors associated with shortened survival times: age greater than 65 years at onset, presence of pyramidal or extrapyramidal dysfunction, high signal intensity in caudate/putamen on MRI, and absence of nasal feeding.

Our findings demonstrate that patient age at disease onset significantly influences survival duration in Chinese sCJD patients. Elderly patients exhibited a 1.379-fold increased mortality risk compared to younger patients, consistent with previous studies documenting age-dependent decreased survival in sCJD (*6*–*7*). This association may be attributed to compromised health status and increased comorbidities in older populations, although some studies have failed to establish a clear correlation between onset age and clinical duration (*8*–*9*). Pyramidal or extrapyramidal dysfunction emerged as a negative prognostic factor, particularly in patients over 65 years at onset. These movement disorders, which encompass tremors, postural and gait abnormalities, limb ataxia, and dystonic spasms, are common in sCJD patients and may increase the risk of falls while complicating daily care management.

The prognostic significance of MRI for sCJD

TABLE 3. Univariate and multivariate regression analysis of factors associated with survival in two groups ≤65 and >65 years.

Factor	Univariate analysis			Multivariate analysis		
	Cases (%)	Median of survival (m) (95% *CI*)	*P*	χ^2	*P*	*HR* (95% *CI*)
sCJD cases ≤65 years (*n*=166)						
Cortical blindness in initial symptoms			0.037*	2.301	0.129	
Yes	8 (4.8)	4 (1.288, 6.772)				1.000
No	158 (95.2)	6 (4.241, 7.759)				0.568 (0.274, 1.180)
Cerebellar disturbance in initial symptoms			0.032*	2.919	0.088	
Yes	56 (33.7)	4 (3.025, 4.975)				1.000
No	110 (66.3)	7 (4.944, 9.056)				0.746 (0.533, 1.044)
Pyramidal or extrapyramidal dysfunction			0.028*	1.871	0.171	
Yes	139 (83.7)	5 (3.641, 6.359)				1.000
No	27 (16.3)	10 (6.183, 13.817)				0.723 (0.454, 1.151)
High signal in caudate/putamen			0.004**	6.628	0.010*	
No	66 (39.8)	7 (4.550, 9.450)				1.000
Yes	100 (60.2)	5 (3.513, 6.487)				1.556 (1.111, 2.178)
Nasal feeding			0.019*	5.686	0.017*	
Yes	84 (50.6)	8 (4.777, 11.223)				1.000
No	82 (49.4)	4 (2.622, 5.378)				1.476 (1.072, 2.033)
sCJD cases >65 years (*n*=134)						
Place of care			0.022*	2.713	0.258	
Professional unit	70 (52.2)	6 (4.366, 7.634)				1.000
At home	54 (40.3)	4 (3.105, 4.895)				1.359 (0.942, 1.961)
Both	10 (7.5)	3 (2.290, 3.710)				1.163 (0.771, 1.755)
Akinetic mutism			0.016*	0.207	0.649	
Yes	107 (79.9)	5 (3.311, 6.689)				1.000
No	27 (20.1)	3 (1.728, 4.272)				1.114 (0.610, 1.372)
Pyramidal or extrapyramidal dysfunction			0.027*	5.031	0.025*	
Yes	109 (81.3)	6 (3.062, 8.938)				1.000
No	25 (18.7)	4 (2.636, 5.364)				1.695 (1.056, 2.721)
Nasal feeding			0.019*	18.464	<0.001***	
Yes	64 (47.8.)	7 (5.041, 8.959)				1.000
No	70 (52.2)	4 (3.154, 4.845)				2.386(1.605, 3.548)

Abbreviaiton: sCJD=sporadic Creutzfeldt-Jakob disease; m=months; *HR*=hazard ratio; *CI*=confidence intervals.
* *P*<0.05;
** *P*<0.01;
*** *P*<0.001.

remains incompletely understood. A recent Korean study demonstrated that caudate nucleus and putamen involvement on diffusion-weighted imaging (DWI) correlates with poor prognosis (*7*). Our findings align with this observation, revealing high signal intensity in the caudate nucleus and putamen as a negative prognostic factor for sCJD survival, particularly in patients ≤65 years at onset. MRI lesion patterns in sCJD cases appear to demonstrate age-dependent characteristics. Previous research indicates that typical cortical and basal ganglia hyperintensities predominate in younger patients, while unilateral hemispheric or isolated cortical lesions occur more frequently in older individuals (*10*). Furthermore, extensive DWI abnormalities, particularly those involving three or more lobes with moderate to extensive cortical and striatal involvement, correlate with notably shortened median survival of approximately 1.7 months (*7*).

Importantly, most sCJD patients in our cohort underwent single evaluations of MRI, electroencephalogram (EEG), and CSF 14-3-3 testing post-onset. Serial examinations, combined with clinical features, would enable more precise stratification and prognostication of sCJD cases.

Nasal feeding demonstrates significant survival benefits for sCJD patients. Japanese research has similarly shown that tube-fed patients experience significantly extended survival compared to non-tube-fed patients, regardless of whether feeding was administered via nasogastric tube or gastrostomy (*7*). Additionally, enteral nutrition through percutaneous endoscopic gastrostomy or radiologically inserted gastrostomy correlates with markedly improved survival across sCJD, gCJD, and acquired CJD patients (*11*). We posit that nasal feeding represents a crucial intervention in the advanced-stage care of CJD patients. While dysphagia frequently compromises nutritional intake in CJD patients, nasal feeding offers a less invasive alternative to gastrostomy that can be readily implemented in small clinical settings or home environments.

Several limitations should be acknowledged in this study. First, all cases were classified as probable sCJD without neuropathological confirmation or PrP^{Sc} detection, which may introduce diagnostic bias. Second, the relatively modest sample size necessitates further validation through expanded cohort studies to confirm the stability of our findings. Third, the implementation of nasogastric feeding is influenced by multiple factors, including family support, patient end-of-life preferences, and physician judgment, which may confound the observed associations. Continued evaluation of these identified survival factors through ongoing CJD surveillance will be crucial for optimizing medical interventions and care strategies for Chinese CJD patients.

Conflicts of interest: No conflicts of interest.

Ethical statement: Received approval from the Ethical Committee of the National Institute for Viral Disease Control and Prevention, China CDC (protocol 2009ZX10004-101).

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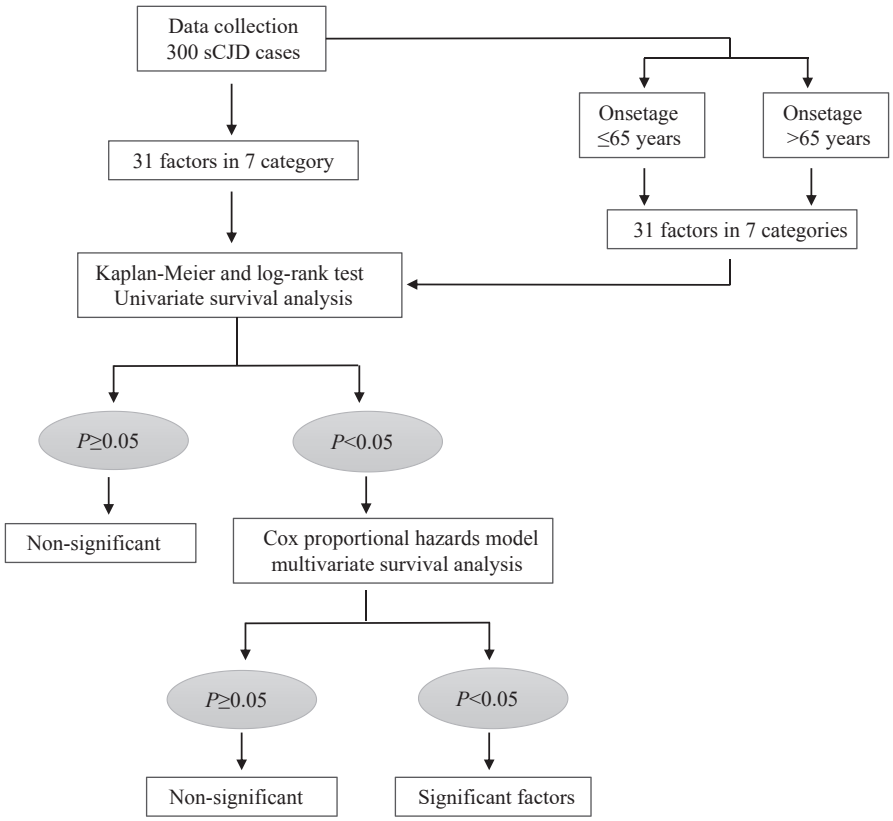
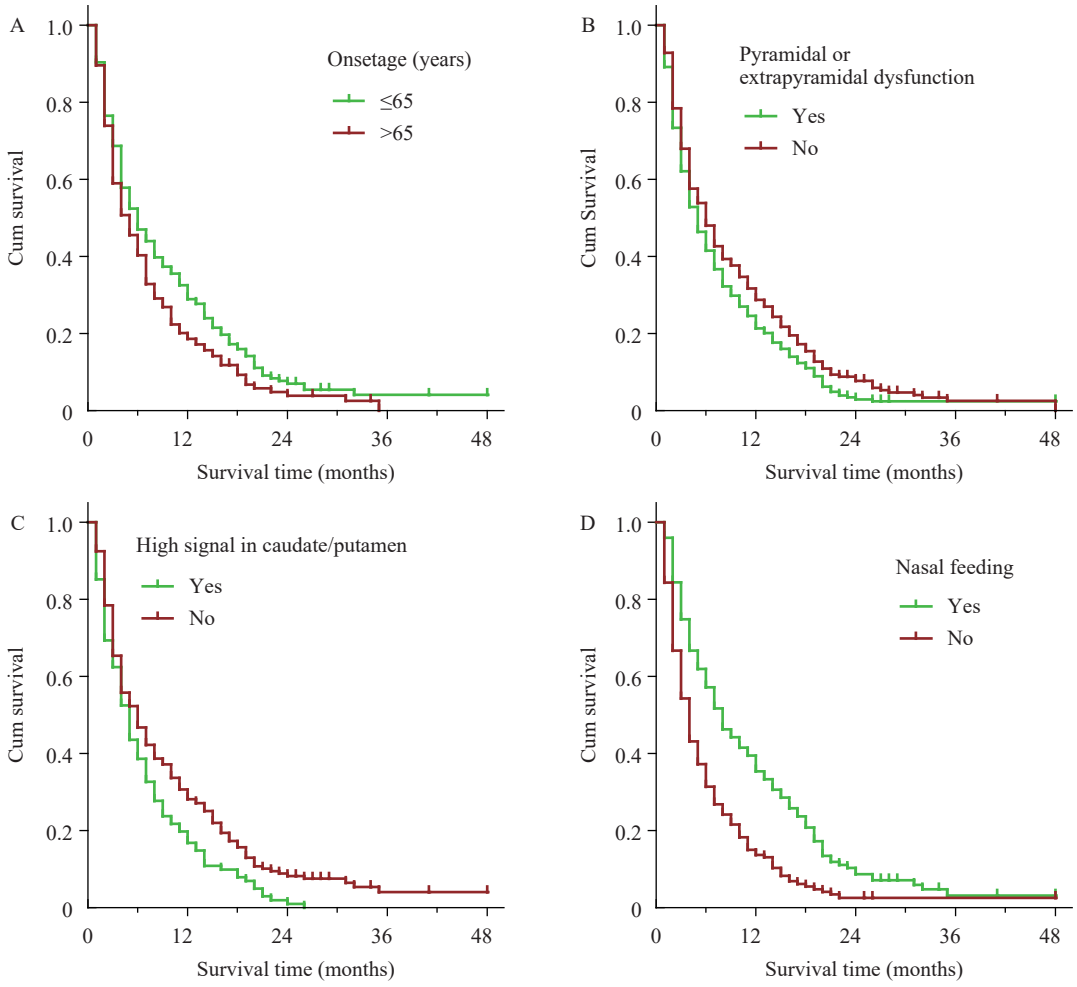
Supplementary Material



SUPPLEMENTARY FIGURE S1. Flowchart showing the data collection of the enrolled 300 sCJD cases and statistical analytic processes for the selected factors potentially associated with the survival of disease.
Abbreviation: sCJD=sporadic Creutzfeldt-Jakob disease.



SUPPLEMENTARY FIGURE S2. Comparative survival curves of sCJD patients (A) between the groups ≤65 years and >65 years at onset, (B) with or without pyramidal or extrapyramidal dysfunction, (C) high signal of caudate nucleus/putamen, (D) with or without nasal feeding.

SUPPLEMENTARY TABLE S1. Univariate analysis of the associations of the frequencies of clinical manifestations and MRI abnormalities with survival.

Factor	Cases	Median of survival time (m) (95% *CI*)	χ^2	*P*
Clinical manifestations			5.756	0.124
Dementia plus 1	17	7 (0.950, 13.050)		
Dementia plus 2	53	6 (3.808, 8.192)		
Dementia plus 3	134	6 (4.586, 7.414)		
Dementia plus 4	96	4 (2.800, 5.200)		
Abnormalities on MRI			4.669	0.198
0	41	6 (3.719, 8.281)		
1	164	6 (4.369, 7.613)		
2	85	5 (3.877, 6.123)		
3	10	4 (0.901, 7.099)		

Abbreviation: MRI=magnetic resonance imaging; m=months; *CI*=confidence intervals.

Outbreak Reports

An Imported Yellow Fever Adverse Events Following Immunization Case Identified by Targeted Next-Generation Sequencing — Guangdong Province, China, October 2024

Xin Zhang[1,&]; Zhe Liu[2,&]; Jieling Wang[1]; Jianhua Huang[1]; Shen Huang[1]; Biao Di[3]; Jiandong Li[4]; Qiqi Tan[1]; Xiaolu Shi[5]; Min Kang[1]; Baisheng Li[1,#]

Summary

What is already known about this topic?

Yellow fever (YF) is a highly lethal mosquito-borne infectious disease endemic to tropical regions for which no antiviral treatments currently exist. Vaccination remains the most effective preventive measure and is recommended by the World Health Organization (WHO) for YF control and prevention. However, the YF vaccination associated Adverse Events following Immunization (AEFI) cases occur globally occasionally.

What is added by this report?

This report describes the first imported suspected YF case in China in 2024, which was a 46-year-old Peruvian man with a recent YF vaccination history. Guangdong CDC employed Targeted Next-Generation Sequencing (tNGS) analysis to determine whether the patient was infected by the wild-type YF virus strain or experienced an AEFI. tNGS analysis successfully yielded a 10.2 kb viral genomic sequence and BLAST analysis revealed high similarity to the YF vaccine strain 17D-213. Phylogenetic analysis classified the sequence within the West Africa II genotype, clustering with the 17D vaccine strain and showing 99.89%–99.79% homology with vaccine strains, while demonstrating only 85.4%–84.9% similarity to wild-type YF virus strains from South America. Based on this evidence, an expert panel consultation concluded that this case represented YF AEFI.

What are the implications for public health practice?

The implementation of tNGS technology enables more precise and expeditious pathogen sequencing, providing critical evidence for accurate disease diagnosis and informed public health interventions.

ABSTRACT

Introduction: Vaccination stands as the most effective preventive measure against yellow fever (YF). However, the YF vaccination associated Adverse Events following Immunization (AEFI) cases occur occasionally.

Methods: The Guangdong Provincial Center for Disease Control and Prevention utilized Targeted Next-Generation Sequencing (tNGS) to determine whether the imported suspected YF case was infected by the wild-type YF virus strain or experienced an AEFI.

Results: tNGS analysis successfully yielded a 10.2 kb viral genomic sequence. Subsequent in - depth analysis revealed high similarity to the YF vaccine strain 17D-213 and classified the sequence within the West Africa II genotype, clustering with the 17D vaccine strain.

Conclusions and Implications for Public Health Practice: This case represented YF AEFI. The implementation of tNGS technology enables more precise and expeditious pathogen sequencing, providing critical evidence for accurate disease diagnosis and informed public health interventions.

Yellow fever (YF) is a mosquito-borne disease preventable through a highly effective, safe, and affordable vaccine (*1*). The YF vaccine, a freeze-dried live-attenuated virus preparation, typically confers lifelong immunity after a single dose (*1–2*). Despite its established safety record spanning more than 80 years, mild adverse effects including fever, flu-like symptoms, muscle aches, and chills have been occasionally reported (*2*). Vaccine recipients may experience viremia between 2 and 6 days post-vaccination (*3*), with peak viremia typically occurring between days 4 and 6 following immunization (*3*).

While Reverse Transcription-Polymerase Chain Reaction (RT-PCR) assay remains widely used for YF virus nucleic acid detection, it lacks the capability to

differentiate between wild-type and vaccine strains. Targeted Next-Generation Sequencing (tNGS), which combines targeted enrichment techniques with high-throughput sequencing, offers enhanced detection sensitivity compared to metagenomic NGS for multiple known pathogenic microorganisms (*4*–*5*). This method employs either multiplex PCR amplification or oligonucleotide probe hybridization to enrich target pathogen genes. The hybrid capture approach demonstrates superior sensitivity and specificity, making it particularly valuable for analyzing complex sequences across large-scale and multi-gene target regions. Consequently, tNGS has become instrumental in biological evolution studies, gene phenotype research, and investigations of genetic and rare diseases (*6*).

Investigation and Results

On October 13, 2024, a 46-year-old Peruvian man tested positive for YF during entry screening at Shenzhen customs. Guangdong CDC received notification from Shenzhen CDC on the evening of October 14, 2024, prompting an immediate epidemiological investigation.

The patient arrived at Hong Kong Airport via Amsterdam at 16:00 on October 13, 2024, proceeded directly to Guangzhou City, Guangdong Province by vehicle, and checked in at his hotel at 22:00. During his brief 30-minute stop at Shenzhen Bay Customs for entry procedures, he presented with a fever of 38.8℃ but no other symptoms. The patient had received YF vaccination on October 7, 2024, as documented in his immunization certificate, and had no travel history to Africa in the preceding 4 weeks. Blood samples analyzed by the Shenzhen Bay Customs Laboratory using RT-PCR assay yielded positive results for YF virus RNA in serum on October 14, 2024, while tests for coronavirus disease 2019 (COVID-19), influenza, Mpox, dengue, Zika, West Nile, and malaria were negative. The patient was immediately transferred via emergency ambulance to Guangzhou Eighth People's Hospital, Guangzhou Medical University, for isolation and symptomatic treatment. Upon admission, his temperature had normalized to 36.4 ℃, and he remained asymptomatic.

On October 15, 2024, Guangdong CDC confirmed YF virus infection in the patient's blood sample received from Guangzhou CDC, detecting viral RNA using a RT-PCR kit [BioGerm (Qingdao), China] with a Ct value of 33. By October 17, 2024, tNGS analysis successfully yielded a 10.2 kb viral genomic sequence. BLAST analysis revealed high similarity to the YF vaccine strain 17D-213 (GenBank Accession Number: U17067.1), with only 10 single nucleotide polymorphism (SNP) sites. Phylogenetic analysis classified the sequence within the West Africa II genotype, clustering with the 17D vaccine strain and showing 99.89%–99.79% homology with vaccine strains, while demonstrating only 85.4%–84.9% similarity to wild-type YF virus strains from South America (Figure 1). The National Institute for Viral Diseases Control and Prevention, China CDC, subsequently confirmed these viral RNA findings. Based on this evidence, an expert panel consultation concluded that this case represented YF Adverse Events following Immunization (AEFI), and the patient was discharged at 22:00 on October 17, 2024.

Public Health Response

Upon receiving confirmation of Yellow fever virus positivity, the Guangdong Provincial, Guangzhou Municipal, and Haizhu District CDCs collaborated to implement comprehensive control measures. These included immediate patient isolation in a mosquito-proof facility, systematic health surveillance of close contacts, and sustained vector monitoring and control in all potentially affected areas.

DISCUSSION

This study documents China's first imported suspected Yellow fever case in 2024. Through comprehensive analysis of epidemiological data, vaccination history, and laboratory findings, we determined that the patient's febrile symptoms and viremia were attributable to Yellow fever vaccine-associated adverse events.

The Eliminate Yellow fever Epidemics strategy represents a global coalition of partners and affected countries established to address YF challenges. As Peru is designated as a YF-risk region, international travelers must present proof of YF vaccination (*1*). The patient developed a fever of 38.8 ℃ at Shenzhen Bay Customs on October 13, 2024 — six days post-vaccination — with YF viral RNA consistently detected in serum samples across multiple independent laboratories. Whole-genome sequencing conclusively demonstrated high sequence homology with the vaccine strain rather than wild-type strains circulating in South America, aligning with previously documented post-vaccination viremia patterns.

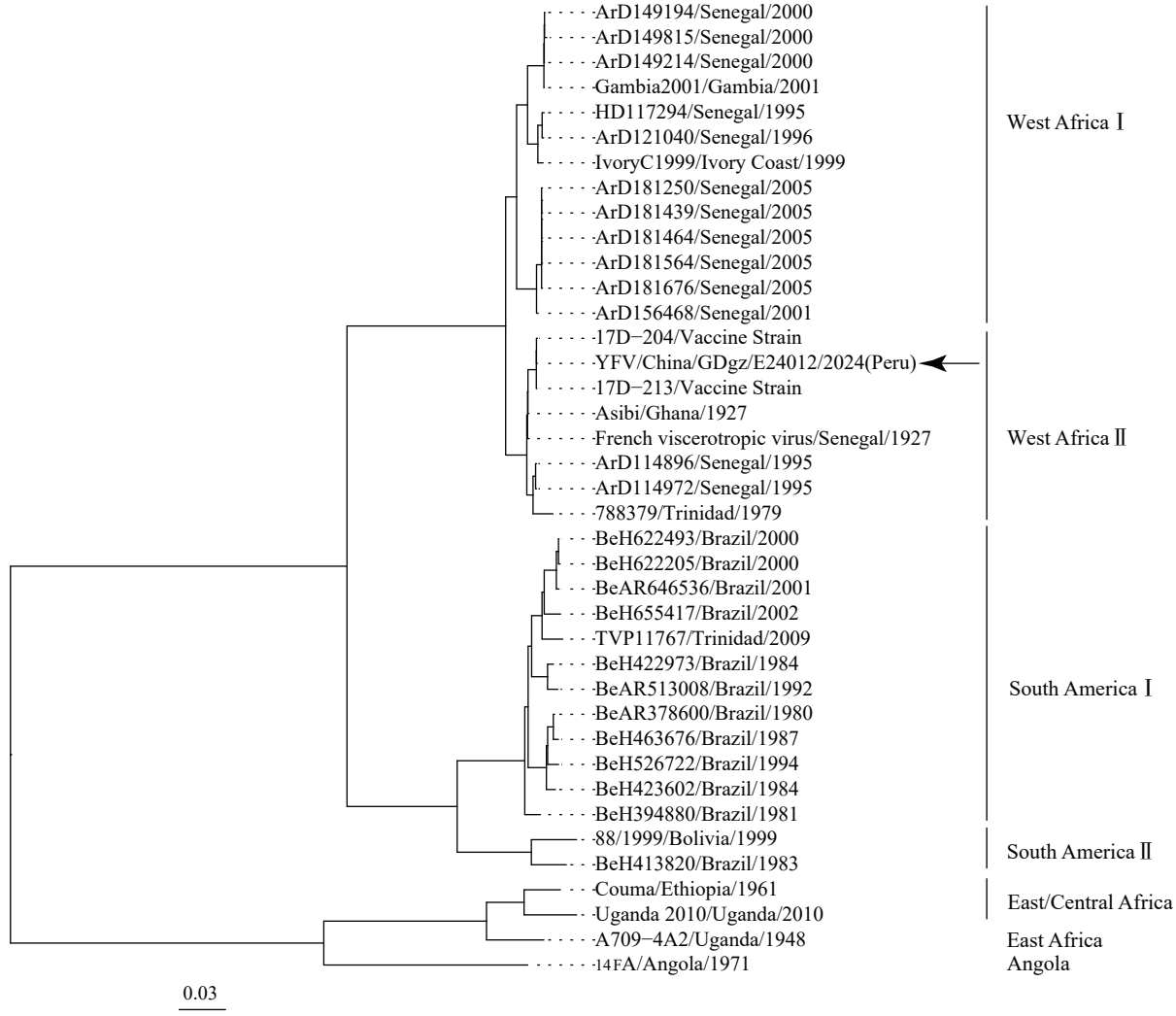


FIGURE 1. Phylogenetic analysis of Yellow fever virus whole genome sequences using the Neighbor-Joining method.
Note: The arrow indicates the sequence obtained in this study.

According to World Health Organization guidelines, a confirmed YF case in an unvaccinated population constitutes an outbreak. The 2016 importation of 11 YF cases to China, all confirmed as wild-type virus infections, prompted enhanced YF surveillance and early warning systems (*7*). In response to the customs alert, we immediately implemented comprehensive epidemiological investigations and rigorous laboratory testing, which confirmed the vaccine-associated nature of this case. To minimize future vaccine-associated adverse events, we recommend earlier administration of YF vaccination for international travelers.

Conflicts of interest: No conflicts of interest.

Ethical statement: Received ethics approval from the Ethical Committee of National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention (No. IVDC2023-19).

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