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ORIGINAL ARTICLE

Impact of COVID-19 on the epidemiology of respiratory viruses in southern Brazil

Impacto da COVID-19 na epidemiologia de vírus respiratórios no Rio Grande do Sul

Impacto epidemiológico de la COVID-19 sobre los virus respiratorios en sur de Brasil

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ABSTRACT

Background and objectives: During the SARS-CoV-2 pandemic, reduction in detection of other Respiratory Viruses (RV) was observed. Epidemiological studies are needed to understand the impact of the pandemic on the circulation of RV. The aim of this study is to analyze the epidemiological profile of cases of severe acute respiratory infection (SARI) associated with the main RV in hospitalized patients from RS, between 2010 and 2019 (period *A*) and between 2020 and 2021 (period *B*). **Methods:** Data related to SARI cases in RS were retrieved from SIVEP-Gripe. **Results:** In period *A* there were more infections with Influenza, Parainfluenza, Adenovirus and Respiratory Syncytial Virus, while in period *B* most cases were of SARS-CoV-2 infection. The most affected age groups were individuals <5 years old (67.1%) in period *A*, and >60 years old (50%) in period *B*. The main symptoms were fever and cough in period *A*, and dyspnea and O_2 saturation <95% in period *B*. The most reported comorbidities were lung diseases and chronic cardiovascular diseases in period *A*, and chronic cardiovascular diseases and diabetes mellitus in period *B*. Importantly, a higher fatality rate was observed in period *B*. Most cases occurred between May and July in period *A*, and in November and December 2021 in period *B*. **Conclusion:** This study reveals that the COVID-19 pandemic changed the epidemiological profile of SARI in RS, and most cases were in the elderly with chronic cardiovascular disease and diabetes mellitus.

Keywords: *Coronavirus Infections. Epidemiological Monitoring. Severe Acute Respiratory Syndrome.*

RESUMO

Justificativa e Objetivos: Durante a pandemia de SARS-CoV-2 foi observada redução na detecção de outros vírus respiratórios (VR). Estudos epidemiológicos são importantes para uma melhor compreensão dos impactos da pandemia sobre a circulação de VR. O objetivo deste estudo foi analisar o perfil epidemiológico dos casos de síndrome respiratória aguda grave (SRAG) associados aos principais VR em pacientes internados no RS, entre 2010 e 2019 (período *A*) e entre 2020 e 2021 (período *B*). **Métodos:** Dados relacionados a casos de SRAG no RS foram obtidos do SIVEP-Gripe. **Resultados:** No período *A* houve mais infecções por Influenza, Parainfluenza, Adenovírus e Vírus Sincicial Respiratório, enquanto no período *B* a maioria foi por SARS-CoV-2. Os grupos etários mais afetados foram de indivíduos <5 anos de idade (67,1%) no período *A*, e >60 anos (50%) no período *B*. Os principais sintomas foram febre e tosse no período *A*, e dispneia e saturação de O_2 <95% no período *B*. As principais comorbidades no período *A* foram pneumopatias e cardiopatias, enquanto no período *B* foram cardiopatias e diabetes mellitus. A mortalidade foi maior no período *B*. A maioria dos casos no período *A* foram entre maio e julho, e no período *B* entre novembro e dezembro de 2021. **Conclusão:** Este estudo revela que a pandemia de COVID-19 alterou o perfil epidemiológico de SRAG no RS, sendo a maioria dos casos em indivíduos idosos com doença cardiovascular e diabetes.

Descritores: *Infecções por Coronavirus. Monitoramento Epidemiológico. Síndrome Respiratória Aguda Grave.*

RESUMEN

Justificación y Objetivos: Durante la pandemia por SARS-CoV-2 se observó reducción en la detección de otros virus respiratorios (VR). Los estudios epidemiológicos son importantes para comprender los impactos de la pandemia en la circulación de VR. Este estudio analizó variables epidemiológicas asociadas al Síndrome Respiratorio Agudo Grave (SRAG) en Rio Grande do Sul (RS), Brasil, antes de la aparición del SARS-CoV-2 (período *A*, 2010-2019) y durante la pandemia (período *B*, 2020-2021). **Métodos:** Los datos relacionados con los casos de SRAG en RS se obtuvieron de SIVEP-Gripe. **Resultados:** En el período *A* hubo más infecciones por Influenza, Parainfluenza, Adenovirus y Virus Respiratorio Sincitial, mientras que en el período *B* la mayoría de los casos fueron causados por SARS-CoV-2. Los grupos de edad más afectados fueron <5 años (67,1%) en el período *A*, y >60 años (50%) en el período *B*. Los principales síntomas fueron fiebre y tos en el período *A*, y disnea y saturación de O_2 <95% en el período *B*. Las principales comorbilidades en el período *A* fueron enfermedades pulmonares y cardíacas, y en el período *B* fueron enfermedades cardíacas y diabetes mellitus. La mortalidad fue mayor en el período *B*. La mayoría de los casos en el período *A* fueron entre mayo y julio, y en el período *B* entre noviembre y diciembre. **Conclusiones:** Este estudio revela que la pandemia de COVID-19 cambió el perfil epidemiológico del SRAG en RS. La mayoría de los casos se dan en personas de edad avanzada con enfermedades cardiovasculares y diabetes.

Palabras Clave: *Infecciones por Coronavirus. Monitoreo Epidemiológico. Síndrome Respiratorio Agudo Grave.*

INTRODUCTION

Acute respiratory infections are a global health problem, with high morbidity and mortality.[1] Respiratory viruses (RVs) can infect the upper and lower respiratory tract, leading to symptoms such as fever, headache, cough, chills, among others. The clinical spectrum can vary from mild cases of acute respiratory infection (ARI) to cases of Severe Acute Respiratory Infection (SARI).[2]

Epidemiological surveillance of RVs is paramount for disease control and prevention. In Brazil, surveillance of RVs is based on case notification and collection of nasopharyngeal samples from patients for laboratorial analysis, which is performed in public laboratories throughout the country, including State Central Laboratories (LACEN) and the National Influenza Centers (NIC). Cases of SARI are notified in the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe) of Brazil.[2]

Rio Grande do Sul (RS) is one of the states with the highest incidence of viral respiratory infections in the country.[3-7] During the first two years of the coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the health network focused efforts for the identification and confirmation of COVID-19 cases, with detection of SARS-CoV-2 becoming a priority over other RV. Therefore, a lower number of SARI cases associated with other RV were reported;[5] noteworthy, pandemic control measures may also have impacted the circulation of other viruses. Moreover, the emergence of a given RV such as SARS-CoV-2 can affect the dynamics of other RVs in the population.[8-10] In this sense, analyses of the circulation of different RV during epidemic and pandemic events are important to better understand the epidemiology of viral respiratory infections in different scenarios and the factors that may contribute for differences in viral circulation. Such studies contribute to the prevention and control of outbreaks and epidemics.

The aim of this study was to analyze the epidemiological profile of cases of respiratory infection associated with the main RVs in hospitalized patients from RS, between 2010 and 2019 (period *A*) and between 2020 and 2021 (period *B*).

METHODS

This study evaluated data from laboratory analyses performed at the Central Public Health Laboratory of Rio Grande do Sul (LACEN-RS) for detection of RVs in nasopharyngeal samples from patients with SARI hospitalized in RS between January 1, 2010 and June 30, 2021. Laboratory data were provided by LACEN-RS, which is responsible for performing surveillance of RVs in RS and diagnosis of viral infection based on viral detection by qPCR, RT-qPCR and

immunofluorescence assays in samples collected from patients in public or affiliated hospitals in all 497 RS municipalities. All analyses are performed based on validated protocols as described elsewhere.[2-4,6,7] It is important to note that samples from period *A* were first tested for influenza viruses; when negative for influenza viruses, samples were tested for other RVs.

Demographic and clinical data related to each SARI case were retrieved from the SIVEP-Gripe system and provided by the State Health Surveillance Center (CEVS-RS). The following data were obtained for epidemiological analysis: sex, age, clinical symptoms, comorbidities, result of RV investigation, outcome, and length of stay in the hospital (LOS). The monthly averages of the maximum and minimum temperatures (in ºC) in RS were obtained from the National Institute of Meteorology (INMET) to associate seasonality with the peak period of each RV.

The databases used contain raw data, which passed inclusion and exclusion criteria, in addition to statistical analyses. The inclusion criteria were: a) total data on SARI cases for absolute numbers; b) data with laboratory examination by qPCR, RT-qPCR or immunofluorescence for any RV and with result "Detected", for analysis of RV; c) the respiratory viruses analyzed were: hPIV, HAdV, RSV, IAV/IBV, SARS-CoV-2; d) cases notified between January 1, 2010 and June 30, 2021. Data from individuals without SARI symptoms and from individuals that were tested only for influenza viruses were excluded.

The database was used for stratification and was later exported for data analysis in the R v.3.6.3 software statistical package. Data presentation was performed through Residual Analysis and Chi-square tests. Results were considered significant when $p<0.0001$ for Chi-square and >1.96 for Residual Analysis. Mean values, percentage or absolute data for quantitative variables were also used. To assess the existence of significant differences in LOS – number of days from date of admission in the hospital to date of evolution (cure or death) –, the Mann-Whitney test was performed for two independent samples; the significance level $\alpha=0.05$ was used.

This study is part of projects approved by the Ethics Committee of UFCSPA which are registered on Plataforma Brasil (CAAE 75118217.9.0000.5345; CAAE 75357417.1.0000.5345; CAAE 30714520.0.0000.5345). The research was conducted in accordance with the required ethical standards from Resolutions 466/2012, 510/2016 and 580/2018, from the Brazilian Ministry of Health.

RESULTS

Data from 29,902 SARI cases from period *A* and 128,642 cases from period *B* were analyzed. Table 1 presents the number of cases according to RV, showing the total number of cases and the percentage in relation to the total number of positive cases for the analyzed RV. The

analysis of adjusted residues (res.adj) reveals that IAV/IBV, hPIV-1, hPIV-2, hPIV-3, HAdV and RSV were more detected in period *A* than period *B* (res.adj=196.81, 31.27, 14.91, 66.07, 62.62, 202.15), while SARS-CoV-2 was the main virus detected in period *B* (res.adj=307.69).

Table 1. Number of SARI cases caused by the respiratory viruses analyzed in this study.

Variable	**Period *A* (2010-2019), N (%)**	**Period *B* (2020-2021), N (%)**
Notified cases	29902	128642
Positive for respiratory viruses[a]	9310 (31.1)	89915 (69.9)
Influenza[b]	3875 (41.6)	18 (0.02)
hPIV[b]	581 (6.2)	6 (0.01)
hPIV-1	108 (18.6)	6 (100)
hPIV-2	23 (4.0)	0 (0)
hPIV-3	450 (77.5)	0 (0)
HAdV[b]	416 (4.5)	10 (0.01)
RSV[b]	4438 (47.7)	370 (0.4)
SARS-CoV-2[b]	0 (0)	89511 (99.6)

N: number of cases.
[a] Percentage of positive cases in relation to the total number of notified cases.
[b] Percentage of cases for the specified respiratory virus in relation to the total number of positive cases for respiratory viruses. In the case of influenza virus, IAV and IBV were not specified.

Regarding the sex of the individuals, 52.5% of SARI cases in period *A* and 53.8% in period *B* were male, with no differences between sexes. Table 2 shows the age profile of SARI cases caused by different respiratory viruses in RS in periods *A* and *B*. In period *A*, there were more cases among individuals aged <1, 1–5, 6–11 and 12–19 (res.adj= 199.19, 123.02, 42.32, 23.25, respectively), while in period B there were significantly more cases in the age groups 20–39, 40–59 and ≥60 (res.adj= 16.27, 50.33, 72.10, respectively). The Chi-square test reveals that there is an association between the age of the patients and the period (pre-pandemic and pandemic, $p<0.0001$).

Table 2. Age profile of SARI cases caused by different respiratory viruses in Rio Grande do Sul between 2010 and 2019 (Period *A*) and between 2020 and 2021 (Period *B*).

Period *A*								
Age (years)	**Influenza, N (%)**	**hPIV-1, N (%)**	**hPIV-2, N (%)**	**hPIV-3, N (%)**	**HAdV, N (%)**	**RSV, N (%)**	**SARS-CoV-2, N (%)**	**All respiratory viruses, N (%)**
<1	519 (13.6)	47 (43.5)	14 (60.9)	333 (74.0)	209 (50.2)	3290 (74.1)	0 (0)	4412 (47.6)
1-5	559 (14.6)	40 (37.0)	2 (8.7)	97 (21.6)	157 (37.7)	949 (21.4)	0 (0)	1804 (19.5)
6-11	217 (5.7)	7 (6.5)	1 (4.4)	4 (0.9)	8 (1.9)	34 (0.8)	0 (0)	271 (2.9)
12-19	177 (4.6)	1 (0.9)	1 (4.4)	2 (0.4)	14 (3.4)	12 (0.3)	0 (0)	207 (2.2)
20-39	589 (15.4)	3 (2.8)	2 (8.7)	1 (0.2)	10 (2.4)	27 (0.6)	0 (0)	632 (6.8)
40-59	868 (22.7)	3 (2.8)	0 (0)	5 (1.1)	12 (2.9)	43 (1.0)	0 (0)	931 (10.1)
≥60	899 (23.5)	7 (6.5)	3 (13.0)	8 (1.8)	6 (1.4)	83 (1.9)	0 (0)	1006 (10.9)
Period *B*								
Age (years)	**Influenza, N (%)**	**hPIV-1, N (%)**	**hPIV-2, N (%)**	**hPIV-3, N (%)**	**HAdV, N (%)**	**RSV, N (%)**	**SARS-CoV-2, N (%)**	**All respiratory viruses, N (%)**
<1	2 (11.1)	3 (50.0)	0 (0)	0 (0)	8 (80.0)	253 (68.4)	219 (0.2)	485 (0.5)
1–5	2 (11.1)	3 (50.0)	0 (0)	0 (0)	1 (10.0)	89 (24.1)	169 (0.2)	264 (0.3)
6–11	1 (5.6)	0 (0)	0 (0)	0 (0)	0 (0)	7 (1.9)	91(0.1)	99 (0.1)
12–19	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	4 (1.1)	327 (0.4)	332 (0.4)
20–39	1 (5.6)	0 (0)	0 (0)	0 (0)	0 (0)	5 (1.4)	11327 (12.7)	11333 (12.6)
40–59	7 (38.9)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.3)	32347 (36.1)	32355 (36.0)
≥60	5 (27.8)	0 (0)	0 (0)	0 (0)	0 (0)	11 (3.0)	45031 (50.3)	45047 (50.1)

N: number of cases of the respective respiratory virus in the specified age group.
%: Percentage of cases in the age group in relation to the total number of cases of the respective respiratory virus.

As shown in Table 3, cough, fever, dyspnea, and sore throat were the symptoms analyzed in both periods, whereas other symptoms were evaluated separately because not all of them were reported in both periods. The frequency of cases with fever and cough was higher in period *A* (res.adj=24.67, 9.27 respectively), while dyspnea and sore throat were more reported in period *B* (res.adj=19.51, 21.26); our analysis revealed an association between patients' symptoms and period ($p<0.0001$). In period *B*, dyspnea was the most predominant symptom, observed in 86% of the cases. Other symptoms were included in the notification forms of SARI in period *B*, including respiratory distress (in 77% of the cases), O_2 saturation <95% (82%), diarrhea (21%) and vomiting (12%).

Table 3. Symptoms observed in SARI cases by different respiratory viruses in Rio Grande do Sul between 2010 and 2019 (Period *A*) and between 2020 and 2021 (Period *B*).

Period *A*							
Symptom N/t[a] (%)	**Influenza**	**hPIV-1**	**hPIV-2**	**hPIV-3**	**HAdV**	**RSV**	**SARS-CoV-2**
Fever	3518/3852 (91.3)	99/108 (91.7)	22/23 (95.7)	424/449 (94.4)	401/415 (96.6)	4012/4423 (90.7)	0/0 (0)
Cough	3578/3849 (93.0)	102/108 (94.4)	23/23 (100)	430/447 (96.2)	398/414 (96.1)	4257/4425 (96.2)	0/0 (0)
Dyspnea	2959/3823 (77.4)	89/108 (82.4)	22/23 (95.7)	418/443 (94.4)	370/414 (89.4)	3977/4396 (90.5)	0/0 (0)
Sore throat	996/3364 (29.6)	13/77 (16.9)	2/12 (16.7)	12/151 (7.9)	37/200 (18.5)	173/2152 (8)	0/0 (0)
Myalgia	1349/2914 (46.3)	11/55 (20.0)	3/9 (33.3)	11/108 (10.2)	33/111 (29.7)	169/1681 (10.1)	0/0 (0)
Period *B*							
Fever	14/18 (77.8)	6/6 (100)	0/0 (0)	0/0 (0)	10/10 (100)	225/335 (67.2)	50481/77738 (64.9)
Cough	13/18 (72.2)	6/6 (100)	0/0 (0)	0/0 (0)	4/10 (40)	326/357 (91.3)	61423/79717 (77.1)
Dyspnea	15/17 (88.2)	5/6 (83.3)	0/0 (0)	0/0 (0)	7/10 (70)	252/337 (74.8)	72180/83555 (86.4)
Sore throat	3/18 (16.7)	0/6 (0)	0/0 (0)	0/0 (0)	1/9 (11,11)	7/285 (2.5)	17103/67250 (25.4)
Respiratory distress	15/17 (88.2)	4/6 (66.7)	0/0 (0)	0/0 (0)	6/10 (60)	274/342 (80.1)	60140/78254 (76.9)
Saturation O_2< 95%	11/17 (64.7)	2/6 (33.3)	0/0 (0)	0/0 (0)	5/9 (55.56)	203/331 (61.3)	67652/82115 (82.4)
Diarrhea	2/17 (11.8)	2/6 (33.3)	0/0 (0)	0/0 (0)	2/9 (22.22)	21/288 (7.3)	14208/67280 (21.1)
Vomiting	2/17 (11.8)	3/6 (50)	0/0 (0)	0/0 (0)	2/9 (22.22)	50/292 (17.1)	8146/65776 (12.4)
Fever	14/18 (77.8)	6/6 (100)	0/0 (0)	0/0 (0)	10/10 (100)	225/335 (67.2)	50481/77738 (64.9)

[a] Number of cases positive for the respective respiratory virus with a given symptom (N) in relation to the total of answers for that symptom (t).

Table 4 presents comorbidities observed in SARI cases in periods *A* and *B*. Chronic cardiovascular disease, chronic kidney disease and immunodeficiency/immunosuppression were reported in all years between periods *A* and *B*. As revealed by the analysis of adjusted residuals, the percentage of cases that presented immunodeficiency/immunosuppression and chronic kidney disease was significantly higher in period *A* (res.adj=30.96, 6.42, respectively). There was no significant difference between the two periods regarding the frequency of patients with chronic cardiovascular disease (res.adj=0.02). The Chi-square test reveals that there is an association between the patients' comorbidities and the period ($p<0.0001$).

Table 4. Comorbidities observed in SARI cases by different RV in RS between 2010 and 2019 (Period *A*) and between 2020 and 2021 (Period *B*).

Period *A* – N/t (%[a])							
Comorbidity/Risk factor	**Influenza**	**hPIV-1**	**hPIV-2**	**hPIV-3**	**HAdV**	**RSV**	**SARS-CoV-2**
Chronic cardiovascular disease	600/3552 (16.9)	7/99 (7.1)	2/20 (10.0)	14/393 (3.6)	12/348 (3.5)	122/3981 (3.1)	0/0 (0.0)
Chronic kidney disease	121/3545 (3.41)	1/99 (1.0)	1/20 (5.0)	1/393 (0.3)	2/349 (0.6)	13/3982 (0.3)	0/0 (0.0)
Immunodeficiency/immunosuppression	263/3534 (7.4)	4/98 (4.1)	1/20 (5.0)	4/393 (1.0)	12/346 (3.5)	55/3978 (1.4)	0/0 (0.0)
Chronic lung diseases (2010–2018)	734/3299 (22.3)	15/94 (16.0)	2/19 (10.5)	73/385 (19.0)	71/325 (21.9)	535/3878 (13.8)	0/0 (0.0)
Smoking (2010–2018)	1/49 (2)	0/10 (0.0)	1/6 (16.7)	0/36 (0)	1/42 (2.4)	10/717 (1.4)	0/0 (0.0)
Asthma (2019)	50/253 (19.8)	2/6 (33.3)	1/1 (100)	3/7 (42.9)	10/23 (43.5)	40/109 (36.7)	0/0 (0.0)
Other chronic lung diseases (2019)	42/253 (16.6)	0/5 (0)	0/1 (0)	2/7 (28.6)	3/23 (13.0)	7/109 (6.4)	0/0 (0.0)
Obesity (2019)	18/249 (7.2)	0/5 (0)	0/1 (0)	0/6 (0)	0/23 (0.0)	1/108 (0.9)	0/0 (0.0)
Period *B* – N/t (%)							
Comorbidity/Risk factor	**Influenza**	**hPIV-1**	**hPIV-2**	**hPIV-3**	**HAdV**	**RSV**	**SARS-CoV-2**
Chronic cardiovascular disease	3/10 (30)	1/3 (33.3)	0/0 (0)	0/0 (0)	0/4 (0)	13/83 (15.7)	31524/51833 (60.8)
Chronic kidney disease	1/10 (10)	0/3 (0)	0/0 (0)	0/0 (0)	0/4 (0)	0/80 (0)	3397/42165 (8.1)
Immunodeficiency/immunosuppression	2/10 (20)	1/3 (33.3)	0/0 (0)	0/0 (0)	0/4 (0)	5/80 (6.3)	2953/42089 (7.0)
Chronic hematological disease	0/10 (0)	1/3 (33.3)	0/0 (0)	0/0 (0)	0/4 (0)	1/81 (1.2)	710/41536 (1.7)
Down's syndrome	0/10 (0)	1/3 (33.3)	0/0 (0)	0/0 (0)	0/4 (0)	4/82 (4.9)	246/41652 (0.6)
Chronic liver disease	0/10 (0)	0/3 (0)	0/0 (0)	0/0 (0)	0/4 (0)	1/80 (1.3)	1044/41564 (2.5)
Asthma	2/10 (20)	1/3 (33.3)	0/0 (0)	0/0 (0)	0/4 (0)	24/83 (28.9)	3735/42446 (8.8)
Diabetes mellitus	2/10 (20)	0/3 (0)	0/0 (0)	0/0 (0)	0/4 (0)	5/83 (6.0)	21893/48674 (44.9)
Chronic neurological disease	1/10 (10)	0/3 (0)	0/0 (0)	0/0 (0)	1/4 (25)	13/83 (15.7)	4784/42700 (11.2)
Other chronic lung diseases	2/10 (20)	0/3 (0)	0/0 (0)	0/0 (0)	1/4 (25)	4/81 (4.9)	4625/42730 (10.8)
Obesity	1/9 (11.1)	0/3 (0)	0/0 (0)	0/0 (0)	0/4 (0)	2/81 (2.5)	12593/44709 (28.2)
Puerperal	0/10 (0)	0/3 (0)	0/0 (0)	0/0 (0)	0/4 (0)	0/81 (0)	187/41506 (0.5)

[a] Number of cases positive for the respective respiratory virus with a given symptom (N) in relation to the total of answers for that comorbidity (t).

In period *A*, 6.7% of the patients with respiratory viral infection died, whereas in period *B* the fatality rate was higher, reaching 37%. In this sense, "cure" was associated with period *A* (res.adj=57.73), while "death" was associated with period *B* (res.adj=57.73). The chi-square test with Yates' correction showed that there is an association between patient outcomes and period (pre-pandemic or pandemic, $p<0.0001$).

The average length of stay in the hospital (LOS) was 11 days in both periods. Statistical analysis revealed a significant difference between periods (W = 1116421728, p-value < 2.2e-16). The mean LOS in period *A* was 11.21 days (± 0.127 days), and in period *B* 11.57 days (± 0.039 days) (data not shown).

The monthly number of SARI cases positive for each respiratory is shown in Table 5. Data related to period *B* was obtained until June 2021; to avoid bias when comparing period *B* with period *A* (which contains data from January to December of all years), period *B* was divided into two segments (period *B*-2020 and period *B*-2021).

In period *A*, most infections occurred between April and August. There was a predominance of Influenza and RSV between April and August (3,453 and 4,238 cases, respectively), with the number of cases decreasing in late winter and early spring (221 and 119 cases, respectively). HAdV circulated mainly in autumn (90 cases) and spring (282 cases). Regarding hPIV, the dominant type was hPIV-3, with peaks in spring (282 cases) and winter (118 cases); whereas most cases of hPIV-1 were observed during fall (53 cases), and of hPIV-2 in winter (9 cases) and autumn (8 cases).

In period *B*, no cases of hPIV-2 and hPIV-3 infection were reported, whereas six (6) cases of hPIV-1 were reported between February and March 2020. Nine (9) cases were positive for HAdV between January and April 2020, and one (1) case in May 2021. There were few cases of RSV in 2020 (9 cases), but in 2021 361 cases of RSV were reported between January and June. Regarding influenza viruses, there were only 18 confirmed cases as of June 2021.

Table 5. SARI cases by RV according to the month in Period *A* (2019-2020) and Period *B* (2020 and 2021)

Period *A* 2010–2019	**Influenza**	**hPIV-1**	**hPIV-2**	**hPIV-3**	**HAdV**	**RSV**	
January	16	4	3	10	12	4	
February	10	2	1	2	5	8	
March	89	17	2	3	12	62	
April	682	19	4	4	33	253	
May	799	17	2	7	45	972	
June	786	10	2	23	26	1392	
July	814	5	1	25	68	1193	
August	372	6	6	70	71	428	
September	167	9	0	114	42	101	
October	54	7	2	109	63	18	
November	59	6	0	59	19	4	
December	26	6	0	24	20	3	
Total	3874	108	23	450	416	4438	
Period *B* 2020	**Influenza**	**hPIV-1**	**hPIV-2**	**hPIV-3**	**HAdV**	**RSV**	**SARS-CoV-2**
January	5	0	0	0	1	2	0
February	3	2	0	0	2	3	0
March	2	4	0	0	5	3	230
April	2	0	0	0	1	0	648
May	0	0	0	0	0	0	1027
June	3	0	0	0	0	0	2644
July	0	0	0	0	0	0	4929
August	0	0	0	0	0	1	4468
September	0	0	0	0	0	0	3050
October	1	0	0	0	0	0	3323
November	0	0	0	0	0	0	5479
December	0	0	0	0	0	0	5698
Total	16	6	0	0	9	9	31496
Period *B* 2021	**Influenza**	**hPIV-1**	**hPIV-2**	**hPIV-3**	**HAdV**	**RSV**	**SARS-CoV-2**
January	1	0	0	0	0	2	4642
February	1	0	0	0	0	5	13812
March	0	0	0	0	0	19	16671
April	0	0	0	0	0	137	8902
May	0	0	0	0	1	136	10912
June	0	0	0	0	0	62	3076
Total	2	0	0	0	1	361	58015

DISCUSSION

The first cases of SARS-CoV-2 infection occurred in China in December 2019. The COVID-19 pandemic was declared in March 2020,[11] and RS had the first case on March 10, 2020.[12] This study analyzed SARI cases associated with RV infection in hospitalized patients along 10 years before the COVID-19 pandemic and during the first 18 months of the pandemic in the State of Rio Grande do Sul (RS), Brazil. Data related to cases notified in the SINAN and SIVEP-Gripe systems between January 2010 and June 2021 were assessed to build two databases, one with data of SARI cases before the COVID-19 pandemic (period *A*, 2010 to 2019: 29,902 cases), and the other with data of SARI cases during the first two years of the COVID-19 pandemic (period *B*, 2020 to 2021: 128,642 cases).

The most detected RVs among SARI patients in period *A* were IAV/IBV and RSV, which is in accordance with data from epidemiological bulletins in the state.[13] These RV were also detected in some cases in period *B*, with more cases of RSV than of Influenza (370 and 18 cases, respectively). In 2021, RSV was the only RV detected in samples of patients with SARI that were negative for SARS-CoV-2, and 335 of 361 RSV-positive cases occurred during autumn and winter, when temperatures are a little above 10ºC. Between September and December, when minimum and maximum temperatures in RS are around 15ºC–21ºC and 23ºC–29ºC, respectively, there were more cases of Influenza than RSV.

In period *A*, a significant number of SARI cases during spring was associated with hPIV-3 infection; hPIV-1, on the other hand, circulates mainly during the autumn. This finding corroborates a previous study that analyzed cases of hPIV-1, hPIV-2, and hPIV-3 along 28 years in RS that found hPIV-3 to be the most common type of parainfluenza virus among hospitalized individuals.[7]

HAdV had a peak in the number of cases in July and August, however with fewer cases than other RVs. Cases of HAdV were also reported in January, like other HAdV studies in RS in years prior to 2020.[4]

In 2020, the first year of the COVID-19 pandemic, a significant number of SARS-CoV-2 infections were observed during winter (July and August), however the months with the highest number of cases in 2020 were November and December, which may be associated with non-seasonal causes posed by the pandemic.

In period *B*, circulation of other RVs in RS was more common during autumn and winter, corroborating other studies.[4,6,7,14] The seasonal occurrence of RV diseases in temperate regions, with more respiratory diseases during colder seasons, as is the case of RS, may be related to factors such as higher replication of some RV at lower temperatures and higher transmission among individuals because of closed and less-ventilated environments.

Regarding the age of patients with SARI associated with RV infection, the most affected age group was <1 year in period *A*, and ≥60 years in period B. Additionally, in period *A* there were more patients aged <5 years (67.1%), while in period B most cases were in adults aged 20 to 59 years (48.6%) and elderly ≥60 (50.1%). Our results corroborate studies performed in RS and in other Brazilian regions.[3,8,15,16] In our study, only 0.54% of the individuals with SARI due to SARS-CoV-2 were children. As discussed in other studies, the prevalence of asymptomatic COVID-19 in children is likely to be underestimated.[17,18]

The most common symptom presented in period *A* was cough, reported by 95% of patients, followed by fever (91%). In period *B*, dyspnea and O_2 saturation <95% were the most

common symptoms, corroborating other findings in Brazil.[19] Fever and cough are the most common symptoms in cases of RV infection, however dyspnea and low O_2 saturation are criteria for classification of SARI.[2] Therefore, the COVID-19 pandemic clearly caused an increase in cases of SARI.

Individuals with comorbidities such as cardiovascular disease and chronic respiratory diseases, and with other risk factors such as smoking, pregnancy and immunosuppression, are more susceptible to severity in case of respiratory viral infection.[1,4,6,20] In the present study, the most common comorbidities in period *A* were respiratory diseases (asthma, lung diseases and other chronic lung diseases), with 58% of the patients having at least one of these comorbidities. In period *B*, the most common comorbidities were chronic cardiovascular disease, diabetes and obesity (present in 60.7%, 44.9% and 28.1% of the patients, respectively). The findings of the present study corroborate previous studies reporting chronic cardiovascular disease as the most common comorbidity associated with COVID-19, also being a risk factor for adverse prognosis.[20-22]

In period *A*, the percentage of individuals with a given comorbidity was similar among the SARI cases regardless of the viral type; in contrast, the most common comorbidities observed in period *B* were mainly in individuals infected by SARS-CoV-2. This might have contributed for a higher fatality in period *B* compared to period *A* (37% and 6.7%, respectively), considering that patients with some comorbidities are more susceptible to developing severe COVID-19.[15,20-24]

Positive cases for IAV/IBV, hPIV-1, hPIV-2, hPIV-3, HAdV and RSV viruses decreased significantly after the emergence of SARS-CoV-2, corroborating findings of another study in RS.[8,10] Studies conducted in other countries also found a decrease in the circulation of other respiratory viruses during the first months of the COVID-19 pandemic, which has been attributed to the effectiveness of the public health measures adopted to reduce SARS-CoV-2 transmission.[9,25]

This study analyzed data from the epidemiological surveillance of respiratory infection in Brazil. Prior to 2020, surveillance of respiratory viruses in Brazil, and globally, primarily focusing on detecting influenza viruses. This limited the ability to comprehensively analyze the epidemiology of other RVs and also hindered the identification of co-infection cases and their interactions.[2,13,16] The COVID-19 pandemic demanded health management and diagnosis efforts to control the spread of SARS-CoV-2, posing even more limitations to detection of other RVs in period *B*.[2,16] The fact that this study was based on the analysis of a few respiratory viruses and missed many cases of co-infections represents a limitation of the study and reinforces the need of a continuous surveillance of respiratory viruses for control and prevention of epidemics. Despite these limitations, the findings presented herein are important to support policies and guidelines for

the continuous surveillance of different RVs along the year, to better plan prevention strategies according to viral seasonality and circulation.

In addition to actions aimed at preventing viral infections, it is crucial to strengthen the diagnostic and epidemiological structure to improve monitoring and control of RV in RS, including genomic surveillance, which provides information about circulating viral strains and even strains that might emerge in the region.[26-28] To achieve this, public policies and health planning and management actions need to be aligned with the population's needs. This would allow for greater accessibility to viral detection tests for suspected cases, along with the implementation of organized and standardized data recording systems.

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Fernanda P. S. Carpeggiani: data analysis and interpretation; writing the draft; writing the manuscript. **Thiago Menezes Cézar:** data analysis and interpretation; description of results; preparation of tables; writing the draft. **Tatiana Schäffer Gregianini:** concept of the study; collection of samples and molecular analyses in the laboratory; reviewing the manuscript. **Felipe Grillo Pinheiro:** statistical analysis and interpretation of results; writing the draft. **Letícia Garay Martins:** data acquisition. **Ana Beatriz Gorini da Veiga:** study design; project administration and acquisition of funds; data analysis; reviewing draft and writing the manuscript.

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