


RESEARCH ARTICLE

Epidemiological and clinical profile of viral respiratory infections in children under 5 years at pre- and post-COVID-19 era in Praia, Cabo Verde

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Abstract

Background: The coronavirus disease-19 (COVID-19) pandemic has affected global health, influencing the prevalence of different respiratory pathogens. The aim of this study is to evaluate the distribution of agents causing acute respiratory infections in children under 5 years old before and after the COVID-19 pandemic in Praia, Cabo Verde, and to describe associated clinical variables.

Methods: Conducted at the University Hospital Dr. Agostinho Neto, this study replicated methods from a previous work from 2019 (Correia et al. 2021). Nasopharyngeal samples were analysed using FilmArray[®] Respiratory Panel 2.1 (BioFire) to identify agents of acute respiratory infections. Molecular identification of human respiratory syncytial virus subtypes was performed using a real-time duplex reverse transcription polymerase chain reaction. Statistical analysis was performed using IBM SPSS version 29 and R 3.5.1 software.

Results: In 2022, 86.5% (83/96) of nasopharyngeal samples were positive for at least one pathogen. Human rhinovirus/human enterovirus was the most frequent agent, followed by human respiratory syncytial virus, adenovirus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Co-infections were observed in 43.3% of positive cases. Infection rates were significantly higher in children under 1 year of age, particularly for SARS-CoV-2 and human respiratory syncytial virus. Seasonal variations were observed, with human respiratory syncytial virus predominating in November, SARS-CoV-2 in January and human parainfluenza virus-4 in May. Molecular analysis of human respiratory syncytial virus revealed a shift in subtype prevalence, with both human respiratory syncytial virus-A and -B co-circulating in the pre-pandemic period, whereas only human respiratory syncytial virus-B was detected in the post-pandemic period.

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Conclusion: Our data indicate changes in the distribution of respiratory viruses in the post-pandemic period compared to pre-pandemic period. The high prevalence of co-infections highlights the complexity of acute respiratory infection aetiology, emphasising the need for enhanced respiratory virus surveillance systems in Cabo Verde. Identifying seasonal trends and risk factors can contribute to targeted interventions and improved public health strategies to mitigate the burden of acute respiratory infections in young children.

KEYWORDS

acute respiratory infections, ARI surveillance, Cabo Verde, children, COVID-19 pandemic, hRSV, paediatric infectious diseases

INTRODUCTION

While the coronavirus disease-19 (COVID-19) pandemic continues to pose global health challenges, other viral infections also affect millions of people, causing an estimated 4 million deaths annually [1, 2]. Non-pharmaceutical interventions (NPIs) implemented to hinder COVID-19 spread have affected the transmission of other respiratory pathogens [3, 4]. In Cabo Verde, governmental policies, societal collaboration and international support have helped manage the pandemic's impact, with the country reporting 64,109 COVID-19 cases, 63,591 recoveries and 414 fatalities until 2024. These numbers correspond to a mortality rate of ~0.65%, highlighting the substantial impact of the COVID-19 pandemic on the country [5].

Studies suggest that strict NPIs influenced the transmission and seasonal circulation of respiratory pathogens, such as influenza (Flu) and human respiratory syncytial virus (hRSV), particularly after the relaxation of restrictions in 2021 [6–9]. Notably, there has been a significant global reduction in hRSV cases since March 2020 [10–12]. Globally, hRSV is recognised for causing severe infections, particularly in children under 5 years old [13–17]. The two antigenic groups, hRSV-A and hRSV-B, generally co-circulate with a switch of the predominant subtype every 2–3 years. Epidemiological surveillance of hRSV genotypes is vital due to the potential long-term impact of genetic variations on the effectiveness of preventive interventions like Nirsevimab against severe infections [9, 13, 14, 18–21].

This study aims to evaluate and compare the distribution of pathogens responsible for acute respiratory infections (ARI) in children under 5 years of age, pre- and post-COVID-19 pandemic, the associated clinical variables and describe molecular characteristics of hRSV in the two study periods. In a previous study conducted in 2019, we identified the pathogens causing ARI at different periods of the year [22]. In 2022, 2 years after the onset of the pandemic, we repeated the study to assess potential changes in the prevalence and diversity of ARI pathogens in our population. This comparison seeks to understand the pandemic's impact on the epidemiological distribution of common respiratory viruses, providing useful information for disease prevention and control at local and regional levels.

MATERIALS AND METHODS

We gathered cross-sectional data in January, May and November 2022 from children under 5 years old who attended the paediatrics' emergency at University Hospital Dr. Agostinho Neto (UHAN) in Praia with suspicion of ARI. In order to participate in the study, children had to be identified by healthcare providers. Children were included in this study only after a thorough explanation of the study's purpose to their guardians/parents. Following this, if informed consent was obtained, a biological sample and a questionnaire with socio-demographic and clinical data were collected. Naso-pharyngeal swabs (NPS) were collected in Viral Transport Medium (VTM) (Delta lab, Barcelona, Spain), stored at -80°C and afterwards transported to the laboratory of the Instituto Universitario de Enfermedades Tropicales y Salud Pública de Canarias, Universidad de La Laguna (IUETSPC-ULL) in Tenerife, Spain. The exclusion/inclusion criteria for this study were defined according to those described by Fitzner et al., 2018 [23]. Inclusion criteria were children under 5 years of age, of both sexes, who exhibited at least three typical symptoms of ARI, such as nasal obstruction, cough, headache, chest pain, difficulty breathing, conjunctivitis and/or fever $\geq 38^{\circ}\text{C}$, with symptom onset occurring between 3 and 7 days before seeking medical attention and without any symptomatic or antibiotic treatment for ARI prior to inclusion. Exclusion criteria encompassed children with severe illnesses and those in critical or terminal conditions, whose health status could interfere with the accurate assessment of study outcomes.

To ensure consistency and comparability, we replicated the study periods (January, May and November) and methods from Correia et al. (2021) [22], as well as the same health structure (UHAN). Sociodemographic data were also collected using identical questionnaires. The same criteria and techniques were used for processing NPS, employing FilmArray[®] Respiratory Panel 2.1 (FARP 2.1 BioFire Diagnostics LLC 390; Wakara Way, Salt Lake City, UT, USA). FARP 2.1 is a multiplex polymerase chain reaction (PCR) assay that detects a wide range of respiratory pathogens, including viruses and bacteria (full list in the legend of Table 1).

A molecular identification study of hRSV was also carried out, using the samples collected in 2019 (pre-pandemic)

TABLE 1 Frequency (%) of the respiratory pathogens by age, sex, study period and geographic areas in Praia, during 2022.

Pathogen	Prevalence's			Age, +/n (%)			Sex, +/n (%)			Study period, +/n (%)			Geographic areas in Praia, +/n (%)						
	+/n (%)	(95% CI)	Sig.	<1 year	1-4 years	Sig.	Female	Male	Sig.	January	May	November	Sig.	North	West	South	East	Other	Sig.
HRV/HEV	40/96 (41.7)	(31.7–52.2)	n.s.	25/58 (43.1)	15/38 (39.5)	n.s.	21/52 (40.4)	19/44 (43.2)	n.s.	12/30 (40.0)	13/30 (43.3)	15/36 (41.7)	n.s.	6/25 (24.0)	6/12 (50.0)	14/26 (53.9)	11/18 (61.1)	3/15 (20.0)	0.02
hRSV	21/96 (21.9)	(14.1–31.5)	n.s.	16/58 (27.6)	5/38 (13.2)	n.s.	10/52 (19.2)	11/44 (25.0)	n.s.	2/30 (6.7)	0/30 (0.0)	19/36 (52.8)	<0.00	7/25 (28.0)	1/12 (8.3)	3/26 (11.5)	4/18 (22.2)	6/15 (40.0)	n.s.
Adv	15/96 (15.6)	(9.0–24.4)	n.s.	7/58 (12.1)	8/38 (21.1)	n.s.	8/52 (15.4)	7/44 (15.9)	n.s.	6/30 (20.0)	1/30 (3.3)	8/36 (22.2)	n.s.	3/25 (12.0)	0/12 (0.0)	3/26 (11.5)	5/18 (27.8)	4/15 (26.7)	n.s.
SARS-CoV-2	14/96 (14.6)	(8.2–23.3)	n.s.	12/58 (20.7)	2/38 (5.3)	n.s.	5/52 (9.6)	9/44 (20.5)	n.s.	10/30 (33.3)	1/30 (3.3)	3/36 (8.3)	<0.01	3/25 (12.0)	3/12 (25.0)	3/26 (11.5)	5/18 (27.8)	0/15 (0.0)	n.s.
hMPV	9/96 (9.4)	(4.4–17.1)	n.s.	5/58 (8.6)	4/38 (10.5)	n.s.	7/52 (13.5)	2/44 (4.5)	n.s.	3/30 (10.0)	2/30 (6.7)	4/36 (11.1)	n.s.	0/25 (0.0)	3/12 (25.0)	3/26 (11.5)	1/18 (5.6)	2/15 (13.3)	n.s.
PIV 3	8/96 (8.3)	(3.7–15.8)	n.s.	5/58 (8.6)	3/38 (7.9)	n.s.	7/52 (13.5)	1/44 (2.3)	n.s.	2/30 (6.7)	5/30 (16.7)	1/36 (2.8)	n.s.	1/25 (4.0)	2/12 (16.7)	2/26 (7.7)	2/18 (11.1)	1/15 (6.7)	n.s.
PIV 4	5/96 (5.2)	(1.7–11.7)	n.s.	2/58 (3.4)	3/38 (7.9)	n.s.	5/52 (9.6)	0/44 (0.0)	n.s.	0/30 (0.0)	5/30 (16.7)	0/36 (0.0)	<0.01	2/25 (8.0)	0/12 (0.0)	3/26 (11.5)	0/18 (0.0)	0/15 (0.0)	n.s.
CoV NL63	4/96 (4.2)	(1.1–10.3)	n.s.	2/58 (3.4)	2/38 (5.3)	n.s.	3/52 (5.8)	1/44 (2.3)	n.s.	0/30 (0.0)	3/30 (10.0)	1/36 (2.8)	n.s.	1/25 (4.0)	0/12 (0.0)	0/26 (0.0)	2/18 (11.1)	1/15 (6.7)	n.s.
CoV OC43	3/96 (3.1)	(0.6–8.9)	n.s.	2/58 (3.4)	1/38 (2.6)	n.s.	3/52 (5.8)	0/44 (0.0)	n.s.	0/30 (0.0)	0/30 (0.0)	3/36 (8.3)	n.s.	1/25 (4.0)	0/12 (0.0)	0/26 (0.0)	1/18 (5.6)	1/15 (6.7)	n.s.
CoV HKU1	2/96 (2.1)	(0.3–7.3)	n.s.	2/58 (3.4)	0/38 (0.0)	n.s.	0/52 (0.0)	2/44 (4.5)	n.s.	2/30 (6.7)	0/30 (0.0)	0/36 (0.0)	n.s.	1/25 (4.0)	0/12 (0.0)	1/26 (3.9)	0/18 (0.0)	0/15 (0.0)	n.s.
FluA H12009	2/96 (2.1)	(0.3–7.3)	n.s.	1/58 (1.7)	1/38 (2.6)	n.s.	2/52 (3.8)	0/44 (0.0)	n.s.	2/30 (6.7)	0/30 (0.0)	0/36 (0.0)	n.s.	0/25 (0.0)	0/12 (0.0)	1/26 (3.9)	0/18 (0.0)	1/15 (6.7)	n.s.
C. pneumoniae	1/96 (1.0)	(0.0–5.7)	n.s.	0/58 (1.7)	1/38 (2.6)	n.s.	0/52 (0.0)	1/44 (2.3)	n.s.	1/30 (3.3)	0/30 (0.0)	0/36 (0.0)	n.s.	0/25 (3.2)	0/12 (4.5)	0/26 (2.3)	0/18 (0.0)	1/15 (6.7)	n.s.
PIV 1	1/96 (1.0)	(0.0–5.7)	n.s.	0/58 (0.0)	1/38 (2.6)	n.s.	1/52 (1.9)	0/44 (0.0)	n.s.	0/30 (2.9)	1/30 (3.3)	0/36 (0.0)	n.s.	0/25 (0.0)	0/12 (0.0)	1/26 (3.9)	0/18 (0.0)	0/15 (0.0)	n.s.
PIV 2	1/96 (1.0)	(0.0–5.7)	n.s.	0/58 (0.0)	1/38 (2.6)	n.s.	0/52 (0.0)	1/44 (2.3)	n.s.	0/30 (0.0)	1/30 (3.3)	0/36 (0.0)	n.s.	1/25 (4.0)	0/12 (0.0)	0/26 (0.0)	0/18 (0.0)	0/15 (0.0)	n.s.
≥1 pathogen	83/96 (86.5)	(78.0–92.6)	0.04	54/58 (93.1)	29/38 (76.3)	0.04	46/52 (88.5)	37/44 (84.1)	n.s.	25/30 (83.3)	22/30 (73.3)	36/36 (100.0)	<0.01	19/25 (76.0)	11/12 (91.7)	22/26 (84.6)	17/18 (94.4)	14/15 (93.3)	n.s.

Note: Positive cases and total samples are expressed as +/n (%). Sig. indicates statistical significance in the comparison of prevalence between groups. Non-significant differences are marked as n.s. (not significant). 95% CI represents the confidence interval for the prevalence of each pathogen with 95% certainty.

Abbreviations: Adv, adenovirus; C. pneumoniae, Chlamydia pneumoniae; hMPV, human metapneumovirus; hRSV, human respiratory syncytial virus; FluA H1 2009, influenza A H1 2009; PIV 1, parainfluenza virus 1; PIV 2, parainfluenza virus 2; PIV 3, parainfluenza virus 3; PIV 4, parainfluenza virus 4.

and 2022 (post-pandemic) in order to obtain a comprehensive assessment of the circulation of hRSV subtypes. For this, viral RNA was purified using QIAamp Viral RNA Mini Kit (Qiagen, Germany), following the supplier's instructions. To identify the hRSV subtype, a real-time duplex reverse transcription polymerase chain reaction (RT-PCR) was employed as proposed by Todd et al. (2021) [24]. To ensure the accuracy of hRSV subtyping and minimise false results, we tested all collected samples, including the negative ones according to FARP testing, those previously positive for other respiratory viruses and those with co-infections involving hRSV. As positive controls, AMPLIRUN® RESPIRATORY SYNCYTIAL VIRUS RNA CONTROL (Subtype A and B) and AMPLIRUN® TOTAL RESPIRATORY VIRAL PANEL CONTROL (VIRCELL Microbiologists) were used, and also RNase-, DNase- and protease-free water were used in negative controls.

Statistical analysis was performed using IBM SPSS (version 29) and R (version 3.5.1). Continuous variables were presented as means and standard deviations (\pm SD), while categorical variables were expressed as proportions with 95% Clopper–Pearson confidence intervals (CI). To evaluate the association between the presence of pathogens and certain sociodemographic variables, the Chi-square test, the Fisher exact test or the Fisher–Freeman–Halton exact test were applied, as appropriate. A logistic regression model was applied to determine which sociodemographic variables were associated with the presence of ARI. First, an association study was conducted between each variable and ARI, identifying the variables to be included in the multivariate logistic regression model. Crude odds ratios (COR) with 95% CI were obtained by fitting a univariate logistic regression model for each variable identified in the previous analysis and the response variable (ARI). Finally, a multivariate logistic regression model was applied using stepwise techniques to study the association between all predictor variables and the outcome variable (ARI), obtaining adjusted odds ratios (AOR) with 95% CI. The Hosmer–Lemeshow goodness-of-fit test was used to assess the fit of the models. Statistical significance was set at 0.05 for all tests.

RESULTS

Up to 96 NPS were collected and analysed during the three study periods in 2022. Their demographic characteristics are described in Supplementary Table S1. According to clinical signs and symptoms, most patients presented with cough (96.9%), nasal obstruction (91.7%) and fever $\geq 38^{\circ}\text{C}$ (67.7%). A total of 56.3% of patients exhibited first symptoms 6–7 days before attending UHAN, 34.4% at 3–5 days and 9.4% presented first symptoms 1–2 days before seeking medical attention (Supplementary Table S2).

Of the NPS examined, 83/96 tested positive for one or more of the pathogens detected in FARP 2.1. HRV/HEV was identified as the most prevalent respiratory pathogen (41.7%), followed by hRSV (21.9%), Adv (15.6%) and SARS-

CoV-2 (14.6%) (Table 1). Detection rates for the remaining pathogens tested were below 10%. Among positive samples, a single respiratory pathogen was detected in 56.6%, while multiple pathogens were identified in 43.4%. These often included combinations of HRV/HEV, Adv, SARS-CoV-2 or hRSV with a different infectious agent, with the most common combination being HRV/HEV+hRSV (11.1%) (Supplementary Table S3). The coexistence of two respiratory pathogens accounted for 80.5% of the cases of co-infection, while coinfection with three pathogens represented 11.1% (Supplementary Table S3). Interestingly, one sample exhibited up to five different pathogens (Adv+HRV/HEV+SARSCoV-2+hMPV+hRSV) (Supplementary Table S3).

For data analysis, the children were stratified into two age groups: under 1 year (0–11 months) and aged 1–4 years (12–59 months). The distribution of pathogens was generally comparable between both age groups throughout the study periods in 2022 (Table 1). However, analysis of the infection rate (any pathogen detected) by age revealed a statistically significant difference, indicating a higher prevalence of respiratory infections among infants under 1 year compared to children aged 1–4 years ($p = 0.04$) (Table 1). This difference suggests that infants are more susceptible to the respiratory infections detected by the diagnostic panel used in the study. It is noteworthy that a considerable proportion of positive cases for SARS-CoV-2 (20.7%) and hRSV (27.6%) were observed in children < 1 year of age, as opposed to children aged 1–4 years (5.3% and 13.2% respectively), although no statistically significant differences were observed. Similarly, no statistically significant differences were observed in infection rates between boys and girls during the 2022 study periods (Table 1).

When analysing the overall infection rates across the study months, a significant difference in positive cases was observed ($p < 0.01$). November had the highest prevalence of respiratory infections caused by pathogens detectable with FARP 2.1, compared to other months (Table 1). Among the 14 detected pathogens, three exhibited statistically significant differences across the three sampling periods: SARS-CoV-2 was the most prevalent in January, PIV 4 most frequently found in May and hRSV was predominant in November (Table 1).

For all patients, epidemiological and sociodemographic data were compiled. To analyse the association with ARI, we compared the proportion of children with each potential risk factor between ARI-positive and ARI-negative groups (Table 2). Variables such as age, number of children under 5 years old sleeping in the same room with an adult, household crowding, presence of domestic animals and method of garbage treatment exhibited $p < 0.2$ and were included in the multivariable logistic regression model.

Factors associated with ARI were identified using forward stepwise binary logistic regression models, yielding a model that explained 23.5% of the variation in prevalence (Nagelkerke's $R^2 = 0.235$). A significant association was observed between ARI and the number of children under

TABLE 2 Risk factors associated with ARI in children under 5 years of age included in the study.

	Risk factors	ARI negative –/n (%)	ARI positive +/n (%)	COR (95% CI)	p-value	AOR (95% CI)
Month	January	5/30 (16.7)	25/30 (83.3)			
	May	8/30 (26.7)	22/30 (73.3)	0.5 (0.16–1.93)	0.35	
	November	0/36 (0.0)	36/36 (100.0)	n/a	0.99	
Age	<1	4/58 (6.9)	54/58 (93.1)			
	1–4	9/38 (23.7)	29/38 (76.3)	0.23 (0.06; 0.84)	0.02	
No. of children <5 years old that sleep with an adult	0 children	2/3 (66.7)	1/3 (33.3)			
	1 child	9/65 (13.8)	56/65 (86.2)	12.44 (1.02; 151.83)	0.04	16.27 (1.26; 208.82)*
	>1 children	2/28 (7.1)	26/28 (92.9)	26.00 (1.58; 426.84)	0.02	29.46 (1.65; 524.34)*
Household crowding	<4	5/27 (18.5)	22/27 (81.5)		0.23	
	4–5	3/44 (6.8)	41/44 (93.2)	3.10 (0.67; 14.23)	0.14	
	>5	5/25 (20.0)	20/25 (80.0)	0.90 (0.22; 3.61)	0.89	
Presence of domestic animals	No	6/64 (9.4)	58/64 (90.6)			
	Yes	7/32 (21.9)	25/32 (78.1)	2.70 (0.82; 8.87)	0.10	
Method of treating garbage	Container	7/75 (9.3)	68/75 (90.7)			
	Collection truck	3/16 (18.8)	13/16 (81.3)	0.44 (0.10; 1.95)	0.28	0.54 (0.10; 2.67)
	Burning	3/5 (60.0)	2/5 (40.0)	0.06 (0.01; 0.48)	<0.01	0.06 (0.01; 0.44)**

Abbreviations: AOR, adjusted odds ratio; COR, crude odds ratio; n/a, not applicable.

* $p < 0.05$; ** $p < 0.01$.

5 years old sharing a bedroom with an adult: compared to households where no children under 5 years sleep with an adult, the AOR was 16.27 for one child (95% CI: 1.26; 208.82) and 29.46 for more than one child (95% CI: 1.65; 524.34) (Table 2). The AOR of ARI caused by detectable pathogens decreased with garbage collection by truck (AOR: 0.54, 95% CI: 0.10; 2.67) and burning garbage (AOR: 0.06, 95% CI: 0.01; 0.44) compared to using containers (Table 2).

For the molecular characterisation of hRSV, 244 nasopharyngeal swabs, that is, the 96 from 2022 described in this study plus the 148 collected in 2019 [22] were analysed using the subtype identification assay described by Todd et al. (2021). Our results show that 37 samples were positive, 16 from 2019 and 21 collected in 2022. Both hRSV subtypes (A and B) were identified, with different prevalence across the years (Table 3). In the pre-pandemic period, both subtypes co-circulated, with hRSV-A accounting for 62.5% of the positive samples and hRSV-B for 37.5%. However, in the post-pandemic period, only subtype B was identified, comprising 100% (21/21) of the positive samples.

The prevalence of both subtypes was notable in November compared to other months, but the differences were not statistically significant (Table 3). There were no statistically significant differences when we analysed hRSV-A or hRSV-B positive cases according to age group or sex (Table 3).

DISCUSSION

Strict preventive COVID-19 interventions like mask-wearing and social distancing reduced SARS-CoV-2 transmission and

TABLE 3 Distribution of hRSV subtypes by year, month, age and sex.

Factor		hRSV-A, +/n (%)	Sig.	hRSV-B, +/n (%)	Sig.
Years	2019	10/16 (62.5)	<0.001	6/16 (37.5)	<0.001
	2022	0/21 (0.0)		21/21 (100.0)	
Month	January	0/2 (0.0)	n.s.	2/2 (100.0)	n.s.
	May	0/1 (0.0)		1/1 (100.0)	
	November	10/34 (29.4)		24/34 (70.6)	
Age	<1	4/23 (17.4)	n.s.	19/23 (82.6)	n.s.
	1–4	6/14 (42.9)		8/14 (57.1)	
Sex	Female	6/21 (28.6)	n.s.	15/21 (71.4)	n.s.
	Male	4/16 (25.0)		12/16 (75.0)	

Note: Positive cases and total samples are expressed as +/n (%). Sig. indicates statistical significance in the comparison of prevalence between groups ($p < 0.001$). Non-significant differences are marked as n.s. (not significant).

Abbreviations: hRSV-A, human respiratory syncytial virus subtype A; hRSV-B, human respiratory syncytial virus subtype B.

altered the prevalence of other respiratory pathogens [25, 26]. Therefore, with the transition to the post-pandemic era, understanding the impact caused by this situation on the transmission of other respiratory pathogens remains crucial for effective healthcare planning and resource allocation [27].

The data generated in this study complements previous work performed in 2019 by our research group, revealing the etiological aspects of respiratory viral infections in children under 5 years old seeking medical attention for ARI at HUAN. Three years and one COVID-19 pandemic after the first study, our data revealed no variation in the prevalence

of ARI among children under 5 years at UHAN, although the distribution of etiological agents presents some differences [4, 22, 28, 29]. Several authors have hypothesised that the increased incidence of ARI in children post-pandemic may be due to limited exposure to respiratory viruses during the COVID-19 pandemic, which weakened their immune systems [30, 31]. This reduced immunity, combined with the persistence of certain viruses (e.g., HRV/HEV and Adv) and the introduction of SARS-CoV2 as a new etiological agent, may have contributed to the sustained high prevalence of ARI [32, 33]. Additionally, crowded schools and daycare centres likely played a significant role in the pathogens' transmission, even with preventive measures in place [34].

Global changes in respiratory pathogen epidemiology due to the pandemic have been observed. Our study identified some variations in respiratory pathogen epidemiology in the context of Cabo Verde, compared to the pre-pandemic period, particularly in flu and hRSV cases, consistent with findings from China and Italy [9, 25, 35]. HRV/HEV and Adv cases showed slight increases, while other pathogens remained low. The reasons for these shifts are unclear but may involve pandemic restrictions and viral characteristics [36, 37]. Non-enveloped viruses like HRV/HEV and Adv are more resistant to disinfection, maintaining usual circulation levels despite NPIs [38]. In contrast, enveloped viruses such as Flu and hRSV, which are more susceptible to NPIs, were significantly affected. However, hRSV has seen an increase in cases, as documented by Fahim et al. (2023) [39]. This increase may be attributed to limited prior exposure, resulting in short-lived immunity and susceptibility upon re-emergence [39, 40]. Further research is needed to explore the impact of NPIs on children's respiratory pathogens.

Co-infections with respiratory pathogens increased in 2022 compared to prepandemic levels, with HRV/HEV remaining the most frequent pathogen in these cases. Paediatric patients, who are more susceptible due to immune fragility, are more likely to experience multiple infections [41–43]. However, the frequent recurrence of HRV/HEV in co-infections is still not well understood [44–46].

A statistically significant difference was observed in the prevalence of ARI between age groups, diverging from prepandemic findings. Studies consistently report a higher prevalence of ARI in children <1 year of age, likely due to the immaturity of their immune systems and the physiological vulnerability of this age group, which facilitates airway colonisation by pathogens and subsequent infection [47–49]. Several factors contribute to this increased susceptibility. Anatomically, infants have narrower airways and underdeveloped mucosal defences, which increase the risk of obstruction and pathogen invasion [50]. Additionally, exposure to respiratory pathogens in high-risk environments, such as daycare centres and overcrowded households, further exacerbates infection rates [51]. Conversely, the decline in ARI prevalence among children over 1 year may be attributed to the progressive maturation of the

immune system, which enhances the body's ability to mount effective immune responses against respiratory pathogens [14, 52].

Interestingly, hRSV and SARS-CoV-2 infections were more common in children <1 year than in those aged 1–4, although there were no statistically significant differences. However, it is important to consider that hRSV is one of the main causes of severe respiratory disease in children, such as bronchiolitis [15, 16], and SARS-CoV-2 is often asymptomatic in this age group, making them potential carriers of the virus [53]. These results emphasise the need for continuous surveillance and periodic assessments of children's health in order to adapt effective strategies for preventing and treating ARI in children, which require a responsive, evidence-driven approach.

Similar to what was observed in 2019, statistically significant differences in ARI prevalence were noted among study months, with November showing notably higher cases in children under 5 years [22]. Seasonal ARI variations are commonly linked to local climate factors like humidity, temperature and sunlight [54–57]. Located in sub-Saharan Africa, Cabo Verde experiences a warm, arid climate with distinct rainy (August–October) and dry (December–June) seasons. From November to March, the archipelago is shrouded in dense Saharan desert dust, potentially influencing ARI prevalence [58]. Additionally, the archipelago also hosts around 2 million international travellers annually, mainly from Europe during their winter months [58], a period that coincides with the highest incidence of ARI in the region [59, 60]. This situation may be influencing the observed seasonality of ARIs in Cabo Verde; however, more studies will be needed to reach any conclusion.

Of the pathogens that showed statistically significant seasonality in Cabo Verde in 2019 [22], only hRSV maintained this pattern according to study months in 2022, in line with some previously published studies [55, 59–61]. Other viruses such as SARSCoV-2 and PIV 4 showed a seasonal trend in 2022. Interestingly, our findings align with Cabo Verde Ministry of Health's 2022 epidemiological data, showing two peaks of SARSCoV-2 respiratory infections: one between January and February and another from May to July [5]. This suggests a correlation between virus spread and paediatric cases, highlighting children's susceptibility during COVID-19 outbreaks. Although often asymptomatic, more studies are needed to understand the dynamics of SARS-CoV-2 in the paediatric population, as they may act as carriers of the virus within the community [53].

Regarding Flu, during the 2019–2020 season, most influenza viruses in tropical areas were FluA (75%), mainly A (H1N1) pdm09, while FluB accounted for 24.8%, mostly B/Victoria lineage [62]. Our previous study [22] showed a different pattern in 2019: FluA (H3) was predominant, with only a few FluA H1-2009 and FluB detections throughout the year [22]. Again, the new results from 2022 do not align with WHO data, which showed FluA (H3) dominance in May and Flu B (Victoria) in November in the West Africa

region [63]. Only two samples were positive for FluA H1-2009 in January in our study, suggesting a temporal shift due to COVID-19 restrictions. However, further studies are necessary to enhance understanding of this infection's dynamics, supporting health policies aimed at improving children's well-being.

Furthermore, we identified an association between children under 5 years sharing a room with an adult as a risk factor for ARI [22]. While previous studies have not shown such an association, they have linked ARI with poor housing quality [64]. Surprisingly, burning as a garbage disposal method was negatively associated with ARI in children under 5 years of age, contradicting previous studies that linked smoke exposure with ARI [65–67]. Additional studies are needed to gain a deeper understanding of the sociodemographic factors affecting ARI prevalence in this vulnerable age group.

The COVID-19 pandemic has been associated with changes in the predominance of the hRSV subtype [37]. Our data revealed a clear subtype shift from hRSV-A dominance in 2019 to hRSV-B predominance in 2022, a pattern consistent with results from other regions of the world [68, 69]. However, post-pandemic Australia observed a resurgence of hRSV-A [70]. These shifts in subtype prevalence may be driven by immunological pressure, with prior infections and population immunity selectively influencing the circulating strains. hRSV is well-known for its ability to evade immune responses through genetic variability, especially in the G protein, which plays a crucial role in immune recognition by the host [71, 72]. This antigenic diversity allows certain subtypes to temporarily escape pre-existing immunity, facilitating their evasion from immune detection and neutralisation. Such mechanisms hinder both host defence and the development of effective vaccines [73, 74]. The relationship between hRSV subtype or genotype and clinical severity has been a subject of ongoing research, with studies yielding divergent results [74, 75]. Pierangeli et al. (2023) found that children under the age of 2 infected with hRSV-A in 2021–22 required less oxygen and intensive care than those infected with hRSV-B during the 2022–23 season [68]. In contrast, a large multicentre study in the United States involving children hospitalised between 2007 and 2010 reported no significant differences in clinical severity between hRSV-A and hRSV-B infections [76]. The reasons behind these variations in clinical outcomes remain unclear, and further studies are needed to elucidate the factors contributing to these discrepancies [75–77].

Cabo Verde has greatly improved vaccination coverage in its population since the early 2000 showing vaccination rates above 93% for most vaccine-preventable diseases, including pertussis, whose etiologic agent is the respiratory pathogen *Bordetella pertussis* [78, 79]. Similar to our results from the 2019 study, not a single case of pertussis infection was detected in our population, suggesting that the programme was functioning adequately at least until 2022.

CONCLUSION

The COVID-19 pandemic has influenced the profile of pathogens responsible for ARI in children under 5 years old at UHAN. While the diversity of circulating pathogens remained unchanged, the influenza virus was substantially affected, showing a significant decrease in cases. There was also an increase in co-infections compared to the pre-pandemic period, particularly the combination of HRV/HEV and hRSV. SARS-CoV-2 virus circulated widely among children under 5 years of age during this period. The number of children under 5 years old sharing a room with an adult remains a significant risk factor for ARI. Finally, the molecular characterisation of hRSV revealed a shift in the temporal distribution of hRSV subtypes, with subtype B becoming predominant in the post-pandemic period, while subtype A was more prevalent in 2019. This study highlights the urgent need for ongoing surveillance programmes for respiratory diseases, as well as the implementation of effective and efficient diagnostic methods to better understand pathogen dynamics within the population. The results also emphasise the importance of specific prevention and treatment strategies tailored to different types of infections, focusing on improving public health outcomes and optimising resource management in the fight against respiratory infections in children.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Original contributions from this study are available in the article and supplementary material. For further inquiries, please contact the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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