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Pediatric Hospitalizations for respiratory infections: before and after SARS-CoV-2

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Pediatric Hospitalizations for Respiratory Infections: before and after SARS-CoV-2

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Resumo

Introdução: As infeções respiratórias agudas representam uma importante fonte de morbilidade infantil, tendo um grande impacto nos custos hospitalares. Com o surgimento do SARS-CoV-2 e da pandemia COVID-19, várias medidas não farmacológicas foram adotadas para mitigar esta doença respiratória. O objetivo deste estudo foi comparar os internamentos pediátricos por infeções respiratórias antes e depois do aparecimento da SARS-CoV-2.

Métodos: Estudo retrospetivo observacional dos internamentos por infeções respiratórias (não SARS-CoV2 e SARS-CoV2) no serviço de pediatria do Centro Hospitalar Universitário do Porto, entre abril/2018 e março/2021. Foram incluídos os episódios de internamento de pacientes pediátricos (entre 0-17 anos de idade, inclusive) com tempo de internamento > 24 horas, codificados com um código de infeção respiratória do ICD-10. A colheita de dados foi realizada através dos registos clínicos eletrónicos. Os 2 primeiros anos foram considerados anos 'não-COVID-19' (ano 1 e ano 2), e entre abril/2020 e março/2021 o 'ano COVID-19' (ano 3).

Resultados: Registaram-se 783 internamentos de pacientes pediátricos com diagnóstico de infeção respiratória. Houve uma diminuição significativa no número de internamentos no ano 3 em comparação com o ano 1 e 2 (73% de redução do ano 1 para o ano 3; redução de 67% do ano 2 para o ano 3; p <0,001). Houve uma redução significativa na proporção de bronquiolites admitidas no ano 3 (redução de 38% do ano 1 para o ano 3; redução de 42% do ano 2 para o ano 3; p <0,001). O Vírus Sincicial Respiratório foi encontrado apenas em 2% dos pacientes internados no ano 3, enquanto o SARS-CoV-2 foi identificado em 32% dos pacientes no mesmo período.

Conclusões: As medidas não farmacológicas populacionais implementadas entre abril/2020 e março/2021, no contexto de COVID-19 associaram-se a uma redução dos internamentos pediátricos por infeções respiratórias por outros agentes não-SARS-CoV2.

Palavras-chave: Criança, internamento, COVID-19, infeções do trato respiratório.

Abstract

Background: Acute respiratory infections represent an important source of childhood morbidity, having a major impact on hospital costs. With the emergence of SARS-CoV-2 and the COVID-19 pandemic, several non-pharmacological measures were adopted to mitigate this respiratory disease. The aim of this study was to compare pediatric hospitalizations for respiratory infections before and after the appearance of SARS-CoV-2.

Methods: Retrospective observational study of admissions for respiratory infections (non-SARS-CoV2 and SARS-CoV2) in the pediatric ward of Centro Hospitalar Universitário do Porto, between April/2018 and March/2021. Hospitalization episodes of pediatric patients (aged 0-17 years inclusive) with length of stay > 24 hours, coded with an ICD-10 respiratory infection code, were included. Data collection was performed using electronic clinical records. The first 2 years were considered 'non-COVID-19' years (year 1 and year 2), and between April/2020 and March/2021 the 'COVID-19 year' (year 3).

Results: There were 783 admissions of pediatric patients diagnosed with respiratory infection. There was a significant decrease in the number of admissions in year 3 compared to year 1 and 2 (73% reduction from year 1 to year 3; 67% reduction from year 2 to year 3; $p<0.001$). There was a significant reduction in the proportion of bronchiolitis admitted in year 3 (38% reduction from year 1 to year 3; 42% reduction from year 2 to year 3; $p<0.001$). Respiratory syncytial virus was found in only 2% of hospitalized patients in year 3, while SARS-CoV-2 was identified in 32% of patients in the same period.

Conclusions: Population non-pharmacological measures implemented between April/2020 and March/2021, in the context of COVID-19, were associated with a reduction in pediatric hospitalizations for respiratory infections caused by other non-SARS-CoV2 agents.

Keywords: Child, hospitalization, COVID-19, respiratory tract infections.

List of Abbreviations

CHUP - Centro Hospitalar Universitário do Porto

CMIN - Centro Materno-Infantil do Norte

ICD-10 - International Classification of Diseases, 10^{th} revision

LRTI - Lower Respiratory Tract Infections

RV - Rhinovirus

RSV - Respiratory Syncytial Virus

SARS-CoV-2 - Severe Acute Respiratory Syndrome - Coronavirus 2

URTI - Upper Respiratory Tract Infections

WHO - World Health Organization

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Introduction

Acute respiratory infections are the leading cause of pediatric hospitalization worldwide.[1] In children under the age of five, malaria and respiratory tract infections account for more than a third of the causes of death globally.[2] Bronchiolitis, asthma and pneumonia are the main causes of hospital admission in children due to acute illness and correspond to an important burden on hospitalization costs.[3]

Viruses are an important cause of morbidity in children and are the main aetiology of lower respiratory tract disease in infants and young children.[4] Respiratory Syncytial Virus (RSV), Rhinovirus (RV), and influenza virus are the most often detected viruses in respiratory infections in infants.[5] RSV is the leading cause of lower respiratory tract infections worldwide in this age group, causing about 75% of all bronchiolitis admissions in children under five years of age.[4] Almost all children have been infected with RSV by the age of 2.[6] There is a wide variety of other less common viruses that can cause respiratory tract disease, such as parainfluenza viruses, adenovirus, human metapneumovirus, enterovirus, coronavirus and bocavirus.[5]

There is an obvious seasonal variation for certain viruses, even though most respiratory viral infections occur throughout the year. Globally, RSV epidemics move from south to north, starting between March and June and decreasing from August to October in southern hemisphere. In northern hemisphere countries the season of RSV starts between September and December and decreases from February to May. An exception to this patterns are humid countries that have their seasonal waves during rainy season.[7] The influenza virus season occurs during June to August in most temperate locations in the southern hemisphere, and January to March in most temperate locations in the northern hemisphere.[8] Early findings from the World Health Organization (WHO) global RSV surveillance published in march 2020 suggested that the annual season epidemics of RSV overlap with influenza season.[9]

Severe Acute Respiratory Syndrome - Coronavirus 2 (SARS-CoV-2), gained worldwide notoriety after the detection of its first case in December 2019 in Wuhan, Hubei province, China.[10] On 11 of March 2020, the WHO declared COVID-19 a pandemic.[11] The first case in Portugal was registered on March 2. [12]

With the appearance of the pandemic, general measures to prevent and control the transmission of SARS-CoV-2 were introduced, namely measures of social distance, use of protective equipment (masks and visors), reinforcement of personal hygiene measures (hand hygiene and respiratory hygiene/cough etiquette), as well as environmental hygiene measures.[13] This type of measures was not specific for SARS-CoV-2, so it provided a potential impact on the transmission of other respiratory viruses. [14]

The beginning of the adoption of these measures coincided with the end of the 2019-2020 winter season in the countries of the northern hemisphere. A study conducted in Finland found an earlier end of the local season of RSV and influenza virus compared to previous years in the pediatric population.[15] In France, non-pharmacological measures to prevent transmission of COVID-19 were associated with a significant decrease in pediatric infectious diseases spread by droplets and contact, including the common cold, gastroenteritis, acute otitis and bronchiolitis. There was also a significant decrease in the number of pediatric visits and hospital admissions, having decreased by 68% and 45%, respectively.[16]

In the southern hemisphere, measures to mitigate the transmissibility of the new virus were applied prior to the local peak of RSV and influenza infections. Australian and New Zealand data showed historically low levels of influenza.[17] Australia's first regional reports indicated an initial decline in the detection of respiratory viruses and related hospital admissions, immediately after the implementation of the restrictions associated with COVID-19. [18] A study of the pediatric population in Western Australia found an initial reduction in RSV and influenza detection and an almost complete absence during the following months, attesting a low RSV and influenza activity during the winter. [19]

The SARS-Cov-2 pandemic and the non-pharmacological measures implemented were associated with less transmission of all viruses with tropism to the airways. On the other hand, the higher incidence of the new virus may compete with other agents, which may decrease the incidence of other respiratory infections. These two situations mentioned, may be associated with a decrease and alteration of the characteristics of hospitalizations due to respiratory infections.

The aim of this study was to compare pediatric hospitalizations due to respiratory infections before the appearance of SARS-CoV-2 and after. Specific objectives were: a) to analyse the number, type and seasonality of respiratory infections admitted during hospitalization; b) describe the microbiological agents associated with respiratory infections; c) analyse the type of clinical approach (auxiliary diagnostic tests and therapeutic measures).

Methods

Study design and setting

This was an observational retrospective study of the hospitalizations due to respiratory infections (non-SARS-CoV2 and SARS-CoV2) on the pediatric ward of Centro Materno-Infantil do Norte (CMIN), Centro Hospitalar Universitário do Porto (CHUP) between April 2018 and March 2021, inclusive. This study was reviewed and approved by the Ethics Committee of CHUP, Porto, Portugal. Informed consent was waived because this was a retrospective study using data from electronic clinical records only. We followed the STROBE statement for reporting observational studies.[20]

Participants, data collection and variables

Inclusion criteria were all the hospital admission episodes of pediatric patients (between 0-17 years of age, inclusive) with a length-of stay >24 hours with, at least, one of the following main or secondary diagnosis according to International Classification of Diseases, 10th revision (ICD-10): A37, A15, R06.2, H66, M35.81, J00, J01, J02, J03, J04, J05, J06, J09, J10, J11, J12, J12.81, J13, J14, J15, J16, J17, J18, J20, J21, J22. The infections were classified as Upper Respiratory Tract Infections (URTI) or Lower Respiratory Tract Infections (LRTI) by ICD-10 diagnosis of the hospitalization (Table I). If electronic clinical records had no registries, hospital admission should be excluded.

In order to obtain a thorough list of the hospitalizations complying with the inclusion criteria 2 strategies were adopted: 1) via administrative databases of Information Department of CHUP; 2) via clinical databases of Pediatric Department of CHUP. After verification of all admission episodes, data collection was performed using electronic clinical records by the research team.

We analysed demographic and administrative variables, like age, gender and length-of-stay. Also, variables from clinical presentation of the disease, workup and therapeutic performed during the hospitalizations were analysed as presented in results section.

For comparison purposes the years were defined as: year 1 (Y1) from April 2018 to March 2019, year 2 (Y2) from April 2019 to March 2020, year 3 (Y3) from April 2020 to March 2021. The Y3 was considered the 'Covid-19 year'.

Statistical analysis

Statistical analyses were performed using SPSS version 27 (SPSS IBM, New York, NY, USA). Continuous variables were described using mean and standard deviation (SD) whenever the variable had a symmetric distribution, and using mean, 25th centile (P25) and 75th centile (P75) whenever the variable didn't have a symmetric distribution. Categorical variables were described using absolute and relative frequencies, and compared with Pearson's chi-squared test. The comparison of the proportions of hospitalizations per year was performed using on sample proportion test. A p-value <0.05 was considered statistically significant for all the inferential analysis.

Results

All the hospitalization episodes identified according to the inclusion criteria had sufficient information in electronic clinical records and no one was excluded. Between April 2018 and March 2021 there were 783 hospitalizations of pediatric patients with a diagnose of respiratory infection at CMIN, CHUP (Table II). Of these, 687 were from patients with one hospitalization only in these 3 years; the remaining 96 episodes were repeated hospitalizations within the 3 analysed years (40 patients with 2 admissions, 4 patients with 3 admissions and 1 patient with 4 admissions). There was a significantly decrease in the number of hospitalizations in the Y3 (73% reduction from Y1 to Y3; 67% reduction from Y2 to Y3; p<0.001). In the Y3, the median age of admission was significantly higher than the previous years (Y1 - 10 months, Y2 - 5 months, Y3 - 20 months; p<0.001).

There was a significantly reduction of URTI proportion in Y3, and a consequently increasing in the proportion of LRTI. This was manly driven by a significantly reduction in the proportion of bronchiolitis admitted in Y3 (38% reduction from Y1 to Y3; 42% reduction from Y2 to Y3; p<0.001), and a significantly increasing in the proportion of pneumonias admitted in Y3 (96% increasing from Y1 to Y3; 124% increasing from Y2 to Y3; p<0.001).

The clinical presentation was statistically different between Y1, Y2 and Y3, with higher proportion of the following symptoms in the Y3: vomits, diarrhea, abdominal pain. And lower proportion of cough, respiratory distress and hypoxemia (Table III).

Blood workup, specifically hemogram, biochemical assay and blood culture were performed in a higher proportion of hospitalizations in Y3 (p<0.001 for hemogram and biochemical assay; p=0.022 for blood culture; Table IV). Inversely, nasopharynx aspirate for viral identification was performed in a lower proportion of admissions in Y3 (55.4% in Y3, vs 78.1% in Y1 and 86.7% in Y2; p<0.001). Also, CT-scans were performed in a higher proportion of admitted patients in Y3 (2094% in Y3, vs 3.7% in Y1 and 5.6% in Y2; p<0.001).

The main identified aetiology of the respiratory infections within the study period were virus (69.5%), specifically, RSV (35.4%), followed by RV (17.1%) and influenza (6.4%) (Table V). Bacteria (in blood culture or sputum microbiology) were identified in 8.4%, mainly, *Haemophilus influenza* (1.4%), *Streptococcus pneumonia* (0.9%) and *Pseudomonas aeruginosa* (0.9%). In Y3, the proportion of identified viruses and bacteria were significantly lower (p<0.001 and p=0.013, respectively). As expected, there was a significant number of SARS-CoV-2 infections in Y3 (31.7%). Of note, there were also two SARS-CoV2 infections (0.6%) in Y2.

In Y3, fewer hospitalized patients were treated with supplemental oxygen (49.5% in Y3, vs 61.4% in Y1 and 62.3% in Y2; p=0.018) or antivirals (2.0% in Y3, vs 6.1% in Y1 and 9.4% in Y2; p=0.037) (Table IV). In the other way, systemic steroids were used more in Y3 (40.6% in Y3, vs 31.8% in Y1 and 26.3% in Y2; p=0.023).

Discussion

To our knowledge, this was the first study carried out in Portugal that analysed hospitalizations for respiratory infections one full year after the appearance of the first case of COVID-19, on March 2, 2020, and compares them with the previous two years in a pediatric tertiary care hospital.

Our study showed a reduction in the number of hospitalizations between April 2020 to March 2021 compared to the same months of the years 2018-2019 and 2019-2020, with a decrease of 73% and 67%, respectively (Figure1). It also showed that there was no peak in hospital admissions for respiratory infections in the winter months of 2020-2021 in contrast to the previous two years. RSV was only found in 2% of patients admitted from April 2020 to March 2021, while in the same period SARS-CoV-2 was identified in 32% of patients.

In Portugal, on March 16, 2020, all schools and teaching activities were suspended[21], and the first state of emergency was declared on March 19, 2020[22]. On May 1, 2020, the government decreed the mandatory use of masks or visors to access or stay in spaces and commercial and service establishments, in public services and buildings and in educational establishments and day care centers by teaching and non-teaching staff and students over six years of age.[23] These measures may have had immediate impacts, since our study showed a sharp decrease in hospitalizations in April, May, June and July 2020 compared to the same months of the years 2018 and 2019. Therefore, there was an immediate positive impact on the institution of measures to mitigate the transmission of SARS-CoV-2, which coincides with data from the international literature.[15,24]

In September 2020 there was a resumption of schools and classroom activities in person. Regarding the data on hospitalizations in the months of September, October and November of 2020, these are overlapping the numbers of hospitalizations in previous years. This can be explained by the resumption of presential classes, given that schools and day care centers were noted not only as a major source of respiratory infections, but also a vehicle for maintaining the circulation of pathogens.[15,25] On the other hand, this overlap with the number of hospitalizations of previous years in these months can also be explained by the increase in the number of cases of infections of COVID-19 that was noted in the country around October and November[26]. Our study shows that 10 of the hospitalizations that took place in November 2020 were due to COVID-19 (Figure 2).

On January 21, 2021, in a communiqué from the council of ministers, the government declared again the suspension of teaching activities starting January 22, including activities to support early childhood day care, family day care and childcare.[27] Our data for December 2020, January, February and March 2021 showed a marked reduction in hospitalizations compared to the same period in previous years. In other words, there was no peak in hospitalizations for respiratory infections characteristic of the winter months. These data corroborate the thesis that the mitigation measures of SARS-CoV-2, namely non-pharmacological measures also have an effect in reducing the transmissibility of the remaining viruses. Similar data were found in New Zealand, where there was a marked decrease in hospitalizations in the winter months, with the characteristic peak of the winter months not being observed.[28]

Regarding the diagnostic groups, in the period after the appearance of COVID-19, there was a significant reduction in URTI and consequently a percentage increase in LRTI. As for specific diagnoses, there was a clear reduction in bronchiolitis and a significant percentage increase in pneumonia compared to previous years. The increase in pneumonia can be explained by pneumonia caused by the new SARS-CoV-2. As for bronchiolitis, which is usually the most common cause of hospitalization below 12 months[29], several studies have shown an abrupt reduction after the implementation of measures against the transmission of SARS-CoV-2.[16,30] A Belgian study even suggested that infections such as bronchiolitis do not become epidemics when non-pharmacological measures such as those implemented inhibit their transmission.[31]

As for the etiological agents, there was a significant decrease in viral isolations, which were identified in 56.4% of hospitalizations between April 2020 and March 2021, and in 67.1% and 76.6% in the same months in the years 2018-2019 and 2019-2020, respectively. There was a significant reduction in RSV that was only isolated in 2% hospitalizations, and in the past years it had been isolated in 35% and 46.8% admissions. These data are very significant since it is known that RSV is the main agent responsible for bronchiolitis.[29] Knowing that RSV has a seasonality between December and April every year[32], there was an obvious and marked reduction in these months, which is also in line with the clear decrease in hospitalizations recorded between December and March 2020-2021 in our study.

Interestingly, RV was isolated in 22.8% of hospitalization episodes between April 2020 and March 2021, which showed a percentage increase compared to previous years. RV are known to be the responsible pathogens for more than half of the cold-like illnesses, but recently they have been found also as lower bronchial tract pathogens, in particular, in infants, elderly patients, and immunocompromised hosts.[33]Also, RV are a major cause of asthma exacerbations in children and adults. There are various risk factors that increase the susceptibility of patients for more severe lower respiratory complications from an RV infection, such as wheezing, bronchitis, and pneumonia. Among others, these risk factors include low neutralizing antibody titers to RV, being an infant, and being an individual with existing asthma.[34] So a hypothesis to justify this increase in the percentage of hospitalizations with RV infection could be infection in individuals with chronic illness, namely asthma, and the dramatic reduction of hospitalizations due to other viruses.

Our data showed a significant difference in the median age of admitted patients between the period of April 2020 and March 2021 compared to previous years, with the median age of hospitalization in this period increasing to 20 months of age. Between 2018-2019 and 2019-2020, 55.9% and 67.2% of hospitalized patients, respectively, were less than 1 year of age and between the same period of 2020-2021 only 40,6% of hospitalized patients were less than 1 year old. In another study, there was also a significant increase in hospitalizations in older age groups, namely in the group between 6 and 10 years old.[25] This is probably related to the drastic reduction in respiratory infection admissions, shown in our analysis. As bronchiolitis are the main cause of hospital admission in developed countries in the first 12 months of life[29], since there was a decrease in these infections, there was a consequent shift from the average age of hospitalizations to a more advanced age.

As for the clinical characteristics, with regard to symptoms, there was a significant increase in the symptoms of vomiting, diarrhea and abdominal pain. This may be justified by the incidence of SARS-CoV-2 infection, as it has been demonstrated that nearly a quarter of patients with COVID-19 infection have gastrointestinal symptoms, with diarrhea being the most common symptom, followed by vomiting and abdominal pain.[35] Regarding the signs, there was a significant decrease in patients hospitalized with respiratory distress and hypoxemia, possibly because of a change in the hospitalization criteria, since patients with less severe signs were admitted.

Regarding treatments, there was a significant reduction in the use of oxygen therapy, which is consistent with the decrease in hypoxia in hospitalized patients. There was a reduction in treatments with antivirals, which may be related to a reduction in hospitalizations for the Influenza viruses. Our data also showed a significant increase in treatment with systemic steroids, which may be related to the use of corticosteroids in the treatment of patients hospitalized for COVID-19.[36]

This study has limitations due to the fact that it was a retrospective study and was dependent on data collection through clinical records and also dependent on the correct coding of infections in research. In the sample submitted for analysis, patients with primary and secondary diagnoses of respiratory infections were included and we were unable to analyse the specific differences between primary vs secondary diagnoses and their implications in clinical presentation, length-of-stay and treatment. Another limitation in this study is that we do not know which hospitalization episodes of those included in the sample were related to patients who have chronic diseases and, in this sense, may have more hospitalization time or need for other types of treatments, which may also translate in the isolation of certain etiologic agents, for example *Pseudomonas aeruginosa* or *Acinetobacter*, which are bacteria usually associated with infections of individuals with chronic diseases.

Future directions: The effectiveness of non-pharmacological measures for mitigating the transmission of SARS-CoV-2 was shown to reduce the number of hospitalizations for respiratory infections globally. This learning can be very useful in the future, with a view to the implementation of permanent measures capable of reducing the burden of hospitalizations for respiratory infections in the health of children and the consequent reduction of costs in the National Health Service. Specific clinical, population, effectiveness and economical trials should be designed towards a more comprehensive understanding of the adequacy of this or other similar measures.

Conclusion

This study showed a significant reduction of hospitalizations due to respiratory tract infections after the appearance of the new SARS-CoV-2 and the implementation of measures to reduce its transmission. Our data also showed there was no peak in hospital admissions for respiratory infections in the winter months of 2020-2021 in contrast to the previous two years. A dramatic reduction in respiratory infections by the remaining viruses was noted, specially RSV.

This allowed us to conclude that non-pharmacological measures were not only effective in the combat of COVID-19 pandemic but also in the combat of the transmission of other viruses, having direct impact in reducing pediatric hospitalization for respiratory infections.

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Figures and Tables

FIGURE 1

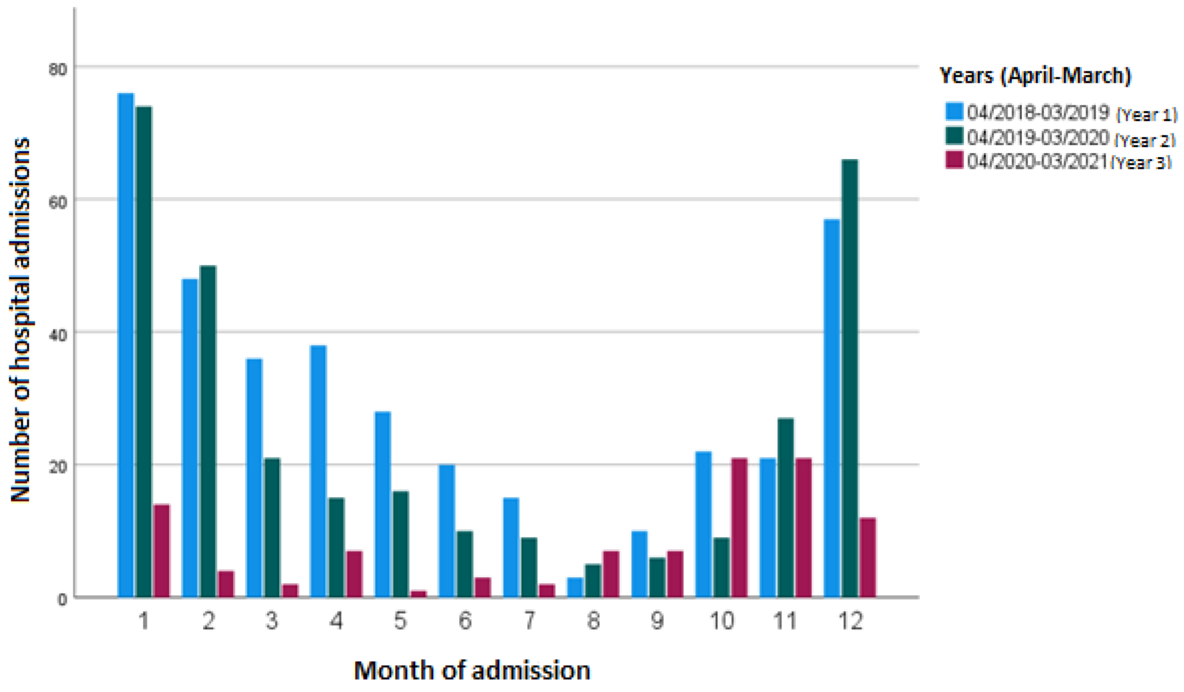

Figure 1 – Number of hospital admissions per month, in each year analysed (April to March)

FIGURE 2

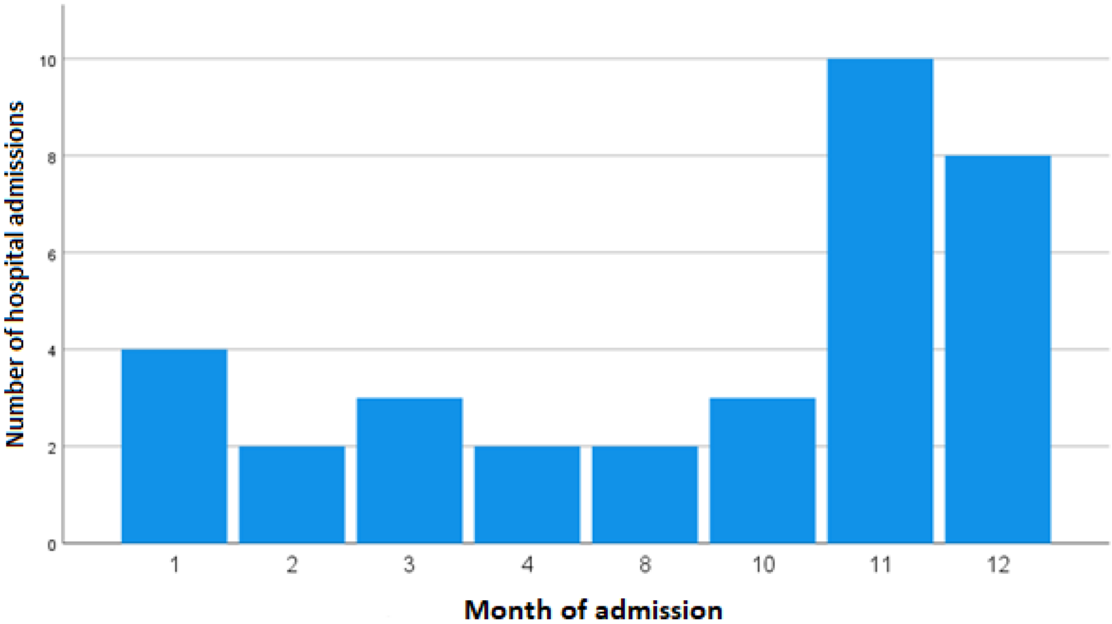

Figure 2 – Number of hospital admissions with SARS-CoV2, per month.

TABLE I

Table I - Classification of Upper and Lower Respiratory Tract Infections Based on the International Classification of Diseases, 10th Revision (ICD-10)

Upper Respiratory Tract Infections		**Lower Respiratory Tract Infections**	
ICD-10	Class	ICD-10	Class
J00	Acute nasopharyngitis (common cold)	J12	Viral pneumonia, not elsewhere classified
J01	Acute sinusitis	J12.81	Pneumonia due to SARS-associated coronavirus
J02	Acute pharyngitis	J13	Pneumonia caused by *Streptococcus pneumoniae*
J03	Acute tonsillitis	J14	Pneumonia caused by *Haemophilus influenzae*
J04	Acute laryngitis and tracheitis	J15	Bacterial pneumonia, not elsewhere classified
J05	Acute obstructive laryngitis (croup) and epiglottitis	J16	Pneumonia due to other infectious organisms, not elsewhere classified
J06	Acute upper respiratory infections of multiple and unspecified sites	J17	Pneumonia in diseases classified elsewhere
H66	Suppurative and unspecified otitis media	J18	Pneumonia, organism unspecified
		J20	Acute bronchitis
		J21	Acute bronchiolitis
		J22	Unspecified acute lower respiratory infection
		A15	Respiratory tuberculosis
		A37	Whooping cough
		R06.2	Wheezing
		M35.81	Multisystem inflammatory syndrome
J09 Influenza			
J10 Influenza due to identified influenza virus			
J11 Influenza, virus not identified			

TABLE II

Table II – Participants characteristics.

	04/2018 - 03/2019	04/2019 - 03/2020	04/2020 - 03/2021	TOTAL
Total admissions	374 (47.8)	308 (39.3)	101 (12.9)*	783
Gender, n (%)				
Female	162 (43.3)	127 (41.2)	46 (45.5)	335 (42.8)
Male	212 (56.7)	181 (58.8)	55 (54.5)	448 (57.2)
Age (months)				
Median (SD)	10 (38)	5 (42)	20 (69)*	8 (46)
Age groups, n(%)				
[0-6[months	148 (39.6)	159 (51.6)	26 (25.7)	333 (42.5)
[6-12[months	61 (16.3)	49 (15.6)	15 (14.9)	124 (15.8)
[12-24[months	61 (16.3)	36 (11.7)	13 (12.9)	110 (14.0)
[2-6[years	74 (19.8)	35 (11.4)	22 (21.8)	131 (16.7)
[6-10[years	7 (1.9)	9 (2.9)	5 (5.0)	21 (2.7)
[10-18[years	23 (6.1)	21 (6.8)	20 (19.8)	64 (8.2)
Length-of-stay (days)				
Median (SD)	5 (6)	5 (7)	5 (6)	5 (7)
Diagnosis groups, n (%)			#	
URTI	46 (12.3)	35 (11.4)	4 (4.0)	85 (10.9)
LRTI	313 (83.7)	261 (84.7)	96 (95.0)	670 (85.6)
Influenza	15 (4.0)	12 (3.9)	1 (1.0)	28 (3.6)
Specific diagnosis, n (%)				
Acute otitis media	13 (3.5)	1 (0.3)	0 (0.0)	14 (1.8)
Nasopharyngitis	23 (6.1)	27 (8.8)	3 (3.0)	53 (6.8)
Pharyngitis/Tonsilitis	7 (1.9)	6 (1.9)	1 (1.0)	14 (1.8)
Laringitis/Croup	4 (1.1)	1 (0.3)	0 (0.0)	5 (0.6)
Bronchitis	2 (0.5)	2 (0.6)	0 (0.0)	4 (0.5)
Bronchiolitis	210 (56.1)	185 (60.1)	35 (34.7)*	430 (54.9)
Pneumonia	115 (30.7)	83 (26.9)	61 (60.4)*	259 (33.1)
Whooping cough	0 (0.0)	3 (1.0)	1 (1.0)	4 (0.5)

*p<0.001, for differences between 04/2020-03/2021 and the previous years

#p=0.015, for differences of diagnosis groups proportion between 04/2020-03/2021 and the previous years

TABLE III

Table III – Clinical characteristics.

	04/2018 - 03/2019	04/2019 - 03/2020	04/2020 - 03/2021	TOTAL
Days of illness before admission, median (SD)	3 (5)	3 (4)	3 (5)	3 (4)
Clinical presentation, n (%)				
Cough	304 (81.3)	256 (83.1)	66 (65.3)*	628 (79.8)
Rhinorrhea	217 (58.0)	227 (73.7)	57 (56.4)	504 (64.0)
Dyspnea	155 (41.4)	160 (51.9)	47 (46.5)	365 (46.4)
Vomits	55 (14.7)	74 (24.0)	30 (29.7)[+]	160 (20.3)
Diarrhea	20 (5.3)	18 (5.8)	16 (15.8)*	55 (7.0)
Abdominal pain	5 (1.3)	12 (3.9)	8 (7.9)[#]	25 (3.2)
Respiratory distress	284 (75.9)	231 (75.0)	56 (54.5)*	573 (72.8)
Fever	241 (64.4)	189 (61.6)	60 (59.4)	492 (62.6)
Hypoxemia	215 (57.5)	191 (62.0)	48 (47.5)[¥]	458 (58.2)

*p<0.001; [+]p=0.012; [#]p=0.004; [¥]p=0.022

TABLE IV

Table IV – Workup and treatment performed.

	04/2018 - 03/2019	04/2019 - 03/2020	04/2020 - 03/2021	TOTAL
Microbiology, n (%)				
Viral Nasopharyngeal	292 (78.1)	267 (86.7)	56 (55.4)*	615 (78.5)
Blood culture	147 (39.3)	107 (34.7)	52 (51.5)¥	306 (39.1)
Sputum microbiology	84 (22.5)	68 (22.1)	18 (17.8)	170 (21.7)
SARS-CoV2 PCR	0 (0)	9 (2.9)	100 (99.0)*	109 (13.9)
Blood, n (%)				
Hemogram	224 (59.9)	197 (64.0)	82 (81.2)*	503 (64.2)
Biochemical	220 (58.8)	195 (63.3)	82 (81.2)*	497 (63.5)
Chest image, n (%)				
X-ray	201 (53.7)	176 (57.1)	64 (63.4)	441 (56.3)
CT scan	14 (3.7)	8 (5.6)	11 (10.9)*	33 (4.2)
Treatments, n (%)				
Supplemental O_2	229 (61.4)	192 (62.3)	50 (49.5)#	471 (60.2)
Inhaled β-agonists	186 (49.7)	140 (45.5)	38 (37.6)	364 (46.5)
Inhaled steroids	97 (25.9)	60 (19.5)	25 (24.8)	182 (23.2)
Systemic steroids	119 (31.8)	81 (26.3)	41 (40.6)+	241 (30.8)
Antibiotics	150 (40.1)	120 (39.0)	46 (45.5)	316 (40.4)
Antiviral	23 (6.1)	29 (9.4)	2 (2.0)++	54 (6.9)

*p<0.001; ¥p=0.022; #p=0.018; +p=0.023; ++p=0.037

TABLE V

Table V – Identified virus and bacteria.

	04/2018 - 03/2019	04/2019 - 03/2020	04/2020 - 03/2021	TOTAL
Virus, n (%)	251 (67.1)	236 (76.6)	57 (56.4)*	544 (69.5)
VSR	131 (35.0)	144 (46.8)	2 (2.0)*	277 (35.4)
Rhinovirus	64 (17.1)	47 (15.3)	23 (22.8)*	134 (17.1)
Influenza	23 (6.1)	26 (8.4)	1 (1.0)	50 (6.4)
Adenovirus	22 (5.9)	15 (4.9)	5 (5.0)	42 (5.4)
Enterovirus	20 (5.3)	19 (6.2)	2 (2.0)	41 (5.2)
Parainfluenza	21 (5.6)	15 (4.9)	1 (1.0)	37 (4.7)
Metapneumovirus	18 (4.8)	18 (5.8)	0 (0.0) ¥	36 (4.6)
Bocavirus	21 (5.6)	13 (4.2)	0 (0.0)	34 (4.3)
Coronavirus	10 (2.7)	1 (0.3)	1 (1.0)	12 (1.5)
CMV	1 (0.3)	4 (1.3)	0 (0.0)	5 (0.6)
EBV	1 (0.3)	1 (0.3)	0 (0.0)	2 (0.3)
SARS-Cov2	0 (0.0)	2 (0.6)	32 (31.7)*	34 (4.3)
Bacteria, n (%)	39 (10.4)	22 (7.1)	5 (5.0)#	66 (8.4)
Haemophilus influenzae	5 (1.3)	6 (1.9)	0 (0.0)	11 (1.4)
Streptococcus pneumoniae	4 (1.1)	3 (1.0)	0 (0.0)	7 (0.9)
Pseudomonas aeruginosa	4 (1.1)	2 (0.6)	1 (1.0)	7 (0.9)
Staphylococcus aureus	2 (0.5)	1 (0.3)	2 (2.0)	5 (0.6)
Moraxella catharralis	2 (0.5)	3 (1.0)	0 (0.0)	5 (0.6)
Mycoplasma pneumoniae	3 (0.8)	1 (0.3)	0 (0.0)	4 (0.5)
Mycobacterium tuberculosis	3 (0.8)	1 (0.3)	0 (0.0)	4 (0.5)
Klebsiella pneumoniae	2 (0.5)	1 (0.3)	0 (0.0)	3 (0.4)
Staphylococcus epidermidis	3 (0.8)	0 (0.0)	0 (0.0)	3 (0.4)
Staphylococcus coagulase -	3 (0.8)	0 (0.0)	0 (0.0)	3 (0.4)
Staphylococcus capitis	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.3)
MRSA	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.3)
Escherichia coli	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.3)
Bordetella pertussis	0 (0.0)	1 (0.3)	1 (1.0)	2 (0.3)
Klebsiella oxytoca	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.1)
Acinetobacter baumanii	0 (0.0)	0 (0.0)	1 (1.0)	1 (0.1)
Bordetella parapertussis	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.1)
Serratia marcescens	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)
Cupriavidus	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)

*p<0.001; #p=0.013; ¥p=0.039