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Molecular epidemiological analysis of Influenza viruses in Influenza-like illness cases: a retrospective study in Chongqing Hi-Tech Zone, China (2021–2024)

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Abstract

Objectives To analyze the molecular epidemiological characteristics of influenza viruses in influenza-like cases in Chongqing Hi-Tech Zone, China, to provide data support and a scientific basis for optimizing influenza prevention and control strategies in the region.

Materials and methods A retrospective analysis was conducted on the molecular epidemiological characteristics of influenza viruses in influenza-like cases at a hospital in Chongqing Hi-Tech Zone from 2021 to 2024. Colloidal gold detection of viral antibodies, fluorescent PCR detection of nucleic acids, and gene sequencing were used to identify the different subtypes.

Results Among 39,986 ILI specimens tested using the immunocolloid gold method, 6,616 influenza viruses were detected, with a detection rate of 16.54%. Infections included 4,464 influenza A viruses (67.50%), 2,033 influenza B viruses (30.73%), and 119 co-infections of influenza A and B viruses (1.77%).In this region, H3N2 was the predominant subtype of influenza A, and Victoria was the main subtype of influenza B.

Conclusion Influenza epidemics in the winter and spring seasons in Chongqing Hi-Tech Zone were predominantly caused by influenza A, with influenza B also circulating. Influenza A strains were mainly H3N2, while influenza B strains were primarily Victoria.

Keywords Molecular epidemiological analysis, Influenza viruses, Influenza-like illness cases, Prevention and control

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Background

Influenza is a pandemic respiratory pathogen from the Orthomyxoviridae family, which can infect humans or other animals [1]. Due to its frequent genetic variation, the antigenicity of pandemic strains often changes annually, posing challenges for vaccine preparation and influenza surveillance. Influenza viruses are classified into four types: A, B, C, and D, based on antigenic differences in their nucleocapsid and nucleoprotein antigens [2]. Among these, influenza A subtypes (H1N1 and H3N2) and influenza B are known as seasonal influenza because they can circulate among populations throughout the year [3]. Influenza epidemics are often associated with significant economic and social burdens [4], making networked surveillance a crucial tool for preventing and controlling pandemics [5]. The World Health Organization analyzes laboratory surveillance data from global influenza surveillance networks annually and recommends vaccine strains for the subsequent year's vaccine preparation [6–9].

Serum amyloid A (SAA) is an inflammation marker that has garnered significant attention recently [10–13]. SAA levels can rapidly and markedly increase following infection, inflammation, or tissue injury, making it valuable for the early diagnosis of infectious diseases, risk assessment, evaluation of therapeutic efficacy, and prognosis determination. The elevation of SAA due to viral infections suggests its potential role in diagnosing influenza A and B [14–18].

This study aims to explore the molecular epidemiological characteristics of influenza viruses in influenza-like cases in Chongqing Hi-Tech Zone from 2021 to 2024. By monitoring and analyzing these cases, the research assesses the potential of inflammatory markers, such as SAA and C-reactive protein (CRP), for use in influenza diagnosis. The findings provide a scientific basis for improving influenza prevention and control strategies in the region and across the country, ultimately helping to mitigate the impact of influenza on public health.

Materials and methods

This study conducted a retrospective analysis of influenza-like illness (ILI) cases in a hospital in Chongqing Hi-Tech Zone, China, from 2021 to 2024. Inclusion criteria were based on the National Influenza Surveillance Programme (2017 version), requiring cases to meet the following conditions: body temperature ≥ 38 °C with symptoms of acute respiratory infection such as cough, sore throat, or sputum. Some cases may exhibit mild symptoms or no fever; physical examinations typically revealed enlarged tonsils and pharyngeal congestion. All cases required signed informed consent and were reviewed and approved by the hospital ethics committee.

We screened cases from the hospital's electronic medical record system that met the ILI definition. Exclusion criteria included non-acute respiratory infectious diseases, known non-influenza viral respiratory diseases, and cases lacking necessary clinical and laboratory data. Additionally, basic patient information such as age, gender, occupation, and place of residence was collected to facilitate subsequent data analysis.

Detection methods

Pharyngeal swabs and sputum samples were collected using sterile swabs. These samples were promptly sent to the laboratory for testing immediately after collection. The colloidal gold method was used to detect viral antibodies, which demonstrating high sensitivity and specificity when compared to real-time RT-PCR, indicating its potential as a reliable screening tool in clinical settings [19, 20].And the fluorescent PCR method was employed to detect nucleic acids(Shanghai Hongshi Automatic Nucleic Acid Analysis System SLAN96P).Gene sequencing was utilized to identify different subtypes.

Statistical processing

" Prior to statistical analysis, the measured data were subjected to a variance chi-square test. Parametric tests were employed for data that satisfied the criteria for normal distribution, while non-parametric tests were utilized for all count data."All data were analyzed utilizing SPSS version 22.0 statistical software. The research results were organized to ensure the logic and completeness of data screening. Descriptive statistics, such as mean ± standard deviation ($\bar{x} \pm s$), were used for continuous data, while frequency and percentage were used for categorical data.

Comparisons between groups for count data were performed utilizing the χ^2 test or Fisher's exact probability method. Comparisons between groups for continuous data were performed utilizing the t-test or ANOVA. A two-sided $P < 0.05$ was considered statistically significant.

Multivariate logistic regression analysis was used to adjust for potential confounders among the independent variables. The correlation between inflammatory indicators, such as SAA and CRP, and influenza virus infection was analyzed to evaluate the sensitivity and specificity of these indicators for influenza. Further statistical analysis was conducted to provide a more accurate assessment of these relationships.

Results

Influenza virus test results

A total of 39,986 ILI specimens were tested using the fluorescent PCR methods, detecting 6,616 influenza viruses, resulting in a detection rate of 16.54%. Among these, 4,464 (67.50%) were influenza A viruses, 2,033 (30.73%) were influenza B viruses, and 119 (1.77%) were

Table 1 Influenza virus test results of ILI specimens

times	*n*	Influenza A virus (*n* = 4464)	Influenza B virus (*n* = 2033)	Influenza A + InfluenzaB virus (*n* = 119)
November 2021	1	0	0	0
December 2021	0	0	0	0
January 2022	4365	1054	23	16
February 2022	3185	43	13	8
March 2022	3769	478	217	11
April 2022	3352	213	245	17
May 2022	2677	208	236	26
June 2022	2356	64	41	5
July 2022	782	53	12	1
August 2022	753	31	9	0
September 2022	1056	132	27	6
October 2022	1369	106	13	4
November 2022	3745	187	23	3
December 2022	6287	1236	541	14
January 2023	5428	647	625	6
February 2023	618	8	5	1
March 2023	243	4	3	1

simultaneous detections of both influenza A and B viruses, as shown in Table 1.

From November 2021 to September 2022, the peak detection of the influenza A virus occurred in January 2022, while the peak detection of the influenza B virus occurred in April 2022. From July 2022 to March 2023, the peak detection of influenza A virus occurred in December 2022, and the peak detection of influenza B virus occurred in January 2023. Notably, the peak of influenza B virus detection lagged behind that of influenza A (Fig. 1).

H1N1 and H2N2 type test results

The positive cases were submitted for second-generation sequencing in order to ascertain the specific type of virus involved.From April 2023 to April 2024, H3N2 was the predominant subtype of influenza A, while Victoria was the main subtype of influenza B. The H1 subtype of influenza A was absent throughout 2023 but accounted for 82% of detections in January 2024 and 16% in February 2024. The Yamagata subtype of influenza B was undetected from 2023 to 2024 (Table 2; Fig. 2).

Data analysis of SAA and CRP levels in patients with influenza A and B

From April 2023 to April 2024, our hospital recorded 241 influenza A and 207 cases of influenza B. The differences in SAA and CRP levels between these groups were statistically significant ($p=0.000$ and $p=0.001$, respectively). SAA and CRP levels were significantly higher in the influenza A group compared to the influenza B group. The increase in SAA levels in the influenza A group was greater than in the influenza B group and higher than in healthy adults. These findings indicate a correlation between influenza positivity and elevated SAA levels (Table 3; Fig. 3).

Comparison of the distribution of influenza viruses by gender in various age groups

The differences in influenza A virus detection rates among genders aged 0–10 years and 60–70 years were statistically significant. In the 0–10 age group, the detection rate for males was 17.34% compared to 14.35% for females ($P<0.05$). In the 60–70 age group, the detection rate for males was 3.52% compared to 6.13% for females ($P<0.05$). For influenza B virus, the detection rate in the 0–10 years age group was 7.34% for males compared to 6.13% for females, also statistically significant ($P<0.05$) (Table 4).

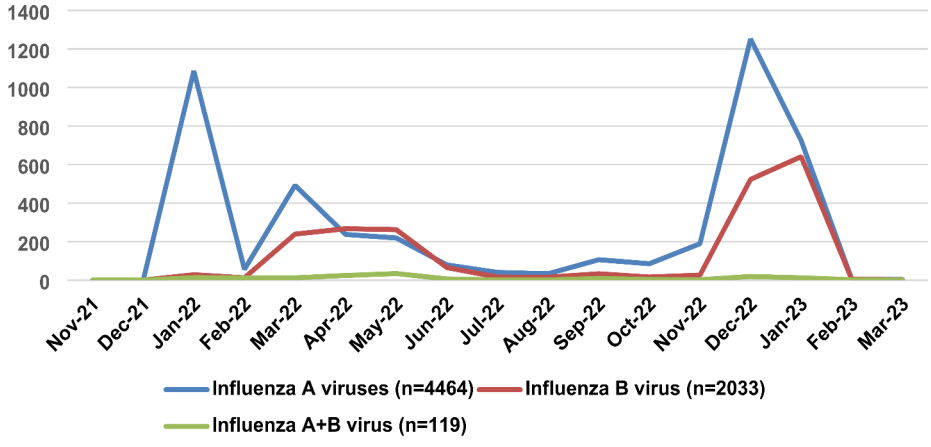

Fig. 1 Temporal distribution of influenza virus epidemics

Table 2 Influenza virus test results of ILI specimens (Subtype of the influenza virus)

times	Influenza A virus		Influenza B virus	
	H1(%)	H3 (%)	Yamagata (%)	Victoria (%)
April 2023	0	100	0	100
May 2023	0	100	0	100
June 2023	0	0	0	0
July 2023	0	0	0	0
August 2023	0	0	0	0
September 2023	0	100	0	0
October 2023	0	100	0	100
November 2023	0	100	0	100
December 2023	0	100	0	100
January 2024	82	18	0	100
February 2024	16	84	0	100
March 2024	87	13	0	100
April 2024	87	13	0	100

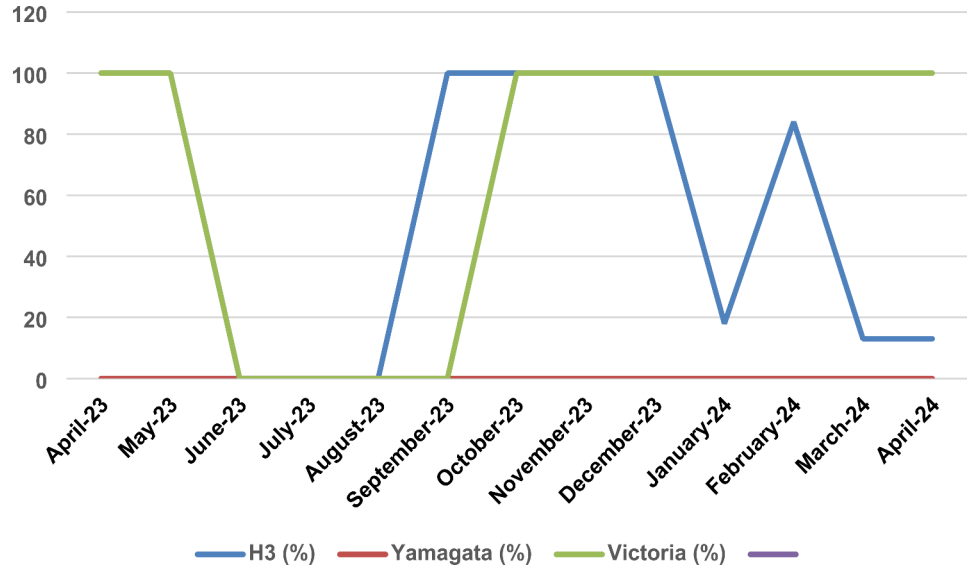

Fig. 2 Percentage of influenza virus test results for ILI specimens

Table 3 Comparison of SAA and CRP levels [M (P25, P75), mg/L] in patients with influenza A and B from April 2023 to April 2024

groups	*n*	SAA	CRP
Influenza A group	241	86.5 (43.6, 128.5)[ab]	18.7 (9.2, 33.7)[ab]
Ethereal group (physics)	207	25.6 (15.7, 75.6)[a]	7.9 (2.4, 15.3)[a]
P		0.000	0.001

Comparison of the distribution of influenza viruses by sex

Among the 32,930 ILI cases, 15,610 were male and 17,320 were female. The detection rates of influenza A and B viruses were higher in males (12.01% and 4.89%, respectively) compared to females (7.83% and 3.69%, respectively). These differences were statistically significant ($P<0.05$)(Table 5).

Colloidal gold and fluorescent PCR results

A total of three hundred patients were randomly selected for testing using both colloidal gold and fluorescent PCR methods in parallel, resulting in 73 influenza virus cases, yielding a detection rate of 24.33%. Among these, 52 cases were influenza A virus (71.23%), and 21 cases were influenza B (28.77%). Using the immunocolloidal gold method to detect influenza virus antigens, 49 cases were detected, with a detection rate of 16.34%. The detection rate of influenza virus using the fluorescent PCR method was significantly higher than that of the immunocolloidal gold method ($\chi^2=5.736$, $P=0.004$), as shown in Table 6.

Discussion

Surveillance of influenza samples in Chongqing High-Tech Zone revealed the molecular epidemiological characteristics of influenza virus strains, including detection

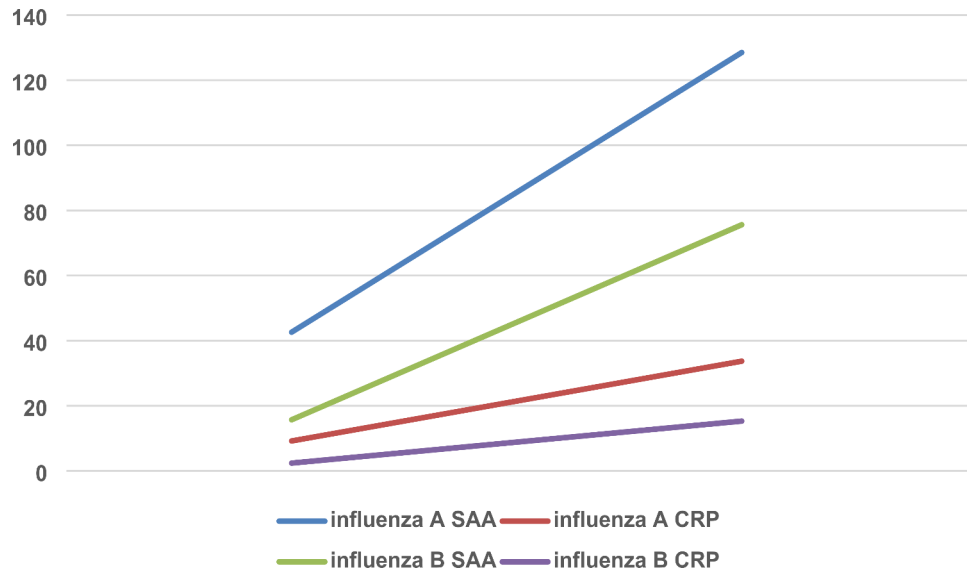

Fig. 3 Ratio of SAA and CRP levels in patients with Stream **A** and Stream **B** from April 2023 to April 2024Comparison of data from [M(P25, P75), mg/L]

Table 4 Comparison of the distribution of influenza viruses by age group and sex

item	Age group	Number of influenza A virus detections (*n*)	Influenza A virus χ^2	*P*	Number of detections of influenza B virus (*n*)	Influenza B virus χ^2	*P*
0 to 10 years	18,752	3275	30.627	< 0.001	1307	5.249	0.036
male	10,865	1856			738		
women	7887	1419			569		
> 10 ~ 20 years old	3875	545	0.387	0.413	325	0.062	0.629
male	1946	327			182		
women	1929	218			143		
> 20 ~ 30 years old	2637	236	0.253	0.721	206	0.136	0.658
male	1214	93			89		
women	1423	143			117		
> 30 ~ 40 years old	3276	258	0.003	0.899	125	0.385	0.472
male	1424	115			53		
women	1852	143			72		
> 40 ~ 50 years old	1321	57	0.005	0.953	23	0.394	0.437
male	589	23			8		
women	732	34			15		
> 50 ~ 60 years old	1629	123	0.936	0.547	13	0.649	0.352
male	757	42			4		
women	872	81			9		
> 60 ~ 70 years old	1753	106	9.978	0.002	21	1.525	0.136
male	697	49			12		
women	1056	57			9		
> 70 years	1928	47	0.659	0.346	11	0.178	0.459
male	745	21			9		
women	1183	26			2		

rates and temporal variations of major genotypes. These findings contribute to understanding influenza virus transmission patterns and trends, support the iterative updating of influenza virus strains, and help predict transmission and pathogenicity, thus providing a scientific basis for public health decision-making [21–24].

Chongqing Hi-tech Zone has a strong population mobility, which increases the likelihood of influenza generation, prevalence, and dissemination. Therefore, monitoring the pathogenetic and epidemiological patterns of influenza in this area is particularly significant. This study analyzed all ILIs reported at Chongqing Hi-Tech Zone

Table 5 Comparison of the distribution of influenza viruses by sex

distinguishing between the sexes	*n*	Influenza A virus		Influenza B virus	
		Number of detections (*n*)	Detection rate (%)	Number of detections (*n*)	Detection rate (%)
male	15,610	1874	12.01	763	4.89
women	17,320	1356	7.83	639	3.69
χ^2		35.623		13.261	
P		< 0.001		< 0.001	

Table 6 Results of colloidal gold and fluorescent PCR assays

immunocolloid gold method	Fluorescent PCR method		add up the total
	positive	negatives	
positive	**42**	**7**	**49**
negatives	31	220	251
add up the total	73	227	300

University Hospital from November 2021 to April 2024. Both influenza A and B peaked during the winter and spring seasons, with influenza B peaking later than influenza A. This finding is consistent with previous literature reports [25–27]. It can be concluded that influenza A predominantly dominates the epidemic season.

From April 2023 to April 2024, there were 241 positive cases of influenza A and 207 positive cases of influenza B. Among the influenza A cases, H3N2 was the predominant subtype, while Victoria was the main subtype for influenza B. The H1 subtype of influenza A was absent throughout 2023 but accounted for 82% of the cases in January 2024 and 16% in February 2024. The Yamagata subtype of influenza B did not appear from 2023 to 2024 [26]. The study found that children aged 0–10 years were affected by influenza. There was a statistically significant difference in the detection rates of influenza A and B viruses between males and females in this age group ($p < 0.05$) [28–30].

The SAA and CRP levels of 241 influenza A positive cases and 207 influenza B positive cases were analyzed, showing statistically significant differences between the two groups ($p = 0.000$ for SAA and $p = 0.001$ for CRP). The CRP levels were 7.9 mg/L in the influenza A positive group and 18.7 mg/L in the influenza B positive group. The SAA levels in the influenza A positive group were significantly higher than in the influenza B positive group. The CRP level in the influenza A positive group was significantly higher than in the influenza B positive group. A correlation was found between influenza A and B positivity and elevated SAA levels, with influenza A positivity showing a stronger correlation with elevated SAA [31–34].

It was shown that inflammation markers were higher in influenza A than influenza B. Studies have shown that patients infected with influenza A exhibit a more pronounced inflammatory response compared to those with influenza B. For instance, a comparative study of severe and critical influenza B in children highlighted that while both types of influenza can lead to significant morbidity, the inflammatory markers associated with influenza A infections tend to be elevated [35]. Additionally, research on the cellular immunophenotype expression during influenza infections indicated that influenza A is associated with a higher fraction of certain immune cell types, such as CD14+and CD4+IL-17 A+cells, compared to influenza B [36].

Moreover, the differential ability of pandemic and seasonal H1N1 influenza A viruses to alter neutrophil function suggests that influenza A may provoke a more robust immune response, potentially leading to increased inflammation [36]. This is further supported by findings that show higher levels of pro-inflammatory cytokines in patients with influenza A, which can contribute to the severity of the disease [37].

In the context of co-infections, it has been observed that influenza A infections are more likely to be complicated by secondary bacterial infections, which can exacerbate the inflammatory response and lead to worse clinical outcomes [38]. The overall immune response to influenza A, characterized by heightened inflammation, underscores the need for vigilant monitoring and management of patients infected with this virus [39].

The correlation between influenza A and B positivity and SAA elevation was notably strong. In summary, winter and spring influenza in Chongqing's High-Tech Zone is predominantly caused by influenza A, though influenza B is also prevalent. Among the positive cases, H3N2 is the primary subtype for influenza A, while Victoria is the primary subtype for influenza B. Elevated SAA levels are correlated with both influenza A and B positivity.

Furthermore, developing and optimizing influenza prevention and control strategies is crucial for mitigating the impact of seasonal and pandemic influenza. Effective strategies must be informed by robust surveillance systems, vaccination programs, and public health interventions. For instance, the Global Influenza Strategy 2019–2030 emphasizes the need for improved surveillance and vaccination efforts in regions like Latin America and the Caribbean, where seasonal influenza is associated with significant morbidity and mortality [1].

Moreover, the application of mathematical models, such as the moving epidemic method, can help define

epidemic thresholds and guide timely interventions. A study conducted in Tunisia demonstrated the utility of this method in determining influenza epidemic and intensity thresholds, which can inform local health authorities about when to implement control measures [2].

In addition to vaccination, nonpharmaceutical interventions play a vital role in controlling influenza transmission. A review of personal protective measures and environmental hygiene in nonhealthcare settings highlighted the importance of hand hygiene and the use of face masks, although evidence from randomized controlled trials suggests limited effectiveness in reducing transmission [3].

Although the study demonstrates the epidemiological characteristics of influenza virus infection and the potential application of inflammatory markers, several limitations exist. The limited sample size may restrict the generalizability of the findings. Additionally, the study did not analyze the effect of different influenza A virus strains on the levels of 14 inflammatory markers or explore the potential influence of other respiratory pathogens on these markers.

Future studies will explore the mechanisms behind these epidemiological features to obtain more comprehensive and objective findings. Additionally, further research is needed on the expression patterns of inflammatory markers in different populations, such as children, the elderly, and patients with chronic diseases, and their role in the preventive mechanisms of influenza vaccination. As research deepens, a clearer understanding of the function and importance of the influenza vaccine and inflammatory markers will provide a solid theoretical basis for influenza prevention and treatment.

Conclusion

The winter and spring influenza virus epidemics in the High-Tech Zone of Chongqing Municipality, China, were dominated by influenza A, with influenza B circulating. The predominant strains were H3N2 for influenza A and Victoria for influenza B. This study provides important data and a scientific basis for developing and optimizing influenza prevention and control strategies in the region.

Author contributions

W.C. and Y. H.D. Conceived the manuscript. W.C. and Y. H.D. wrote the draft manuscript. P.X. curated the data and prepared the figures and tables. J.J.X. critically read and edited the manuscript. P.X. curated the data and prepared the figures and tables. J.J.X. critically read and edited the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

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