Morbidity of Respiratory Syncytial Virus (RSV) Infections: RSV Compared With Severe Acute Respiratory Syndrome Coronavirus 2 Infections in Children Aged 0–4 Years in Cologne, Germany

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The aim of this retrospective analysis was to provide information on how infections with respiratory syncytial virus (RSV) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) differ in symptoms, clinical course, outcome, and utilization of hospital care. We investigated 748 polymerase chain reaction results from symptomatic children aged 0–4 years in Cologne, Germany. One hundred sixty-nine patients tested positive for RSV (22.6%) and 24 children for SARS-CoV-2 (3.2%). Symptomatic patients with RSV infection were hospitalized significantly longer. RSV-positive patients needed oxygen supplementation significantly more often as well as high-flow therapy. With regard to care efforts, RSV-infected patients put higher pressure on the hospital and utilized more hospital resources.

Keywords. Germany; COVID-19; RSV infections; hospitalization; children.

Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections in infants and young children [1]. RSV typically affects children in the first 2 years of life and/or those with limited respiratory or cardiovascular function [2]. During the global coronavirus disease 2019 (COVID-19) pandemic, RSV and other respiratory viruses such as influenza changed dramatically in their incidence. Data from Australia and New Zealand showed a decrease of RSV infections throughout the winter season 2020 (April–June 2020) in the southern hemisphere [3, 4]. Data from the European Centre for Disease

Prevention and Control confirmed these findings for the winter season 2020–2021. Before the COVID-19 pandemic, the highest RSV incidences were usually detected from December to March with first cases occurring in autumn (eg, September–October) [5]. In 2021 we observed an enormous increase of RSV infections worldwide, characterized by an obvious shift of incidence toward late summer with the first cases by the end of July [6–8].

Children with RSV infection usually present with upper respiratory symptoms (eg, fever, rhinitis, and nasal congestion) as well as with lower respiratory symptoms (eg, cough and tachydyspnea) [1]. Therapy of choice is supportive care such as maintaining hydration and nutrition as well as keeping the oxygen saturation >90% [9].

In parallel, the COVID-19 pandemic is still ongoing with increasing numbers of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, especially in the pediatric cohort [10]. The course of disease is often mild [11] and fatal outcomes are rare [12]. However, the symptoms of the respiratory tract reflect the main clinical appearance in SARS-CoV-2 in children as well.

The absolute number of SARS-CoV-2–positive tested patients, but especially RSV-positive tested patients, requiring inpatient treatment and inevitable hygiene measures such as the cohorting of infected patients currently exerts high pressure on hospitals in Germany [13]. This work presents data of 193 children aged 0–4 years collected over a period of 21 months from March 2020 to November 2021 who tested positive for RSV or SARS-CoV-2. The aim of this retrospective analysis was to provide information on how infections with RSV and SARS-CoV-2 differed in terms of symptoms, clinical course, outcome, and incidence over the observation period.

METHODS

We included symptomatic children between 0 and 4 years of age who had shown a positive reverse-transcription polymerase chain reaction (RT-PCR) result for RSV or SARS-CoV-2 and were admitted to our hospital between 13 March 2020 and 30 November 2021. During this period, the wild type of SARS-CoV-2 (the Alpha variant; first cases in January 2021), and the Delta variant (first cases at the end of July 2021) were circulating in Germany. We excluded asymptomatic patients as well as patients aged >4 years. The patients received a nasopharyngeal and/or oropharyngeal swab. All swabs were conducted by trained staff and were tested for RSV, SARS-CoV-2, and influenza A/B. High-flow nasal cannula (HFNC) was defined as a flow >4 L/minute. Former preterm infants as well as multimorbid children and those suffering from chronic renal diseases were regarded as patients at risk.

In the case of numerical variables, the descriptive presentation of the results was performed by specifying the mean value and the standard deviation, or the median indicating the minimum and maximum values of nonnormally distributed variables. We checked for normal distribution by using the Kolmogorov–Smirnov test. Categorical variables were described as a percentage of the underlying collective. Statistical analysis was performed using the Student t test for normally distributed values, the Mann–Whitney U test for nonnormally distributed values, or the χ^2 test for categorical values. Results were regarded as differing significantly when the P value was < .05.

RESULTS

Between March 2020 and November 2021, 748 children between 0 and 4 years of age admitted to our hospital with respiratory symptoms received a naso- and/or oropharyngeal swab. One hundred sixty-nine (22.6%) patients tested positive for RSV, 24 (3.2%) tested positive for SARS-CoV-2, and 2 (0.3%) tested positive for influenza A. We observed the first cases of RSV infections in July 2021 with an enormous increase of cases in October 2021. For more data, see Figure 1.

Only 17 of 748 infants received a more comprehensive multiplex PCR analysis to detect other viruses that may cause respiratory symptoms in infants. These were, in particular, patients who were critically ill at presentation. Multiplex PCR is not performed routinely at our hospital due to high costs. In these 17 patients, infection with rhinovirus was detected in 10 cases,

bocavirus in 7 cases, adenovirus in 2 cases, metapneumovirus in 2 cases, coronavirus NL63 in 2 cases, and parainfluenza type 3 in 1 case (coinfection with >1 virus occurred in 8 cases; 4 of 8 [50%] had a coinfection of bocavirus and rhinovirus). The median age of our patients was 14 months (min, 0 months; max, 59 months).

Statistically, there was no significant difference in age between the groups, even though patients infected with RSV were slightly younger than those infected with SARS-CoV-2. RSV patients presented significantly more often with a cough (88.8% vs 45.8%; $P < .001$), whereas SARS-CoV-2 patients suffered significantly more often from fever (87.5% vs 42.0%; $P < .001$) and gastrointestinal symptoms (25.0% vs 8.3%; $P < .05$). Patients with an RSV infection stayed in hospital significantly longer than patients with a SARS-CoV-2 infection (4 days [min, 0; max, 21] vs 2 days [min, 1; max, 8]; $P < .05$). Moreover, RSV-positive patients needed oxygen supplementation significantly more often (39.6% vs 8.3%; $P < .05$) as well as HFNC (24.3% vs 0.0%; $P < .05$), even though there was no difference with respect to intubation. It is of note that no infant with a positive SARS-CoV-2 test had to be admitted to the pediatric intensive care unit (PICU), whereas 17 infants with RSV required intensive care. By calculating the relative risk (RR), we could show that the risk of PICU admission (RR, 1.16 [95% confidence interval {CI}, 1.10–1.23]), intubation (1.14 [95% CI, 1.08–1.21]), and nasal continuous positive airway pressure (nCPAP) (RR, 1.15 [95% CI, 1.08–1.21]) for RSV patients was almost 20% higher than for SARS-CoV-2 patients. For more data, see Table 1.
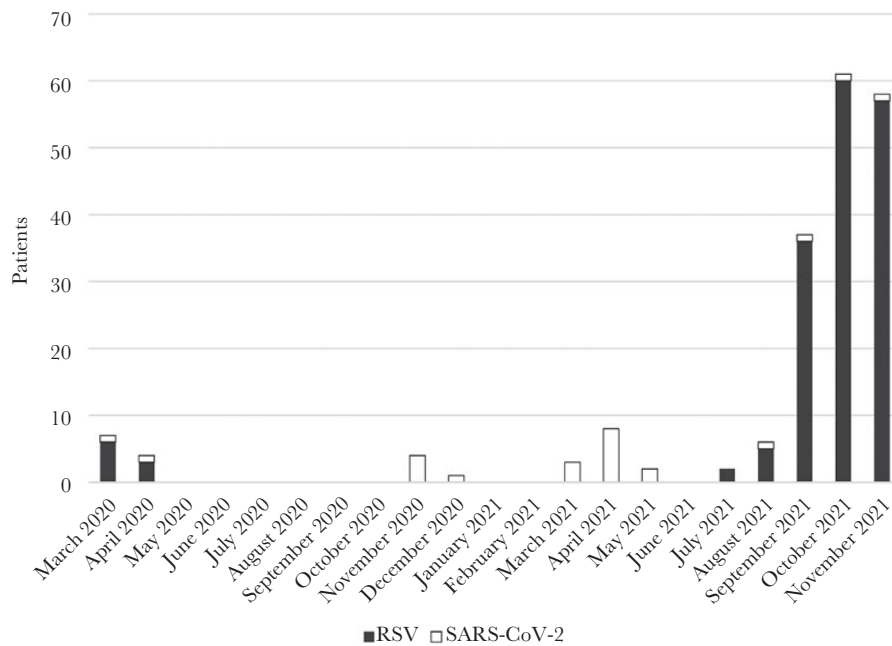

Figure 1. Respiratory syncytial virus (RSV)– and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–positive patients throughout the observation time (n = 193).

Table 1. Comparison of Respiratory Syncytial Virus (RSV)– Versus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)–Infected Patients (n = 193) and Characteristics of Patients With Neither RSV Nor SARS-CoV-2 (n = 555)

Characteristic	RSV (n = 169)	SARS-CoV-2 (n = 24)	P Value	RR (95% CI)
Median age, mo (min; max)	3 (0; 57)	7 (0; 44)	.601	…
Male sex	57.4% (n = 97)	54.2% (n = 13)	.765	1.02 (.91–1.13)
Patients at risk	13.6% (n = 23)	12.5% (n = 3)	.882	1.01 (.87–1.18)
Signs and symptoms				
Dyspnea	20.7% (n = 35)	12.5% (n = 3)	.344	1.07 (.95–1.19)
Fever	42.0% (n = 71)	87.5% (n = 21)	**<.001**	0.80 (.71–.89)
Cough	88.8% (n = 150)	45.8% (n = 11)	**<.001**	1.57 (1.18–2.10)
Rhinitis	50.9% (n = 86)	33.3% (n = 8)	.107	1.09 (.98–1.21)
GI symptoms	8.3% (n = 14)	25.0% (n = 6)	**.012**	0.78 (.58–1.05)
Median time of hospitalization, d (min; max)	4 (0; 21)	2 (1; 8)	**.049**	…
Intensive care treatment	10.1% (n = 17)	0.0% (n = 0)	.104	1.16 (1.10–1.23)
O_2 supplementation	39.6% (n = 67)	8.3% (n = 2)	**.003**	1.18 (1.08–1.29)
HFNC	24.3% (n = 41)	0.0% (n = 0)	**.007**	1.19 (1.11–1.27)
nCPAP	1.8% (n = 3)	0.0% (n = 0)	.511	1.15 (1.08–1.21)
IMV	1.2% (n = 2)	0.0% (n = 0)	.592	1.14 (1.08–1.21)
Mortality	0% (n = 0)	0% (n = 0)	>.999	…

Characteristic	Neither RSV Nor SARS-CoV-2 (n = 555)
Median age, mo (min; max)	16.0 (0; 59)
Male sex	58.9% (n = 327)
Patients at risk	15.3% (n = 85)
Signs and symptoms	
Dyspnea	14.2% (n = 79)
Fever	60.9% (n = 338)
Cough	39.5% (n = 219)
Rhinitis	26.1% (n = 145)
GI symptoms	24.7% (n = 137)
Median time of hospitalization, d (min; max)	3 (0; 72)
Intensive care treatment	4.3% (n = 24)
O_2 supplementation	10.8% (n = 60)
HFNC	7.4% (n = 41)
nCPAP	0.7 (n = 4)
IMV	2.2% (n = 12)
Mortality	0.7% (n = 4)

Abbreviations: CI, confidence interval; GI, gastrointestinal; HFNC, high-flow nasal cannula; IMV, invasive mechanical ventilation; nCPAP, nasal continuous positive airway pressure; O_2, oxygen; RR, relative risk; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Values in bold denote significant P Value (<.05).

DISCUSSION

In our cohort, symptomatic patients with RSV were sicker than patients with SARS-CoV-2 and were hospitalized significantly longer. Moreover, patients with RSV infection required a higher level of medical care and more intensive nursing than patients infected with SARS-CoV-2 due to a higher need of respiratory support with HFNC and oxygen supplementation. It is noteworthy that 11 of 41 patients (26.8%) required >15 L/minute of flow. Therefore, the incidence of nCPAP support might be higher in other centers that limit flow to 10–12 L/minute in young infants, and the need for nCPAP support in RSV infections might be underestimated in our survey. Moreover, we were able to underline the higher need for medical care and more intensive nursing by showing that RSV patients have a higher risk of intensive care treatment at the PICU, a higher risk of nCPAP, and a higher risk of intubation.

This analysis was limited by its retrospective nature and its local cohort. Despite the shown differences in clinical appearance, in times of high prevalence of both infections, clinical symptoms cannot be used to reasonably differentiate between these 2 infections. Thus, RT-PCR testing is necessary for the diagnosis and subsequent cohorting of infected patients. Although the outcome of both infections is good, one should not forget long-term outcome after RSV infections such as preschool wheeze, asthma, and repeated respiratory infections. Long-term outcomes of SARS-CoV-2-infections are unknown or suspected to play a small role with regard to children at present.

In summary, RSV-infected patients require a higher level of medical care and had to stay in hospital for longer than SARS-CoV-2–infected children, thereby placing higher stress on hospital resources and the healthcare system in general.

Notes

Potential conflicts of interest. All authors: No reported conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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