



Epidemiological Study of Respiratory Virus Infections in Pediatric Patients with Systemic Inflammatory Response Syndrome

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Abstract

Background: Respiratory infections are a common cause of systemic inflammatory response syndrome (SIRS) in pediatric patients. However, literature specifically addressing respiratory viruses that lead to SIRS or sepsis in children is limited, primarily consisting of case reports and lacking data for more comprehensive conclusions.

Objectives: This study aims to investigate the relationship between respiratory viral infections and SIRS in children, focusing on virus detection rates, patient profiles, and the incidence of septic shock associated with different respiratory viruses.

Methods: A retrospective analysis was conducted from January 2022 to December 2023 on hospitalized children diagnosed with respiratory infections and SIRS. Respiratory viruses were detected through qualitative PCR testing, and procalcitonin levels were measured using an enzyme-linked fluorescent immunoassay.

Results: A total of 931 pediatric patients with SIRS were tested for respiratory viruses and/or other pathogens. Among these, 298 (32.0%) were positive for respiratory viruses, with 263 (28.2%) cases attributed solely to respiratory viruses. Human rhinovirus (HRV) had the highest infection rate at 37.3% (98/263), followed by human adenovirus (HAdV) at 24.3% (64/263). Seasonal distribution among the 263 SIRS cases associated with respiratory viral infections showed the highest incidence in spring (39.5%), followed by summer (25.5%), winter (17.9%), and autumn (17.1%). Septic shock rates were highest among cases of influenza A) FluA(, human metapneumovirus (hMP), and co-infections, with incidences of 27.8%, 18.2%, and 22.7%, respectively. There was significant variation in septic shock rates across different viral infections in pediatric patients ($P < 0.001$).

Conclusions: Many hospitalized children with respiratory viral infections develop SIRS, and a subset of these cases can progress to septic shock.

Keywords: Respiratory Viral Infections, Systemic Inflammatory Response Syndrome, Children, Septic Shock

1. Background

Systemic inflammatory response syndrome (SIRS) is widely recommended as a screening tool to identify pediatric patients at risk of septic shock who may require resuscitative care. As part of the formal definition of sepsis, SIRS has been effectively utilized in the Pediatric Surviving Sepsis campaign to activate pediatric sepsis protocols, despite some concerns regarding its potential for over-sensitivity in pediatric emergency settings (1, 2). Systemic inflammatory response syndrome encompasses systemic inflammatory responses arising from various severe conditions, including infection, trauma, hypoxia-

ischemia, and shock. Respiratory infections frequently lead to SIRS and sepsis, although many cases of clinical deterioration lack bacterial involvement, suggesting that viruses may also play a significant role (3-5).

The emergence of coronavirus disease 2019 (COVID-19) in China and globally has renewed attention on viral sepsis among clinicians and researchers (6). While advancements have been made in understanding the pathophysiology of viral sepsis, its distinctions from bacterial sepsis remain poorly understood. Moreover, diagnostic methods to reliably differentiate between viral and bacterial sepsis—especially in the early stages—are limited.

Common respiratory viruses include human rhinovirus (HRV), influenza viruses (FluA/B), respiratory syncytial virus (RSV), human parainfluenza viruses (HPIV), human coronaviruses (HCoV), human adenovirus (HAdV), human metapneumovirus (hMPV), and human bocavirus (HBoV). Literature on respiratory viruses associated with SIRS in pediatric patients is notably sparse, primarily consisting of isolated case reports (7, 8). These cases provide valuable but fragmented insights into the impact of respiratory viruses on severe systemic conditions in children. However, the available data remains insufficient to form more generalized conclusions or to guide comprehensive clinical practices.

2. Objectives

This research aims to examine the relationship between respiratory viral infections and SIRS in pediatric patients, focusing on the prevalence of these infections, associated clinical and demographic characteristics, and the rate of septic shock associated with various respiratory viruses.

3. Methods

3.1. Study Population

A retrospective analysis was conducted on hospitalized pediatric patients who met the clinical criteria for both respiratory infections and SIRS from January 2022 to December 2023. Cases were excluded based on the following criteria: (1) neonates and preterm infants; (2) underlying chronic respiratory or other systemic diseases; (3) congenital or genetic disorders affecting respiratory or other systems; (4) co-infections with other pathogens (e.g., bacteria, fungi, mycoplasma, or chlamydia) or concurrent infections at other anatomical sites; (5) insufficient clinical information. The study was approved by the Maternal and Child Health Hospital of Hubei province, with informed consent waived due to its retrospective nature and use of anonymized clinical data.

3.2. Definitions

Acute respiratory tract infections were classified as upper respiratory infection, bronchitis, or pneumonia based on clinical symptoms, physical examination findings, and chest X-ray results where available. The criteria for pediatric SIRS and septic shock were based

on the 2005 Expert Consensus and the 2012 International Guidelines, respectively (1, 2).

3.3. Laboratory Tests

Nasopharyngeal secretions or alveolar lavage fluid collected within 24 hours of admission were analyzed. Respiratory virus detection was conducted using commercial qualitative PCR capillary electrophoresis kits (Ningbo Haiers Gene Technology Co., Ltd., China), targeting FluA/B, HRV, RSV, HPIV, HCoV, HAdV, hMPV, HBoV, *Mycoplasma pneumoniae*, and *Chlamydia*. Microbial culture and identification were conducted within 24 hours of admission, following the hospital's standard diagnostic procedures. Procalcitonin levels in serum were measured via enzyme-linked fluorescent immunoassay using the Vidas BRAHMS PCT kit (bioMérieux, Marcy l'Etoile, France).

3.4. Statistical Analyses

Statistical analyses were performed using SPSS version 21.0 software (SPSS, Inc., Chicago, IL, USA). Comparisons of frequencies between groups were analyzed using Chi-squared tests, with a P-value of less than 0.05 considered statistically significant.

4. Results

4.1. Study Profile

Between January 2022 and December 2023, a total of 931 pediatric patients with SIRS were tested for respiratory viruses and/or other pathogens. Among these, 542 cases (58.2%) were negative for pathogens. Out of the 389 cases that tested positive for pathogens, 298 (32.0%, 298/931) were positive for respiratory viruses, with 263 (28.2%, 263/931) being attributed solely to respiratory viruses. Detailed pathogen detection results are shown in [Figure 1](#).

4.2. Pathogen Detection in Pediatric Respiratory Infections Associated with Systemic Inflammatory Response Syndrome

In the 389 cases with positive pathogen detection, 91 children tested negative for respiratory viruses, representing 23.4% (91/389) of the cases. Of the remaining 298 cases with positive respiratory virus detection, 35 (9.0%, 35/389) involved co-infections with other pathogens, and 263 (67.6%, 263/389) were solely due to respiratory virus infections ([Figure 2A](#)).

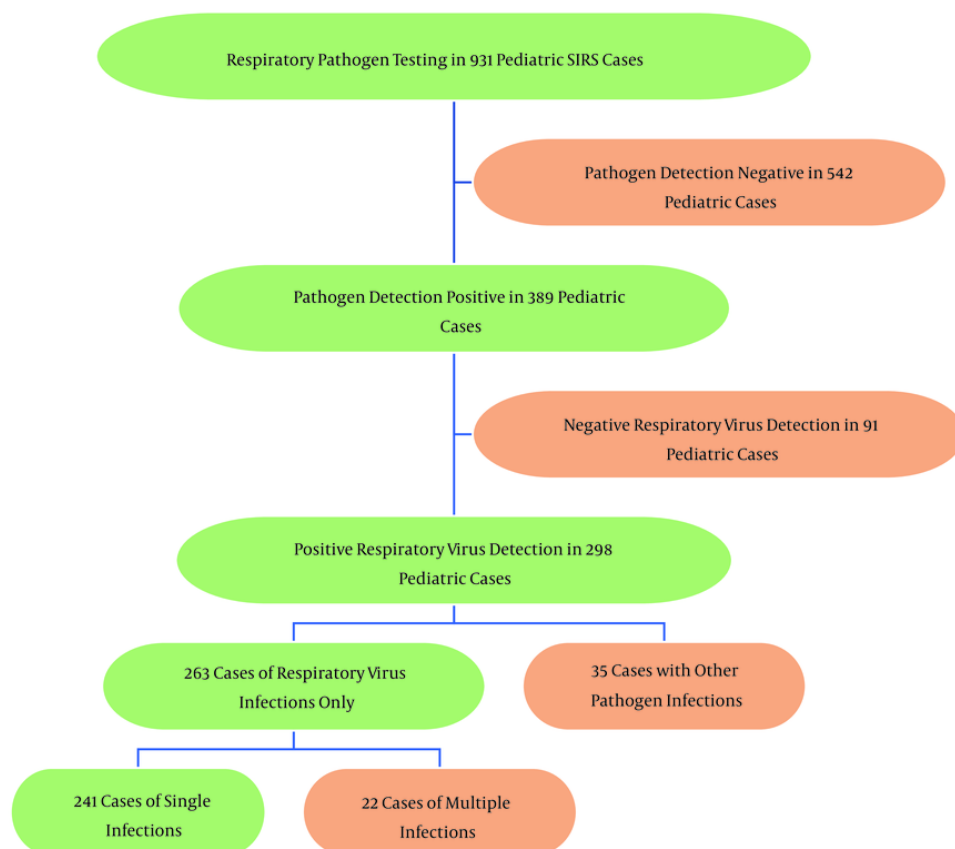


Figure 1. Flowchart of the studied population

4.3. Detection Rates of Respiratory Viruses in Children with Systemic Inflammatory Response Syndrome

As illustrated in [Figure 2B](#), among the 263 cases of respiratory virus infections, HRV had the highest detection rate at 37.3% (98/263), followed by HAdV at 24.3% (64/263). Other notable detection rates included FluA, RSV, HPIV, and mixed infections, all with rates above 5%.

4.4. Demographics of Pediatric Patients with Systemic Inflammatory Response Syndrome Potentially Due to Respiratory Viral Infections

[Table 1](#) presents the demographic and seasonal distribution of the 263 pediatric patients with SIRS potentially caused by respiratory viral infections. Among these patients, 51.0% were male. Ages ranged

from 1 month to 13 years, with a mean age of 2.91 ± 2.26 years and a median of 3 years. The majority (69.2%) were aged between 1 and 5 years, while 17.8% were under 1 year and 13.0% were aged 6 years or older. Seasonally, the highest incidence occurred in spring (39.5%), followed by summer (25.5%), winter (17.9%), and autumn (17.1%).

4.5. Clinical and Demographic Data of Pediatric Systemic Inflammatory Response Syndrome Patients with Respiratory Viral Infections

[Table 2](#) presents the primary clinical characteristics of 263 pediatric patients with SIRS potentially attributed to respiratory viral infections. Fever was prevalent, affecting over 80% of cases for most viruses, with HBoV and hMPV showing the highest incidence at 100%. Increased respiratory rates were notably common, particularly in infections caused by HAdV (92.2%) and

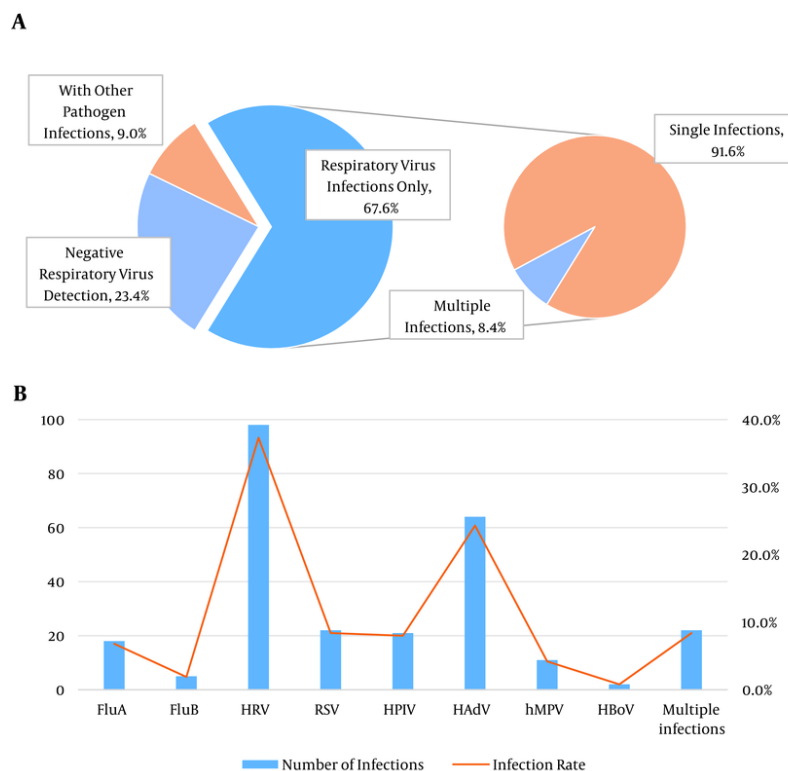


Figure 2. A, Pathogen detection in pediatric respiratory infections associated with SIRS; B: detection rates of respiratory viruses in children with systemic inflammatory response syndrome (SIRS).

hMPV (81.8%). Tachycardia was frequently observed in cases of RSV (90.9%) and hMPV (72.7%). Approximately 20% of patients had normal plasma procalcitonin levels, with no significant elevations detected.

4.6. Incidence of Septic Shock Caused by Various Viral Infections

Among the 263 children with SIRS due to respiratory viral infections, 6.8% (18/263) progressed to septic shock. The highest rates of septic shock occurred with FluA (27.8%, 5/18), hMPV (18.2%, 2/11), and coinfections (22.7%, 5/22). For details on septic shock rates associated with other viral infections, refer to Figure 3. The differences in septic shock rates between various viral infections were statistically significant ($P < 0.001$).

5. Discussion

In this study of 931 children with SIRS, respiratory viruses were detected in 32.0% of cases, increasing to

67.6% among those with positive pathogen tests. A prospective study found that respiratory viral infections were identified in 17% of pediatric sepsis cases and 48.2% of adult sepsis cases (3), highlighting the significant role respiratory viruses play in pediatric SIRS and indicating they are a major factor in its onset. Findings underscore the need for comprehensive viral screening in pediatric intensive care units and the importance of developing targeted antiviral therapies and supportive measures for managing pediatric SIRS.

Respiratory viruses, including Flu A/B, HRV, RSV, HPIV, HAdV, hMPV, and HBoV, can all lead to severe illness in children (9-11). In this study, detection rates of HRV, HAdV, Flu A, RSV, HPIV, and mixed infections were each above 5%, consistent with previous research findings (3, 12). However, a positive viral confirmation of viral sepsis or SIRS; clinicians must consider potential co-infections with other undetected pathogens or the possibility of false positives. Thorough clinical assessment—including

Table 1. Demographics of 263 Pediatric Patients with Systemic Inflammatory Response Syndrome Potentially Due to Respiratory Viral Infections.

Parameter	Values
Sex	
Male	
No. (%)	134 (51.0)
Age	
< 1	
Month (median, range)	6 (1 - 11)
Mean \pm standard deviation	5.70 \pm 3.078
No. (%)	47 (17.8)
1 - 5	
Year (median, range)	3 (1 - 5)
Mean \pm standard deviation	2.73 \pm 1.204
No. (%)	182 (69.2)
≥ 6	
Year (median, range)	6 (6 - 13)
Mean \pm standard deviation	7.26 \pm 2.093
No. (%)	34 (13.0)
Season	
Spring (March, April and May)	104 (39.5)
Summer (June, July and August)	67 (25.5)
Autumn (September, October, and November)	45 (17.1)
Winter (December, January, and February)	47 (17.9)

Table 2. Clinical and Demographic Data of Pediatric Systemic Inflammatory Response Syndrome Patients with Respiratory Viral Infections^a

Parameter	HRV (n = 98)	FluA (n = 18)	FluB (n = 5)	RSV (n = 22)	HAdV (n = 64)	HPIV (n = 21)	hMPV (n = 11)	HBoV (n = 2)	Coinfections (n = 22)
Upper respiratory infection	53 (54.1)	10 (55.6)	2 (40.0)	7 (31.8)	34 (53.1)	4 (19.0)	2 (18.2)	1 (50.0)	7 (31.8)
Tracheitis/bronchitis	17 (17.3)	2 (11.1)	1 (20.0)	3 (13.6)	11 (17.2)	8 (38.1)	1 (9.0)	1 (50.0)	4 (18.2)
Pneumonia/bronchopneumonia	28 (28.6)	6 (33.3)	2 (40.0)	12 (54.5)	19 (29.7)	9 (42.9)	8 (72.7)	0 (0)	11 (50.0)
Fever (> 38.5°C)	79 (80.6)	15 (83.3)	4 (80.0)	16 (72.7)	61 (95.3)	17 (81.0)	11 (100.0)	2 (100.0)	20 (90.9)
Tachycardia	59 (60.2)	10 (55.6)	3 (60.0)	20 (90.9)	37 (57.8)	15 (71.4)	8 (72.7)	0 (0)	8 (36.4)
Mean respiratory rate > 2 SD above normal for age	56 (57.1)	10 (55.6)	3 (60.0)	15 (68.2)	59 (92.2)	13 (61.9)	9 (81.8)	0 (0)	16 (72.7)
Leukocyte count elevated or depressed for age	63 (64.3)	8 (44.4)	3 (60.0)	10 (45.5)	34 (53.1)	10 (47.6)	3 (27.3)	2 (100.0)	11 (50.0)
Plasma procalcitonin < 0.05 ng/mL	21 (21.4)	6 (33.3)	1 (20.0)	5 (22.7)	15 (23.4)	6 (28.6)	2 (18.2)	0 (0)	6 (27.3)

Abbreviations: HRV, human rhinovirus; FluA/B, influenza viruses A/B; RSV, respiratory syncytial virus; HPIV, human parainfluenza viruses; hMPV, human metapneumovirus; HBoV, human bocavirus; HAdV, human adenovirus.

^a Values are expressed as No. (%).

symptoms, lab results, and imaging—is essential for accurate diagnosis and management.

Respiratory viruses often display distinct seasonal patterns (13, 14). Our study showed that HRV peaks in Wuhan from March to July, while HAdV peaks from May to August. In this study, we observed that SIRS detection rates in children were highest for HRV and HAdV, aligning with the majority of virus-related SIRS cases

occurring in spring and summer. Our findings also indicated that 15% to 30% of pediatric patients with respiratory viral infections did not exhibit elevated procalcitonin levels, and even when elevated, the increase was often minimal. Studies have shown that markedly high procalcitonin levels are typically associated with bacterial rather than viral infections (15, 16). Furthermore, a pstrated that patients with sepsis and negative cultures had significantly lower

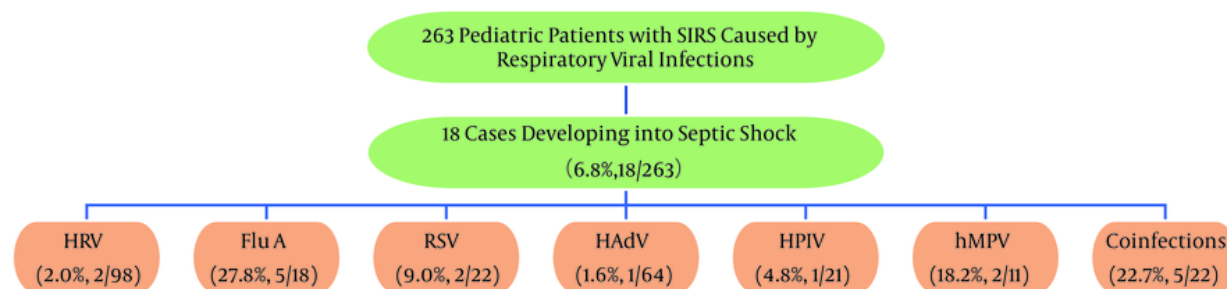


Figure 3. Incidence of septic shock caused by various viral infections

procalcitonin levels (17). Consequently, if procalcitonin levels slightly elevated or normal, a viral infection should be strongly considered.

This finding highlights the complex relationship between viral pathogens and disease severity in pediatric SIRS. Although HRV and HAdV were more prevalent, the higher risk of septic shock associated with FluA, hMPV, and co-infections suggests these viruses may trigger more severe systemic responses. Previous studies have shown that FluA infections are associated with severe sepsis, with adults experiencing influenza infections at a higher risk of septic shock compared to those with HRV infections (18-20). Additional research has confirmed that viral conditions and elevate the risk of shock. However, more studies are needed to further clarify the relationship between co-infections and septic shock (10, 21, 22).

These findings underscore the importance of virus-specific approaches in musative virus may significantly impact the risk of progression to septic shock. Future research should aim to elucidate the mechanisms by which different respiratory viruses interact with the host immune system, providing insight into more effective, targeted therapeutic interventions. Our study has two main limitations. First, as a retrospective analysis with a limited scope for pathogen detection in pediatric patients, certain infections may have been missed, or the pathogens identified may not be the actual causes of the illnesses. Second, a substantial number of febrile children had received antibiotics prior to admission, which may have contributed to negative results in pathogen detection and blood cultures.

5.1. Conclusions

In conclusion, many children hospitalized with respiratory viral infections are at risk of developing SIRS, with some cases potentially progressing to septic shock. For cases where SIRS is present and no bacterial, mycoplasma, or fungal pathogens are detected, it is essential to consider viral infections as a possible cause and conduct appropriate viral pathogen testing.

Footnotes

Authors' Contribution: Y. L. M. and H. B. H.: Conceptualized and designed the study, coordinated and supervised data collection, drafted the initial manuscript, and reviewed and revised the manuscript; Y. C.: Conducted the study and analyzed the data.

Conflict of Interests Statement: The authors declare no conflicts of interest.

Data Availability: The dataset presented in the study is available upon request from the corresponding author during the submission process or post-publication. The data are not publicly accessible due to privacy and confidentiality considerations.

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