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Hospital-based cross-sectional study on the clinical characteristics of children with severe acute respiratory infections in Hungary

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Abstract

Background Severe acute respiratory infection (SARI) is a major cause for hospital admission and associated with high mortality among children worldwide. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza viruses and respiratory syncytial virus (RSV) are the most frequently identified pathogens in children with SARI. The duration of care can be affected by the type of infection and patient characteristics. Therefore, the objective of this study was to identify factors affecting the length of hospitalization in children infected with SARS-CoV-2, influenza A and RSV.

Methods We collected data on 713 children with SARI from the medical databases of a university hospital in Hungary. To examine whether there is a difference in the length of hospitalization in children with the SARI Kruskal-Wallis test was performed. To determine the factors that may have an impact on the duration of care a multiple logistic regression analysis was executed.

Results Our results showed that among RSV infected patients the proportions of children requiring intensive care (8.94%), mechanical ventilation (8.94%) and oxygen therapy (13.01%) and suffering from pneumonia (29.27%) were larger than among cases with SARS-CoV-2 and influenza A infection. Considering the age distribution and the duration of care in children with SARI, cases with RSV were significantly younger ($p < 0.001$) and stayed longer in the hospital (median: 5 days, IQR: 4–7 days, $p < 0.001$) than those with SARS-CoV-2 and influenza A virus. Multiple logistic regression analysis showed that RSV infection (adjusted odds ratio (aOR): 3.25, 95% confidence interval (CI): 1.43–7.38; $p = 0.005$), pneumonia (aOR: 3.65, 95% CI: 2.14–6.24; $p < 0.001$), mechanical ventilation or oxygen therapy (aOR: 3.23, 95% CI: 1.29–8.11; $p = 0.012$) and underlying illnesses (aOR: 2.39, 95% CI: 1.35–4.23; $p = 0.003$) significantly increased the odds of hospitalization for more than 4 days.

Conclusions Our research showed that of the viruses causing SARI, RSV had the greatest clinical relevance, contributing to hospital stays of more than 4 days in a large share of paediatric patients below 1 year of age. Our results supply new information on children with SARI, and provide evidence for health policy makers to allocate additional resources to hospitals during SARI epidemics.

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Keywords Children, Cross-sectional study, Influenza, Length of hospitalization, RSV, Respiratory infection, SARS-CoV-2, SARI

Background

Severe acute respiratory infection (SARI) is defined by the World Health Organization (WHO) as "an acute respiratory illness leading to hospitalization and characterized by cough and fever equal to or higher than 38°C developed no longer than 10 days before admission" [1]. SARI has been shown to contribute to a large number of hospitalization and associated with high death rate worldwide [2, 3]. Among the conditions related to SARI, acute lower respiratory infections (ALRIs), such as pneumonia and bronchiolitis, are significant causes of morbidity and mortality in children under five years [4–6]. Globally, ALRIs were estimated to be responsible for 0.74 million deaths in children under five years in 2019 [7]. Although several microorganisms have been reported as etiological agents of SARI in children, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza viruses (types A, B), and respiratory syncytial virus (RSV) are the most commonly identified pathogens [4, 8–10].

In 2020, SARS-CoV-2, the pathogenic microorganism responsible for the novel coronavirus disease 2019 (COVID-19), has been identified as a new virus causing SARI in children [11–13]. SARS-CoV-2 infections have contributed to a major global epidemic resulting in significant morbidity and mortality [11, 14, 15]. Globally, as of September 21th, 2024, there were 776,205,140 confirmed cases of COVID-19 with 7,064,380 deaths [16]. According to epidemiological research, 1–6% of all SARS-CoV-2 cases have been reported among children under the age of 15 [17, 18]. Although COVID-19 may present with milder symptoms in children, studies have shown that adverse effects of the disease are not negligible in younger age groups [17, 19–21]. Children with SARS-CoV-2 have been frequently reported to have high fever, upper respiratory symptoms including cough and sore throat, diarrhoea and vomiting [18–20]. Besides coronavirus infections, seasonal influenza viruses often cause SARI [22, 23]. Data obtained from Global Burden of Disease Study (GBD) demonstrate that influenza virus infections caused nearly 9.5 million hospitalizations and 145,000 deaths in 2017 [24]. The WHO estimates that seasonal influenza epidemics result in 3 to 5 million severe infections each year [25]. An analysis by the WHO also showed that hospitalization rate and mortality were the highest for patients under 5 years of age and adults aged 65 years or older with influenza infection [24, 25]. A study examining data on influenza-associated care across 40 countries and administrative regions found hospitalization rates of 224.0 and 96.8 per 100,000 persons among children under 5 years and adults 65 years or older, respectively [25]. RSV is one of the respiratory pathogens that often cause ALRIs in children [26, 27]. Results from hospital-based investigations have shown that RSV is a frequent cause of hospital admissions in children under 5 years with ALRIs [26, 28]. Li et al. in a systematic analysis estimated that globally, there were 33 million RSV related ALRIs in children less than 5 years in 2019 [29]. The same study found that RSV-associated ALRIs contributed to the hospitalization of 3.6 million children below the age of 5 and accounted for 26,300 deaths with 39% of hospital care and 51% of mortality occurring among children under 6 months of age [29].

Several studies have shown that SARS-CoV-2, influenza and RSV are the most frequently detected respiratory pathogens that cause SARI in children [2, 9, 10, 19, 30–36]. However, only a few studies have compared the characteristics of SARI due to these viruses in paediatric patients [33, 36]. In addition, there have been only a limited number of investigations that have provided data on patients and studied the factors affecting disease severity and length of hospitalization [37]. According to our knowledge, there are no studies in the scientific literature that have used comprehensive statistical analyses to identify which of the respiratory infections and patient characteristics have a significant impact on the duration of hospital stay in children with SARI.

To fill this gap, we have obtained data from a university hospital in Hungary on 713 hospitalized children with SARI due to SARS-CoV-2, influenza A and RSV. The primary goal of our research was to report the characteristics of these patients with SARI. We also aimed to compare the length of hospitalization among patients diagnosed with SARI due to the respiratory viruses investigated. The third objective of our research was to identify factors that influence the duration of hospitalization in children with SARI.

Methods

Study design and sampling

A cross-sectional study was conducted at the Nagyerdei Campus of the University of Debrecen Clinical Centre (NC UDCC) in Hungary from the 40th week of 2021 to the 20th week of 2022 (from October 4th, 2021 to May 22nd, 2022). Our study collected data on patients infected with SARS-CoV-2, influenza and RSV. All children admitted to the hospital with respiratory symptoms were tested for SARS-CoV-2 infection with a rapid antigen test (RAT). In addition, a nasopharyngeal sample was obtained for PCR testing from children with a positive

COVID-19 RAT result and clinical symptoms suggesting the presence of Influenza A/B or RSV co-infection. When the COVID-19 RAT yielded a negative result, an RSV RAT was performed. Patients whose result was negative for both viruses were subject to further testing for infections with other respiratory viruses using a PCR analysis.

Acquisition of patient data

To identify individuals with SARI, we retrieved data on infections of SARS-CoV-2, influenza, and RSV from the Medbacter and UD MED IT systems of the NC UDCC. These systems provide detailed information on microbiological test results and patients' anamnesis. The period of data collection was from the 40th week of 2021 to the 20th week of 2022. Medical information collected for each patient included age, sex, place of residence, date of admission and discharge, place of treatment (hospital ward), date of sampling, type of specimen, microbiological result, and underlying diseases. In addition, information related to the therapy of the patients were also collected including the presence or absence of pneumonia, mechanical ventilation and oxygen therapy. Next, patient records were reviewed and those matching the case definition of SARI (cough and fever ≥ 38 °C developed no longer than 10 days before admission) were obtained for further analysis. Subsequently, SARI cases with positive test result for SARS-CoV-2, influenza and RSV infection were included in our study. Last, the underlying diseases of the selected SARI patients were classified into illness categories using the 10th revision of International Classification of the Diseases.

To process patient data, ethical approval was obtained from the Regional and Institutional Ethics Committee of the University of Debrecen (DE RKEB/IKEB: 5677 − 2021).

Database development

The total number of inpatients with SARI was 1464 in our study. Adult patients were excluded from our database as our study concentrated exclusively on children with SARI. Therefore, adults infected with SARS-CoV-2 (n = 734) and influenza (n = 17) viruses were not included in our database. There were no cases of RSV infection among adults. Consequently, our database comprised data on 713 children with SARI due to SARS-CoV-2, influenza A and RSV infections. Patients with influenza B or C virus were not detected. Apart from the respiratory viruses investigated, no other pathogen causing SARI in children was detected in our sample. All children with SARI were treated at the Department of Paediatrics of the NC UDCC. Figure 1 shows the selection of study population for statistical analysis.

Data analysis

To examine the temporal distribution of infections investigated, the number of weekly cases was divided by the number of children hospitalized each week at the Department of Paediatrics for the period between the 40th week of 2021 and the 20th week of 2022. The results were expressed as the weekly number of cases per 1000 inpatients. The weekly number of inpatients at the Department of Paediatrics was retrieved from data reported by the Department of Medical Documentation of the NC UDCC.

First, a descriptive statistical analysis was conducted to determine the share of children with SARS-CoV-2, influenza A and RSV infections. The percentage of children was also calculated by gender, age groups, factors indicating the severity of the disease (intensive care, pneumonia, mechanical ventilation, oxygen therapy and underlying disease) and outcome of illness (see Table 1). Next, the duration of care for each child with SARI was computed. Then, the median duration of hospitalization and corresponding interquartile ranges (IQR) were calculated separately for children with SARS-CoV-2, influenza A and RSV infections. Prior to performing group comparisons, data was assessed for normality by the Shapiro-Wilk test and found to be not normally distributed. We performed a Kruskal-Wallis test with Bonferroni post hoc analysis to examine whether there is a difference in the length of hospitalization in children with the respiratory infections investigated. A multiple logistic regression model was developed to identify factors that can affect the duration of care for children with SARI. The regression model included the median number of days of care as a dependent variable (< median; median ≤). Independent variables were sex, age, type of infection, and factors indicating disease severity such as intensive care, pneumonia, mechanical ventilation/oxygen therapy and underlying diseases. Logistic regression analysis was carried out using the forced entry procedure. Variables were incorporated into the initial model if the univariate analysis indicated a statistically significant association among them. Gender and age were included as general confounding variables in the final model. Results with p values less than 0.05 were considered statistically significant. IBM SPSS version 28.0.1 (IBM Inc, Armonk, New York, NY, USA) was used to carry out statistical analyses.

Results

Table 1 depicts that the proportion of children with SARS-CoV-2, influenza A and RSV was 76.58% (n = 546), 6.17% (n = 44) and 17.25% (n = 123), respectively. It is also shown that the share of boys and girls with SARS-CoV-2 (54.58%; 45.42%), influenza A (52.27%; 47.73%) and RSV (47.97%; 52.03%) infection was similar (Table 1). The mean age ± standard deviation (SD) of children

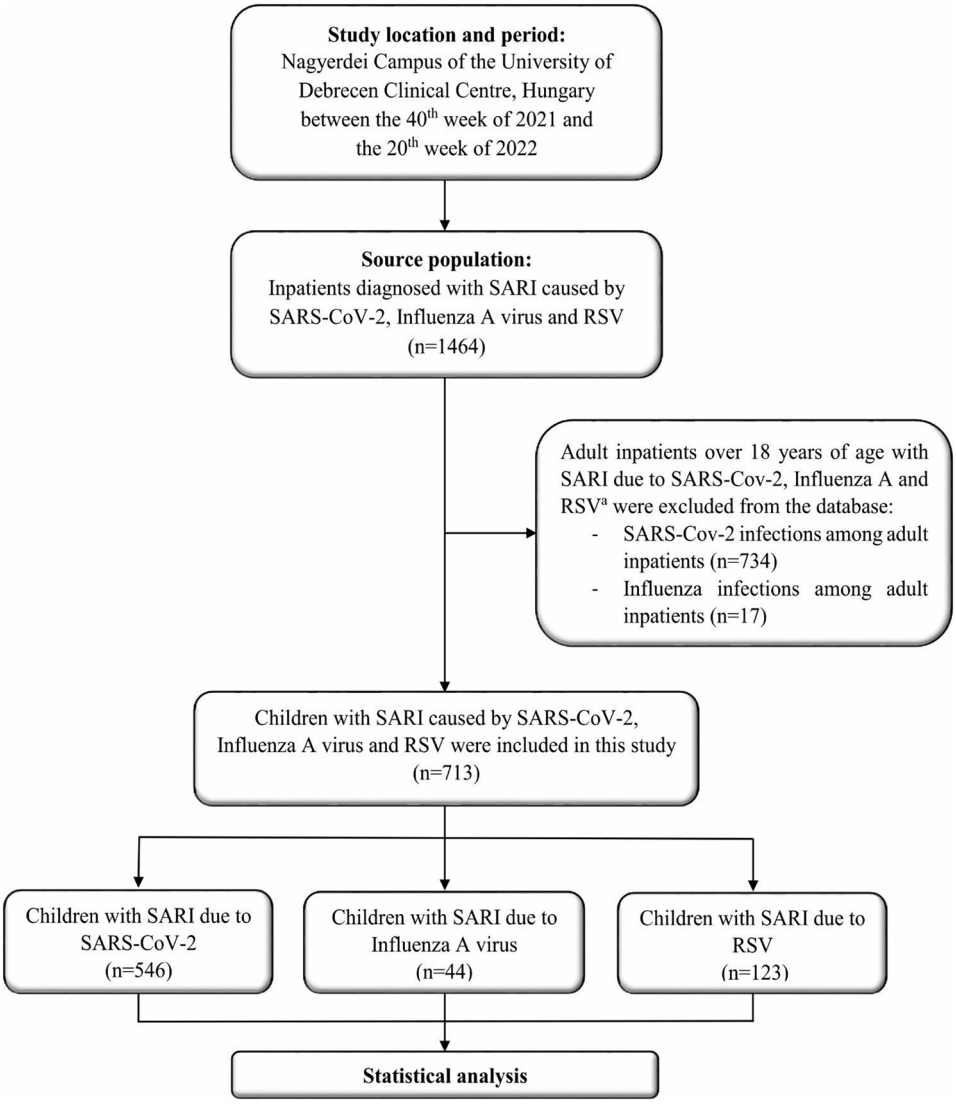

Fig. 1 Flowchart showing the selection of study population for statistical analysis. Abbreviations SARI: severe acute respiratory infection, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, RSV: respiratory syncytial virus. [a] There were no cases of respiratory syncytial virus infection among adults

diagnosed with SARS-CoV-2, influenza A and RSV infection was 3.47 ± 5.14 years, 5.41 ± 4.35 years and 0.12 ± 0.52 years, respectively (Table 1). Analysis of data showed that patients with SARI between 1 and 6 years (30.43%, $n=217$) and under 1 year of age (51.75%, $n=369$) were present in the largest proportion in our sample (Table 1). In addition, infants under 1 year of age had the highest share among cases infected with SARS-CoV-2 (45.79%, $n=250$) and RSV (93.50%, $n=115$) (Table 1). In contrast, the proportion of paediatric patients between 1 and 6 years of age was the largest among children with influenza A virus (65.91%, $n=29$) (Table 1). The proportion of cases requiring intensive care (8.94%), mechanical ventilation (8.94%) or oxygen therapy (13.01%) was the highest among those with SARI due to RSV (Table 1). Furthermore, pneumonia (29.27%) was the most frequent among children with this infection (Table 1). The proportion of children with underlying illnesses were 15.02%, 2.27% and 4.88% among cases infected by SARS-CoV-2, influenza A and RSV, respectively (Table 1). Table 1 presents that there was no in-hospital mortality in children with influenza A and RSV infection. However, two patients with SARS-CoV-2 infection (0.37%) died (Table 1). Considering all children with SARI, the median length of care was 4 days (IQR: 3–5 days). Table 1 demonstrates that patients infected with RSV had the longest hospitalization with a median of 5 days (IQR: 4–7 days). It is also shown that the median length of hospitalization was the same (4 days) among children with SARI due to SARS-CoV-2 and influenza A infection (Table 1).

As shown in Table 2, the category of the diseases of the respiratory system including allergy, asthma and lung

Table 1 Characteristics of children with severe acute respiratory infection by SARS-CoV-2, influenza a virus and RSV

	SARS-CoV-2		Influenza A		RSV	
Variables	**n**	**%**	**n**	**%**	**n**	**%**
Total number and share of cases	546	76.58	44	6.17	123	17.25
Sex distribution						
Male	298	54.58	23	52.27	59	47.97
Female	248	45.42	21	47.73	64	52.03
Mean age ± SD	3.47 ± 5.14		5.41 ± 4.35		0.12 ± 0.52	
Age group distribution (years)						
< 1	250	45.79	4	9.09	115	93.50
1–6	181	33.15	29	65.91	8	6.50
7–12	52	9.52	5	11.36	0	0
13–18	63	11.54	6	13.64	0	0
Frequency of factors influencing the course of the disease *						
Treatment at intensive care unit	19	3.48	1	2.27	11	8.94
Patients requiring mechanical ventilation	11	2.01	0	0	11	8.94
Patients requiring oxygen therapy	30	5.49	0	0	16	13.01
Patients diagnosed with pneumonia	85	15.57	7	15.91	36	29.27
Patients with underlying diseases	82	15.02	1	2.27	6	4.88
Outcome of illness						
Recovered	544	99.63	44	100	123	100
In hospital mortality	2	0.37	0	0	0	0
Length of hospital stay median and interquartile range (days)	4 [3–5]		4 [3–6]		5 [4–7]	

Abbreviations SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, RSV: respiratory syncytial virus * The frequency of factors affecting the course of the disease should be interpreted independently from each other

disease had the highest proportion (20%). In addition, asthma (17%), mental retardation (14%), obesity (10%) and prematurity (10%) were the most common underlying diseases in paediatric patients (Table 2). Figure 2 depicts that the number of new SARS-CoV-2, influenza A and RSV cases per 1000 inpatients was the highest on the 4th week of 2022 (118.11 SARS-CoV-2 cases/1000 inpatients), the 8th week of 2022 (27.30 influenza A cases/1000 inpatients) and the 44th week of 2021 (45.48 RSV cases/1000 inpatients), respectively. Figure 3 illustrates a significant difference in the age distribution of paediatric patients infected with SARS-CoV-2, influenza A and RSV ($p<0.001$). Figure 4 shows that the duration of care for cases with RSV ($p<0.001$) was significantly longer when compared to that of in children with SARS-CoV-2 and influenza A infection. Our regression model showed that RSV infection (adjusted odds ratio (aOR): 3.25, 95% confidence interval (CI): 1.43–7.38; $p=0.005$) and pneumonia (aOR: 3.65, 95% CI: 2.14–6.24; $p<0.001$) significantly increased the odds of hospitalization longer than 4 days (Table 3). It is also illustrated that patients requiring mechanical ventilation or oxygen therapy (aOR: 3.23, 95% CI: 1.29–8.11; $p=0.012$) and cases with underlying illnesses (aOR: 2.39, 95% CI: 1.35–4.23; $p=0.003$) had significantly higher odds for inpatient care longer than 4 days (Table 3).

Discussion

Children with SARI often require treatment at intensive care units including mechanical ventilation or oxygen therapy [34, 37–40]. Furthermore, the occurrence of complications including pneumonia and thereby longer hospital stay in children with this disease have been reported to be more frequent [37, 39, 40]. However, limited research exists that simultaneously investigated the factors that influence the duration of inpatient care among children with SARI due to SARS-CoV-2, influenza and RSV [37]. Therefore, our study aimed to confirm and extend the results of previous investigations by developing a regression model incorporating the clinical data of 713 children with SARI and determining which of the patient characteristics contribute to increased length of hospitalization. Our result showed that significantly higher proportion of patients with RSV infection required intensive care (8.94%), mechanical ventilation (8.94%), oxygen therapy (13.01%), and suffered from pneumonia (29.27%) than those with SARS-CoV-2 and influenza A infection. In addition, our findings demonstrated that the share of children below one year of age was higher among RSV infected cases (93.50%) than among those with the other respiratory infections studied. The median duration of care was also found to be the highest among children with RSV infection (median: 5 days). Our results showed that one in eight children (12.5%) in our sample had an underlying disease, the

Table 2 Underlying diseases among children with severe acute respiratory infection caused by SARS-CoV-2, influenza a virus and RSV

Disease category*	Underlying disease	Number of underlying diseases ($n = 100$)+	% of total number of underlying diseases
II. Neoplasms	Malignant neoplasm of brain	7	7
	Leukaemia		
	Malignant lymphoma		
	Malignant neoplasm of liver		
	Rhabdomyosarcoma		
	Malignant neoplasm of kidney		
III. Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	Anaemia	3	3
	Autoimmune haemolytic disease		
IV. Endocrine, nutritional and metabolic diseases	Metabolic disease	4	14
	Diabetes mellitus		
	Gilbert syndrome		
	Obesity	10	
V. Mental and behavioural disorders	Autism	3	17
	Mental retardation	14	
VI. Diseases of the nervous system	Disorder of brain	7	10
	Sleep apnoea		
	West syndrome		
	Hydrocephalus		
	Degenerative disease of nervous system		
	Epilepsy	3	
IX. Diseases of the circulatory system	Hypertension	3	3
	Heart disease		
X. Diseases of the respiratory system	Asthma	17	20
	Allergy	3	
	Lung disease		
XVI. Certain conditions originating in the perinatal period	Prematurity	10	10
XVII. Congenital malformations, deformations and chromosomal abnormalities	Down syndrome	5	12
	Hirschsprung disease		
	Plagiocephaly		
	Ventricular septal defect		
	Tetralogy of Fallot	3	
	Other congenital malformations of brain	4	

* Based on the International Classification of Diseases 10th Revision: 2019. Only those disease categories are shown that included children with underlying diseases.
+ Among the children nine had 2, one had 3 and one had 4 underlying diseases. The total number of underlying disease were 100. This was used to calculate the proportion of underlying diseases in one category. To ensure patient anonymity, categories with less than 3 underlying diseases were merged. Where this was not possible, the category was deleted. This way 3 categories with 4 underlying diseases were omitted

most common being asthma (17%). Considering the age distribution of children with SARI, cases with RSV were significantly younger than those with SARS-CoV-2 and influenza A. Furthermore, the duration of hospitalization was shown to be significantly longer in children with RSV infection (median: 5 days, IQR: 4–7 days) when compared to those with SARS-CoV-2 and influenza A. Using regression analysis, we have identified four factors significantly increasing the odds of hospital care longer than 4 days and these were RSV infection, pneumonia, mechanical ventilation or oxygen therapy, and underlying disease.

Our findings are in accordance with those of previous investigations. Several hospital based epidemiological studies from the United States of America (USA), Lithuania, Italy, China and the Netherlands have shown that RSV was the most commonly detected pathogen in paediatric patients with SARI requiring treatment at intensive care unit (share of RSV positive cases: 3–36%), and mechanical ventilation or oxygen therapy (share of RSV positive cases: 2-42.7%) [33, 37, 41–46]. In addition, pneumonia was also a common complication among hospitalized children with RSV infection with a proportion varying between 16.1% (USA) and 24% (China) [37, 43]. Furthermore, our research supports the

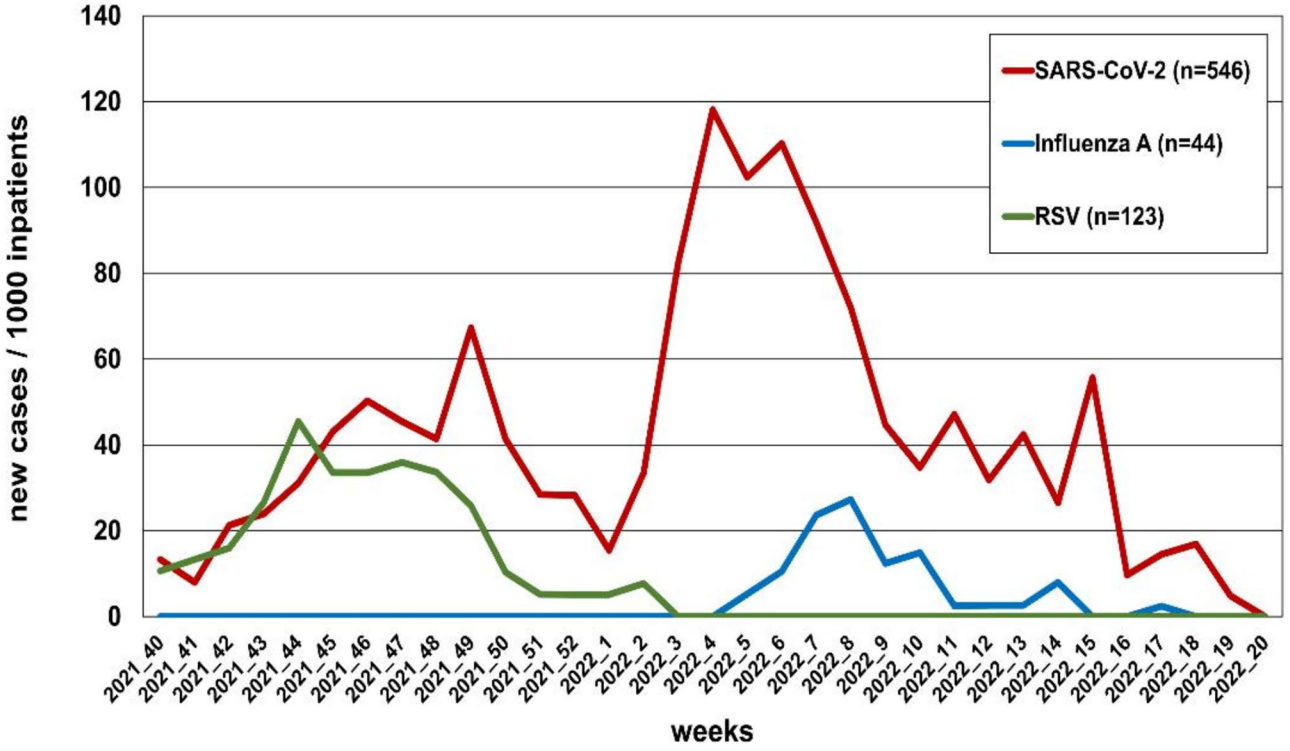

Fig. 2 Temporal distribution of severe acute respiratory infections due to SARS-CoV-2, influenza A virus and RSV cases per 1000 inpatients between the 40th weeks of 2021 to the 20th weeks of 2022. Abbreviations SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, RSV: respiratory syncytial virus

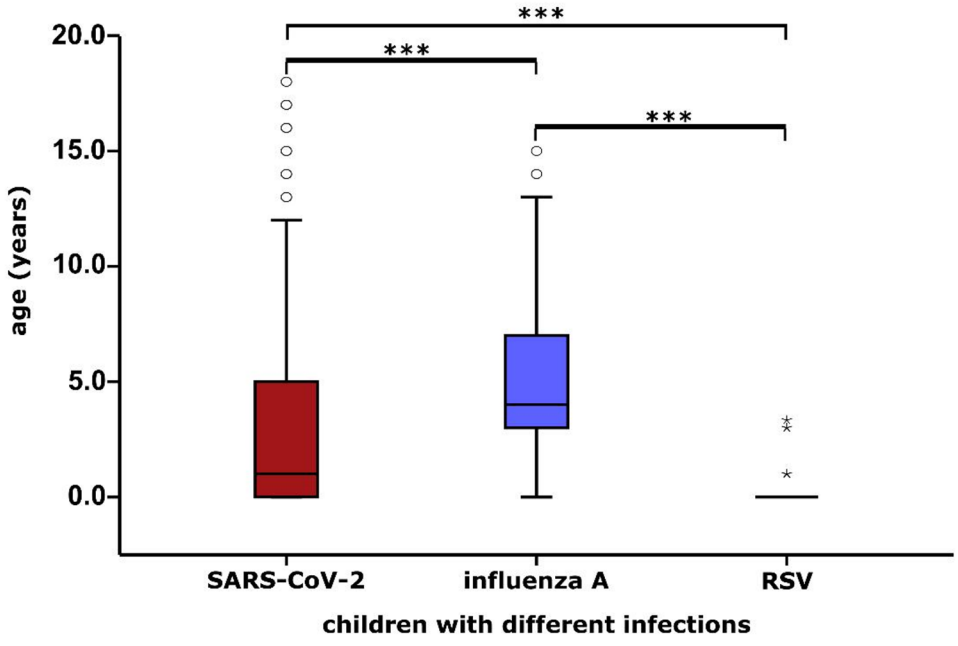

Fig. 3 Age distribution of children with severe acute respiratory infections. Abbreviations SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, RSV: respiratory syncytial virus. Median, interquartile ranges and 1.5 times of interquartile ranges as whiskers are shown. Open circles and asterisks indicate outlier values. *** $p < 0.001$

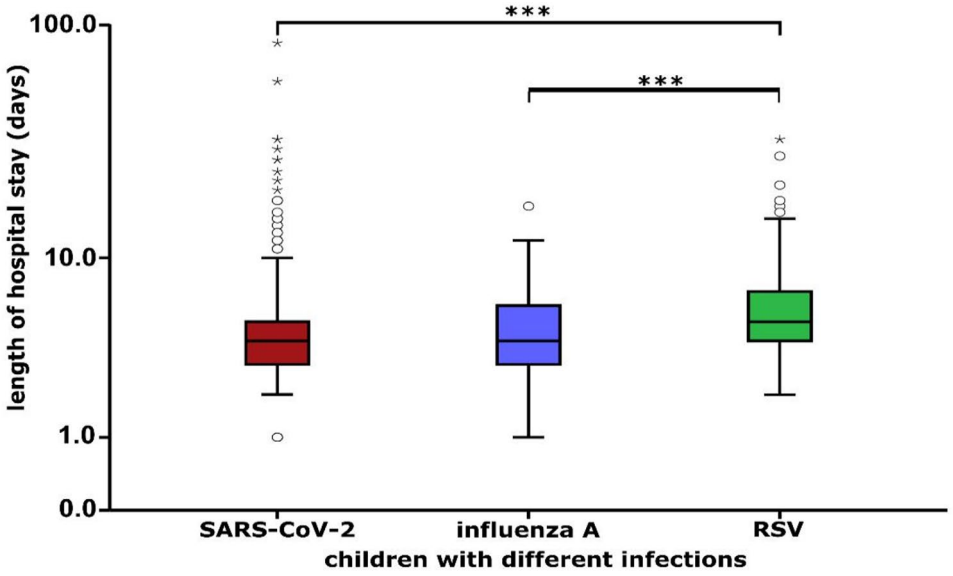

Fig. 4 Distribution of length of hospitalization in children with severe acute respiratory infections. Abbreviations SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, RSV: respiratory syncytial virus. Median, interquartile ranges and 1.5 times of interquartile ranges as whiskers are shown. Open circles and asterisks indicate outlier values. *** $p < 0.001$

Table 3 Factors influencing the length of hospital stay in children with severe acute respiratory infection based on a multiple logistic regression model

Multiple logistic regression model						
variable	**β**	**S.E.**	**aOR**	**95% CI for aOR**		***p*-values**
				Lower	**Upper**	
Female	-0.18	0.17	0.84	0.60	1.16	0.289
Age	-0.02	0.02	0.98	0.95	1.02	0.377
SARS-CoV-2	-0.18	0.33	0.84	0.44	1.60	0.595
RSV	**1.18**	**0.42**	**3.25**	**1.43**	**7.38**	**0.005**
Treatment at intensive care unit	1.81	1.08	6.08	0.74	50.19	0.094
Pneumonia	**1.30**	**0.27**	**3.65**	**2.14**	**6.24**	**< 0.001**
Mechanical ventilation/ Oxygen therapy	**1.17**	**0.47**	**3.23**	**1.29**	**8.11**	**0.012**
Underlying disease	**0.87**	**0.29**	**2.39**	**1.35**	**4.23**	**0.003**

Abbreviations: S.E.: standard error, aOR: adjusted odds ratio, CI: confidence interval, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, RSV: respiratory syncytial virus, Values of $p < 0.05$ were considered statistically significant. The reference categories of the variables shown in the table are male, patients without SARS-CoV-2 infections, patients without respiratory syncytial virus infection, patients not requiring treatment at intensive care unit, patients without pneumonia, patients without mechanical ventilation or oxygen therapy, and patients without underlying diseases, respectively. Influenza infection was not included in the model because it did not show a statistically significant association with the duration of hospitalisation in the univariate analysis

findings of previous investigations showing that more than 2/3 of children suffering from RSV infection were under one year of age [26, 37, 47]. It has been reported that infants are at higher risk of acquiring RSV infection due to their immature immune and respiratory system [48, 49]. Prematurity has also been linked to the severe form of respiratory disease caused by RSV [48, 49]. The clinical significance of RSV infection is further demonstrated by the fact that the median length of hospitalization in children with that disease has been found one day longer in all available studies when it was compared to that of SARS-CoV-2 and influenza [33, 37, 47]. This is in line with our own result. Although the proportion of underlying diseases is not known in the general Hungarian children population, studies on comorbidities among children in France and Germany reported a prevalence of 4% and 3-3.8%, respectively [50, 51]. Assuming a similar disease prevalence in Hungary, it is possible that the frequency of underlying diseases is 3 or 4 times higher among hospitalized children with SARI (12.5%) than in their healthy counterparts. However, further studies are needed to support this hypothesis. Furthermore, we have found that the proportion of children with underlying diseases was the highest among those with SARS-CoV-2 (15.02%). This is in accordance with the results of previous investigations showing that the presence

of comorbidities, especially asthma, increase the risk of hospitalization in children infected with the novel coronavirus [52, 53]. However, it is important to note that the effect of asthma in children with SARI due to SARS-CoV-2 infection on the risk of hospitalisation has not been confirmed by a previous Australian study [54].

Prolonged hospital stay has been shown to increase the risk of nosocomial infections and the cost of treatment [55, 56]. However, only a few studies carried out regression analysis to identify factors influencing the duration of care in children with SARI. Of the research available, a recent investigation from Germany reported that children with RSV infections had significantly higher odds of hospitalization longer than 5 days when they were preterm born (OR: 3.37 [95% CI: 1.22–9.27]), required oxygen supplementation (OR: 5.09 [95% CI: 2.72–9.54]) and suffered from pneumonia (OR: 2.33 [95% CI:1.30–4.15]) [57]. Another study showed that children infected with RSV had significantly increased risk (relative risk: 1.40 [95%: 1.12–1.76) for treatment longer than 4 days using patients with SARS CoV-2 infection as reference [37]. Although previous studies have separately examined the effects of the type of respiratory infection, mechanical ventilation/oxygen therapy, pneumonia and certain comorbidities on the length of hospitalization in paediatric patients with SARS-CoV-2, influenza and RSV, these factors have not been studied in the same multiple logistic regression model. Besides providing further evidence on factors leading to prolonged hospital stay, our study goes beyond the existing research by comprehensively analysing patient characteristics influencing the duration of care.

The strengths and limitations of this study should also be taken into account. Our study is the first that compared data on paediatric patients with SARI due to common respiratory viruses in a Hungarian university hospital. In addition, our research compared the duration of hospitalization in children infected with SARS-CoV-2, influenza and RSV. We extended the results of previous studies using multiple regression to identify independent factors that can increase the duration of care in children with SARI. Limitations of our research should also be considered. Data on patients with SARI were collected only from one hospital in Hungary, thus limiting our ability to generalize our findings to children treated in other healthcare facilities. Second, our investigation was limited to cases detected in one season between the 40th week of 2021 and the 20th week of 2022. In addition, it was not possible to take into consideration differences in clinical phenotypes relating to seasonal genetic changes in pathogens. A further limitation of the present investigation is that the standard definition of SARI was used to identify patients [58]. However, this criteria may not capture children with severe RSV infection who may not present with fever. Last, we were not able to examine the effects of each underlying disease on the length of hospital stay separately.

Conclusion

In summary, of the viruses causing SARI in children, RSV had the greatest clinical relevance in our study. By comparing the age distribution of children with SARI we have also shown that cases with RSV were significantly younger than those with SARS-CoV-2 and influenza A infection. In addition, a significantly higher proportion of patients with RSV infection required intensive care and had longer hospitalisation compared to children with SARI due to other viruses. The results of the regression model suggest that RSV infection, pneumonia, mechanical ventilation or oxygen therapy, and underlying medical conditions significantly increased the odds of a hospital stay longer than 4 days. However, more research is needed to determine how patient characteristics, especially individual underlying diseases, influence the duration of care in children with SARI.

Our results provide new information on children with SARI, contributing to the better understanding of the epidemiology of these infections. Our research can support the development of hospital-level SARI surveillance systems. The findings described also draw attention to children below 1 year of age with RSV infection, who should be payed particular attention by paediatricians during epidemic seasons. This study can provide evidence for health policy makers to allocate additional resources to hospitals, so they can cope with the increased burden of care during SARI epidemics.

Abbreviations

ALRIs	Acute lower respiratory infections
aOR	Adjusted odds ratio
CI	Confidence interval
COVID-19	Novel coronavirus disease 2019
GBD	Global Burden of Disease Study
IQR	Interquartile range
NC UDCC	Nagyerdei Campus of the University of Debrecen Clinical Centre
RAT	Rapid antigen test
RSV	Respiratory syncytial virus
SARI	Severe acute respiratory infection
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SD	Standard deviation
USA	United States of America
WHO	World Health Organization

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Author contributions

Conceptualization, methodology, study design: NO, AN; Data curation, formal analysis, investigation, project administration, writing—original draft preparation, visualization: NO; Resources, supervision, validation: GG, AN; Writing—review and editing: GG, UB, AN; All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study is a secondary data analysis based on clinical data. The research was approved by the Regional and Institutional Ethics Committee of the University of Debrecen (5677 – 2021). Given the retrospective and non-interventional nature of the study, along with the use of anonymized data, informed consent from participants was not required as per national legislation and institutional guidelines.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Fitzner J, Qasmieh S, Mounts AW, Alexander B, Besselaar T, Briand S, et al. Revision of clinical case definitions: influenza-like illness and severe acute respiratory infection. Bull World Health Organ. 2018;96:122–8.
2. Lamrani Hanchi A, Guennouni M, Rachidi M, Benhoumich T, Bennani H, Bourrous M, et al. Epidemiology of respiratory pathogens in children with severe Acute Respiratory infection and impact of the Multiplex PCR Film array respiratory panel: a 2-Year study. Int J Microbiol. 2021;2021:1–9.
3. Razanajatovo NH, Guillebaud J, Harimanana A, Rajatonirina S, Ratsima EH, Andrianirina ZZ, et al. Epidemiology of severe acute respiratory infections from hospital-based surveillance in Madagascar, November 2010 to July 2013. PLoS ONE. 2018;13:e0205124.
4. Li Z-J, Zhang H-Y, Ren L-L, Lu Q-B, Ren X, Zhang C-H, et al. Etiological and epidemiological features of acute respiratory infections in China. Nat Commun. 2021;12:5026.
5. Nair H, Simões EA, Rudan I, Gessner BD, Azziz-Baumgartner E, Zhang JSF, et al. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: a systematic analysis. Lancet. 2013;381:1380–90.
6. Wang X, Li Y, Mei X, Bushe E, Campbell H, Nair H. Global hospital admissions and in-hospital mortality associated with all-cause and virus-specific acute lower respiratory infections in children and adolescents aged 5–19 years between 1995 and 2019: a systematic review and modelling study. BMJ Glob Health. 2021;6:e006014.
7. Perin J, Mulick A, Yeung D, Villavicencio F, Lopez G, Strong KL, et al. Global, regional, and national causes of under-5 mortality in 2000–19: an updated systematic analysis with implications for the Sustainable Development Goals. Lancet Child Adolesc Health. 2022;6:106–15.
8. Kozinska A, Wegrzynska K, Komiazyk M, Walory J, Wasko I, Baraniak A. Viral Etiological Agent(s) of respiratory tract infections in symptomatic individuals during the Second Wave of COVID-19 pandemic: a single drive-thru Mobile Collection Site Study. Pathogens. 2022;11:475.
9. Correia W, Dorta-Guerra R, Sanches M, Almeida Semedo C, de JB, Valladares B, de Pina-Araújo IIM, et al. Study of the etiology of Acute Respiratory infections in Children under 5 years at the Dr. Agostinho Neto Hospital, Praia, Santiago Island, Cabo Verde. Front Pediatr. 2021;9:716351.
10. Zhu G, Xu D, Zhang Y, Wang T, Zhang L, Gu W, et al. Epidemiological characteristics of four common respiratory viral infections in children. Virol J. 2021;18:10.
11. Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges. Int J Antimicrob Agents. 2020;55:105924.
12. Mohanty SK, Satapathy A, Naidu MM, Mukhopadhyay S, Sharma S, Barton LM, et al. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and coronavirus disease 19 (COVID-19) – anatomic pathology perspective on current knowledge. Diagn Pathol. 2020;15:103.
13. Synowiec A, Szczepański A, Barreto-Duran E, Lie LK, Pyrc K. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): a systemic infection. Clin Microbiol Rev. 2021;34:e00133–20.
14. Gebru AA, Birhanu T, Wendimu E, Ayalew AF, Mulat S, Abasimel HZ, et al. Global burden of COVID-19: situational analyis and review. Hum Antibodies. 2021;29:139–48.
15. Feng W, Zong W, Wang F, Ju S. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): a review. Mol Cancer. 2020;19:100.
16. World Health Organization Coronavirus (COVID-19). Dashboard. https://data.who.int/dashboards/covid19/cases?n=c. Accessed 21 Sept 2024.
17. Alteri C, Scutari R, Costabile V, Colagrossi L, Yu La Rosa K, Agolini E, et al. Epidemiological characterization of SARS-CoV-2 variants in children over the four COVID-19 waves and correlation with clinical presentation. Sci Rep. 2022;12:10194.
18. Alnajjar AA, Dohain AM, Abdelmohsen GA, Alahmadi TS, Zaher ZF, Abdelgalil AA. Clinical characteristics and outcomes of children with COVID-19 in Saudi Arabia. Saudi Med J. 2021;42:391–8.
19. Zhang Z, Chen D, Liu Q, Gan C, Jiang L, Zhu K, et al. Clinical features of Chinese children with COVID-19 and other viral respiratory infections. Pediatr Pulmonol. 2022;57:49–56.
20. Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19: an overview of the epidemiology, clinical features, diagnosis, treatment and Prevention options in Children. Pediatr Infect Dis J. 2020;39:355–68.
21. Chaiyakulsil C, Sritipsukho P, Satdhabudha A, Bunjoungmanee P, Tangsathapornpong A, Sinlapamongkolkul P, et al. An epidemiological study of pediatric COVID-19 in the era of the variant of concern. PLoS ONE. 2022;17:e0267035.
22. Macias AE, McElhaney JE, Chaves SS, Nealon J, Nunes MC, Samson SI, et al. The disease burden of influenza beyond respiratory illness. Vaccine. 2021;39:A6–14.
23. Maltezou HC, Papanikolopoulou A, Vassiliu S, Theodoridou K, Nikolopoulou G, Sipsas NV. COVID-19 and respiratory virus co-infections: a systematic review of the literature. Viruses. 2023;15:865.
24. Troeger CE, Blacker BF, Khalil IA, Zimsen SRM, Albertson SB, Abate D, et al. Mortality, morbidity, and hospitalisations due to influenza lower respiratory tract infections, 2017: an analysis for the global burden of Disease Study 2017. Lancet Respir Med. 2019;7:69–89.
25. Paget J, Staadegaard L, Wang X, Li Y, Van Pomeren T, Van Summeren J, et al. Global and national influenza-associated hospitalisation rates: estimates for 40 countries and administrative regions. J Glob Health. 2023;13:04003.
26. Cai W, Buda S, Schuler E, Hirve S, Zhang W, Haas W. Risk factors for hospitalized respiratory syncytial virus disease and its severe outcomes. Influenza Other Respir Viruses. 2020;14:658–70.
27. Xie Z, Qin Q, Shen K, Fang C, Li Y, Deng T. The burden of respiratory syncytial virus associated with acute lower respiratory tract infections in Chinese children: a meta-analysis. Transl Pediatr. 2020;9:496–506.
28. González-Granado LI, Martín-Nalda A, Alsina L, Neth O, Santamaría M, Soler-Palacín P. Respiratory syncytial virus infections requiring hospitalization in patients with primary immunodeficiency. Pediatría Engl Ed. 2022;96:492–500.
29. Li Y, Wang X, Blau DM, Caballero MT, Feikin DR, Gill CJ, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. Lancet. 2022;399:2047–64.
30. Lamrani Hanchi A, Guennouni M, Ben Houmich T, Echchakery M, Draiss G, Rada N, et al. Changes in the epidemiology of respiratory pathogens in children during the COVID-19 pandemic. Pathogens. 2022;11:1542.
31. Ye Q, Wang D. Epidemiological changes of common respiratory viruses in children during the COVID-19 pandemic. J Med Virol. 2022;94:1990–7.
32. Zhu L, Luo T, Yuan Y, Yang S, Niu C, Gong T, et al. Epidemiological characteristics of respiratory viruses in hospitalized children during the COVID-19 pandemic in southwestern China. Front Cell Infect Microbiol. 2023;13:1142199.

33. Steponavičienė A, Burokienė S, Ivaškevičienė I, Stacevičienė I, Vaičiūnienė D, Jankauskienė A. Influenza and respiratory Syncytial Virus infections in Pediatric patients during the COVID-19 pandemic: a single-center experience. Children. 2023;10:126.
34. Ogunbayo AE, Mogotsi MT, Sondlane H, Nkwadipo KR, Sabiu S, Nyaga MM. Pathogen Profile of Children Hospitalised with severe Acute Respiratory infections during COVID-19 pandemic in the Free State Province, South Africa. Int J Environ Res Public Health. 2022;19:10418.
35. Diesner-Treiber SC, Voitl P, Voitl JJM, Langer K, Kuzio U, Riepl A, et al. Respiratory infections in children during a Covid-19 pandemic winter. Front Pediatr. 2021;9:740785.
36. Encinosa W, Figueroa J, Elias Y. Severity of hospitalizations from SARS-CoV-2 vs influenza and respiratory syncytial virus infection in children aged 5 to 11 years in 11 US States. JAMA Pediatr. 2022;176:520.
37. Rao S, Armistead I, Tyler A, Lensing M, Dominguez SR, Alden NB. Respiratory Syncytial Virus, Influenza, and Coronavirus Disease 2019 hospitalizations in children in Colorado during the 2021–2022 respiratory virus season. J Pediatr. 2023;260:113491.
38. Mazumdar S, Nerella S, Mitra S, Roy BC. Clinical and viral profile of children admitted in the paediatric intensive care unit due to severe acute respiratory infection during seasonal surge from a tertiary care centre in Eastern India. Sri Lanka J Child Health. 2023;52:175–81.
39. Malveste Ito CR, Moreira ALE, Silva PAND, Santos MDO, Santos APD, Rézio GS, et al. Viral coinfection of children hospitalized with severe Acute Respiratory infections during COVID-19 pandemic. Biomedicines. 2023;11:1402.
40. Relan P, Garbern SC, O'Reilly G, Bills CB, Schultz M, Kivlehan S, et al. Emergency care interventions for paediatric severe acute respiratory infections in low- and middle-income countries: a systematic review and narrative synthesis. J Glob Health. 2023;13:04065.
41. Glaser EL, Hariharan D, Bowser DM, Gervasio RM, Rowlands KR, Buckley L et al. Impact of Respiratory Syncytial Virus on Child, Caregiver, and Family Quality of Life in the United States: Systematic Literature Review and Analysis. J Infect Dis. 2022;226 Supplement_2:S236–45.
42. Bianchini S, Silvestri E, Argentiero A, Fainardi V, Pisi G, Esposito S. Role of respiratory Syncytial Virus in Pediatric Pneumonia. Microorganisms. 2020;8:2048.
43. Zhang Q, Guo Z, Langley JM, Bai Z. Respiratory syncytial virus - associated intensive care unit admission in children in Southern China. BMC Res Notes. 2013;6:447.
44. Linssen RS, Bem RA, Kapitein B, Rengerink KO, Otten MH, Den Hollander B, et al. Burden of respiratory syncytial virus bronchiolitis on the Dutch pediatric intensive care units. Eur J Pediatr. 2021;180:3141–9.
45. Rao S, Armistead I, Messacar K, Alden NB, Schmoll E, Austin E, et al. Shifting epidemiology and severity of respiratory Syncytial Virus in Children during the COVID-19 pandemic. JAMA Pediatr. 2023;177:730.
46. Faraguna MC, Lepri I, Clavenna A, Bonati M, Vimercati C, Sala D, et al. The bronchiolitis epidemic in 2021–2022 during the SARS-CoV-2 pandemic: experience of a third level centre in Northern Italy. Ital J Pediatr. 2023;49:26.
47. Hedberg P, Karlsson Valik J, van der Werff S, Tanushi H, Requena Mendez A, Granath F, et al. Clinical phenotypes and outcomes of SARS-CoV-2, influenza, RSV and seven other respiratory viruses: a retrospective study using complete hospital data. Thorax. 2022;77:1–10.
48. Anderson J, Do LAH, Wurzel D, Quan Toh Z, Mulholland K, Pellicci DG, et al. Severe respiratory syncytial virus disease in preterm infants: a case of innate immaturity. Thorax. 2021;76:942–50.
49. Kang J, Lee J, Kim Y, Cho HK, Park SE, Kim K, et al. Pediatric intensive care unit admission due to respiratory syncytial virus: retrospective multicenter study. Pediatr Int. 2019;61:688–96.
50. Pergeline J, Lesuffleur T, Rey S, Fresson J, Rachas A, Tuppin P. Long-term chronic diseases and 1-year use of healthcare services by children under 18 years of age during 2018–2019: a French nationwide observational study. Arch Pédiatrie. 2023;30:48–58.
51. Schröder H, Brückner G, Schüssel K, Breitkreuz J, Schlotmann A, Günster C, Monitor. Gesundheitliche Beeinträchtigungen - Vorerkrankungen mit erhöhtem Risiko für schwere Verläufe von COVID-19. Verbreitung in der Bevölkerung Deutschlands und seinen Regionen. Berlin. 2020.
52. Størdal K, Ruiz PL-D, Greve-Isdahl M, Surén P, Knudsen PK, Gulseth HL, et al. Risk factors for SARS-CoV-2 infection and hospitalisation in children and adolescents in Norway: a nationwide population-based study. BMJ Open. 2022;12:e056549.
53. Farrar DS, Drouin O, Moore Hepburn C, Baerg K, Chan K, Cyr C, et al. Risk factors for severe COVID-19 in hospitalized children in Canada: a national prospective study from March 2020–May 2021. Lancet Reg Health - Am. 2022;15:100337.
54. Williams P, Koirala A, Saravanos GL, Lopez LK, Glover C, Sharma K, et al. COVID -19 in New South Wales children during 2021: severity and clinical spectrum. Med J Aust. 2022;217:303–10.
55. Haque M, Sartelli M, McKimm J, Abu Bakar MB. Health care-associated infections – an overview. Infect Drug Resist. 2018;Volume 11:2321–33.
56. Jia H, Li L, Li W, Hou T, Ma H, Yang Y, et al. Impact of Healthcare-Associated infections on length of Stay: a study in 68 hospitals in China. BioMed Res Int. 2019;2019:1–7.
57. Hartmann K, Liese JG, Kemmling D, Prifert C, Weißbrich B, Thilakarathne P, et al. Clinical burden of respiratory Syncytial Virus in Hospitalized Children aged ≤ 5 years (INSPIRE study). J Infect Dis. 2022;226:386–95.
58. World Health Organization Global Influenza Programme. RSV surveillance case definitions. https://www.who.int/teams/global-influenza-programme/global-respiratory-syncytial-virus-surveillance/case-definitions. Accessed 21 Sept 2024.

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