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Risk factors associated with poor outcomes in children with Severe Acute Respiratory Infection (SARI) in a state in the Brazilian Amazon

Fatores de risco associados a desfechos desfavoráveis em crianças com Síndrome Respiratória Aguda Grave (SRAG) em um estado da Amazônia brasileira

Factores de riesgo asociados a desenlaces desfavorables en niños con Síndrome Respiratoria Aguda Grave (SRAG) en un estado de la Amazonía brasileña

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ABSTRACT

Objective: To identify independent risk factors for death, need for mechanical ventilation, and prolonged hospitalization in children with severe acute respiratory infection (SARI). **Methods:** Data were analyzed from the National Health Information System of a state in the Brazilian Amazon, collected between May 2020 and May 2022. Univariate and multivariate Poisson regressions were applied to estimate adjusted relative risks (RR), with significance set at $p < 0.05$. Model calibration and discrimination were evaluated using the Hosmer-Lemeshow and Stukel tests, as well as ROC curves. **Results:** A total of 226 children were included, with a mortality rate of 14.2%. Death was associated with invasive mechanical ventilation (RR = 6.81), presence of comorbidities (RR = 2.25), and respiratory syncytial virus (RSV) infection (RR = 2.38). The need for mechanical ventilation was related to ICU admission (RR = 4.14), RSV infection (RR = 1.68), and influenza H3N2 infection (RR = 1.59). Prolonged hospitalization was associated with oxygen saturation < 95% (RR = 1.47), infection by other respiratory viruses (RR = 1.86), and H3N2 infection (RR = 1.67). **Conclusion:** It is concluded that respiratory viruses are important independent predictors of adverse outcomes in pediatric SARI cases.

Keywords: Hospitalized child, Severe Acute Respiratory Infection, Viral infections, Risk factors, Cohort studies.

RESUMO

Objetivo: Identificar fatores de risco independentes para óbito, necessidade de ventilação mecânica e internação prolongada em crianças com síndrome respiratória aguda grave (SRAG). **Métodos:** Foram analisados dados do Sistema Nacional de Informação em Saúde de um estado da Amazônia Brasileira, entre maio de 2020 e maio de 2022. Aplicaram-se regressões de Poisson univariadas e multivariadas para estimar riscos relativos ajustados (RR), com significância de $p < 0,05$. Avaliaram-se calibração e discriminação dos modelos pelos testes de Hosmer-Lemeshow, Stukel e curvas ROC. **Resultados:** Foram incluídas 226 crianças com mortalidade de 14,2%. O óbito associou-se à ventilação mecânica invasiva (RR = 6,81), presença de comorbidades (RR = 2,25) e infecção por vírus sincicial respiratório (VSR) (RR = 2,38). O uso de ventilação mecânica foi relacionado à admissão em UTI (RR = 4,14), infecção por VSR (RR = 1,68) e influenza H3N2 (RR = 1,59). Internações prolongadas associaram-se à saturação de oxigênio < 95% (RR = 1,47), infecção por outros vírus respiratórios (RR = 1,86) e H3N2 (RR = 1,67). **Conclusão:** Conclui-se que vírus respiratórios são importantes preditores de desfechos adversos em SRAG pediátrica.

Palavras-chave: Criança hospitalizada, Síndrome respiratória aguda grave, Infecções virais, Fatores de risco, Estudos de coorte.

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RESUMEN

Objetivo: Identificar los factores de riesgo independientes de muerte, necesidad de ventilación mecánica y hospitalización prolongada en niños con síndrome respiratoria aguda grave (SRAG). **Métodos:** Se analizaron datos del Sistema Nacional de Información en Salud de un estado de la Amazonia brasileña, entre mayo de 2020 y mayo de 2022. Se aplicaron regresiones de Poisson univariadas y multivariadas para estimar riesgos relativos ajustados (RR), con significancia de $p < 0.05$. La calibración y la discriminación de los modelos se evaluaron mediante las pruebas de Hosmer-Lemeshow, Stukel y curvas ROC. **Resultados:** Se incluyeron 226 niños, con una mortalidad del 14.2%. La muerte se asoció con ventilación mecánica invasiva (RR = 6.81), presencia de comorbilidades (RR = 2.25) e infección por virus sincitial respiratorio (VSR) (RR = 2.38). El uso de ventilación mecánica se relacionó con ingreso en UCI (RR = 4.14), infección por VSR (RR = 1.68) e influenza H3N2 (RR = 1.59). Las hospitalizaciones prolongadas se asociaron con saturación de oxígeno < 95% (RR = 1.47), infección por otros virus respiratorios (RR = 1.86) y H3N2 (RR = 1.67). **Conclusión:** Se concluye que los virus respiratorios son importantes predictores de desenlaces adversos en casos pediátricos de SRAG.

Palabras clave: Niño hospitalizado, Síndrome respiratoria aguda grave, Infecciones virales, Factores de riesgo, Estudios de cohorte.

INTRODUCTION

Acute viral respiratory infections (AVRI) in children under five years old are a major public health issue worldwide due to the high hospitalization and lethality rates (FRAZI R, et al., 2024; SUN, YP, et al., 2022). Since the onset of the COVID-19 pandemic, various epidemiological patterns of respiratory viruses have raised questions about transmission and prevention, justifying the continuous prevalence and monitoring (OLSEN SJ, et al., 2021). The most frequent etiological agents of AVRI in children are the respiratory syncytial virus (RSV), adenovirus, influenza A, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (DALLMEYER LK, et al.,2024; MOREIRA AL, et al., 2023; TAYLOR S, et al., 2017).

ARVIs can range from a flu-like syndrome (mild symptoms in the upper respiratory tract, fever, chills, sore throat, runny nose, headache, and olfactory or taste disturbances) to a severe acute respiratory infection (SARI). SARI is a flu-like condition associated with dyspnea, respiratory discomfort, peripheral oxygen saturation (SpO_2) < 95%, and central cyanosis that may progress to multiple organ failure and require mechanical ventilation (SUN YP, et al., 2022; OLSEN SJ, et al., 2021).

Investigating the risk factors for poor outcomes in children with AVRI is crucial to appropriately allocating resources and multidisciplinary task forces (DALLMEYER LK, et al., 2024). Previous studies observed divergences among risk factors due to differences in age groups, geographical regions, epidemiological time, and virus types (TRUSINKA D, et al., 2024; LI Y, et al., 2022). Also, several studies identified age, sex, race, country or region, comorbidities, fever, hypoxemia, platelet count, leukocyte count, and type of virus as independent risk factors for unfavorable poor outcomes in children with AVRI due to respiratory viruses (TRUSINKA D, et al., 2024; DIAS CS, et al., 2024; NUNZITA F, et al., 2023; SENA GR, et al., 2021; HAVDAL LB, et al., 2022; GRAHAM HR, et al., 2024; AGARWAL A, et al., 2024; DEL VALLE R, et al., 2022). However, despite advances in the strategies for improving living conditions, nutrition, and provision of vaccines for the pediatric population, some Brazilian regions still present a high prevalence of hospitalization and unfavorable outcomes in children with AVRI (SOBRINHO FLDV, et al., 2021; OLIVEIRA EA, et al., 2021).

The Brazilian states located in the North region, especially Amapá, have difficult geographic conditions that limit the access of the population to healthcare services (GARNELO L, et al., 2020; GARNELO L, et al., 2018). In 2022, the state of Amapá presented the lowest vaccine coverage compared with other states from the North region and the highest lethality rate among children under four years old due to avoidable causes, such as lack of immunization, poor assistance during labor and post-natal care, failure in early diagnosing respiratory conditions, and insufficient health promotion initiatives in the primary care level (BRASIL, 2022; BRASIL, 2022).

Although studies conducted in low- and middle-income countries have described the risk factors for poor outcomes in children with SARI due to respiratory viruses, the literature encompassing poor regions, mainly those with restricted access to basic health services influencing behaviors and health outcomes (e.g., North of Brazil), is scarce (OLIVEIRA AE, et al., 2021; GARNELO L, et al., 2020). Therefore, this study aimed to identify the independent risk factors associated with poor outcomes (death, need for mechanical ventilation, and prolonged hospitalization time) in children hospitalized with SARI due to respiratory viruses in the state of Amapá. We hypothesized that respiratory virus etiology was an independent risk factor for poor outcomes in this population.

METHODS

This retrospective cohort study was approved by the research ethics committee of the Instituto de Medicina Integral Professor Fernando Figueira (N° 5.834.186/2022 e CAAE: 65799022.2.0000.5201). The analysis was conducted based on secondary data from children hospitalized with SARI due to respiratory viruses in the public health system of the state of Amapá. Notified cases of SARI were collected from the influenza surveillance network, while other respiratory viruses were obtained from the Information System of Influenza Syndrome of the National Information System on Epidemiological Surveillance of Influenza (SIVEP-GRIPE, Ministry of Health, Brazil). The SIVEP-GRIPE is a public domain database and the primary source of information and surveillance on deaths and SARI cases caused by respiratory viruses in Brazil. The files from 2020 to 2022 available on the webpage of the database were used for this study (BRASIL, 2023).

The state of Amapá is located in the North region of Brazil, mostly within the Amazon rainforest, and has approximately 733 thousand people distributed in 16 municipalities (human development index of 0.688) (BRASIL, 2024); a total of 27% of the population has between 0 and 14 years old According to the Brazilian Ministry of Health, approximately 4,200 children were treated for respiratory complaints during the period of this study.

The records of children under 12 years old with a confirmed diagnosis of SARI (reverse transcriptase polymerase chain reaction technique [RT-PCR]) (BRASIL, 2020) and hospitalized in the public health system of Amapá between May 2020 and May 2022 were defined as eligible. Records with no data on virus classification were excluded. The sample size was calculated using the OpenEpi software (version 3.01) and based on data related to deaths from a study conducted with patients under 20 years old infected with respiratory viruses (OLIVEIRA EA, et al., 2021). Therefore, admitting an expected mortality of 15%, the required sample size would be at least 191 children hospitalized with SARI due to respiratory viruses.

The independent variables evaluated were age (0 to 2, 2 to 5, and 5 to 12 years old), sex, ethnicity (brown or not brown), number of symptoms upon admission (one to three, four to six, and seven to nine), signs and symptoms upon admission (cough, fever, dyspnea, and hypoxemia), comorbidities, vaccine against influenza, admission to pediatric intensive care length of ICU stay, length of hospital stay and mortality. According to the RT-PCR, the following types of respiratory viruses were recorded: influenza and its subtypes, human metapneumovirus, RSV, parainfluenza and its subtypes, and SARS-CoV-2. The respiratory viruses were also categorized into four classes based on their prevalence: influenza H3N2, RSV, SARS-CoV-2, or other (i.e., human metapneumovirus, adenovirus, rhinovirus, parainfluenza virus and its subtypes, enterovirus, or bocavirus). The dependent variables for poor outcomes were death, need for mechanical ventilation, and prolonged hospitalization time; the latter was defined by a median of the total hospitalization time (i.e., the difference in days between the date of hospital admission and the date of hospital discharge or death) greater than or equal to six days.

Data were exported to an electronic database using STATA version 12.1 (StataCorp. Texas, USA) and presented as absolute and relative frequencies, mean and standard deviation, or median and 25%-75% interquartile range. Relative frequencies were compared using the Chi-square test or Fisher's exact test. Univariate and multivariate Poisson regression models with robust variance were used to identify the factors associated with death, need for mechanical ventilation, and prolonged hospitalization time. The relative risk (RR) and 95% confidence intervals (95%CI) were reported. Independent variables with a p-value < 0.20 in the univariate analysis were included in the multivariate models. Adjusted relative risks (aRR) were

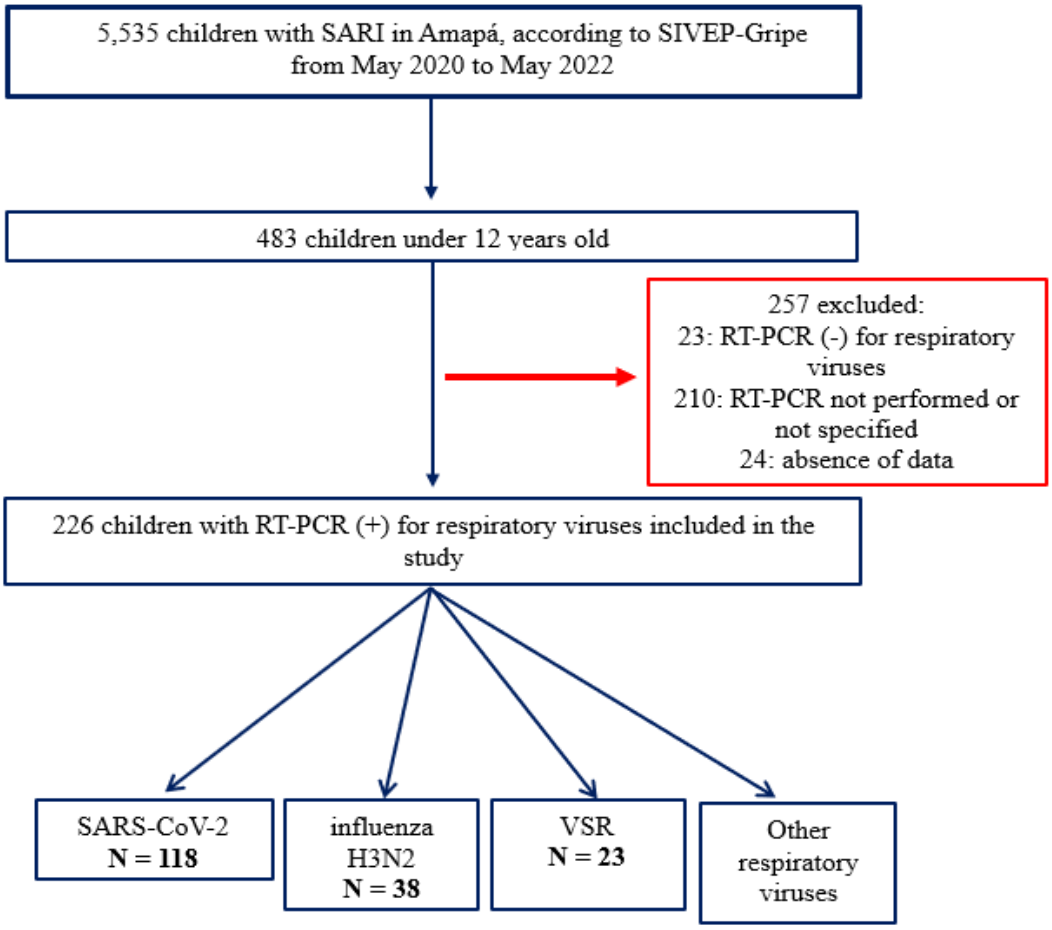
calculated for each factor, representing the strength of the association between independent factors and outcomes, while controlling for possible confounding effects of the other factors included in the model.

Subsequently, a logistic regression was used to evaluate the calibration (Hosmer-Lemeshow and Stukel tests) and discrimination (receiver operating characteristic [ROC] curve) of the adjusted multivariate models. The Hosmer-Lemeshow classification was used to determine the quality of the discrimination as follows: ROC = 0.5 (no discrimination), 0.5 < ROC < 0.7 (poor), 0.7 ≤ ROC < 0.8 (acceptable), 0.8 ≤ ROC < 0.9 (excellent), and ROC ≥ 0.9 (exceptional) (DAVID W, et al.,2013). A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 5,535 cases of SARI were notified in the SIVEP-Gripe from Amapá between May 2020 and May 2022. Among these, 483 (8.73%) cases referred to children under 12 years old. After excluding 257 children due to RT-PCR results (23 were negative, 210 were not performed or not specified, and 24 lacked information), the final cohort consisted of data from 226 children (**Figure 1**).

Figure 1 - Flowchart of the sample selection. SARI = severe acute respiratory infection; SIVEP-gripe = Syndrome of the National Information System on Epidemiological Surveillance of Influenza; RT-PCR (-) = negative reverse transcriptase polymerase chain reaction; RT-PCR (+) = positive reverse transcriptase polymerase chain reaction; SARS-Cov-2 = severe acute respiratory syndrome 2 Coronavirus; Influenza A subtype H3N2 (influenza H3N2); RSV = respiratory syncytial virus.



Source: Nogueira FGSB, et al., 2026.

The epidemiological and clinical characteristics of the children included are presented in **Table 1**. The mean age upon hospital admission was 4.2 (± 3.2) years; only 1.8% were younger than one year old, and 60.6% were younger than five years old. Comorbidities were observed in 15% of children. Of these, 35.3% had neurological diseases, 29.4% had asthma, 14.7% had cardiac disease, 8.8% had kidney disease, 5.9%

had immunodeficiency, and 5.9% had other lung diseases. Approximately 44% of children required mechanical ventilation, and this proportion increased to 60% among those older than five years old. The median hospitalization time was six days; however, when stratified by virus type, influenza H3N2 had a median time of 11.5 days compared with RSV (eight days), other respiratory viruses (seven days), and SARS-CoV-2 (five days).

Table 1 - Epidemiologic and clinical characteristics of children hospitalized by respiratory viruses from May 2020 to May 2022 in the state of Amapá, Brazil.

Variable	Total (n = 226)
Age (years), mean (± SD)	4.2 (±□3.2)
0 to 2, n (%)	63 (27.9)
2 to 5, n (%)	74 (32.7)
5 to 12, n (%)	89 (39.4)
Gender male, n (%)	116 (51.3)
Ethnicity: Brown, n (%)	170 (75.2)
Number of symptoms upon admission, n (%)	
One to three	91 (40.3)
Four to six	125 (55.3)
Seven to nine	10 (4.4)
Symptoms upon admission, n (%)	
Cough	189 (83.6)
Fever	176 (77.8)
Dyspnea	140 (61.9)
SpO_2< 95%	68 (30.0)
Presence of comorbidity, n (%)	34 (15.0)
Vaccination against influenza, n (%)	38 (19.5)
Admission to pediatric ICU, n (%)	88 (38.9)
Mechanical ventilation, n (%)	
Invasive	52 (23.1)
Non-invasive	42 (18.7)
None	131 (58.2)
Virus type, n (%)	
Influenza H3N2	38 (16.8)
RSV	23 (10.2)
SARS-CoV-2	118 (52.2)
Other respiratory viruses	47 (20.8)
Length of ICU stay, in days (mean and SD)	11.4 (±10.5)
Length of hospital stay, in days (median and $IQR_{25\%-75\%}$)	6 (4 to 11)
Death	32 (14.2)

Data are presented as relative and absolute frequencies, mean and standard deviation, or median with $IQR_{25\%-75\%}$. SD = standard deviation; $IQR_{25\%-75\%}$ = interquartile range; SpO2 < 95% = peripheral oxygen saturation lower than 95%; ICU = intensive care unit; Influenza H3N2 = influenza A virus subtype H3N2; RSV = respiratory syncytial virus; SARS-Cov-2 = acute respiratory syndrome 2 Coronavirus. **Source:** Nogueira FGSB, et al., 2026.

Although the mortality rate was 14.2%, variations were observed according to age: 25% were younger than two years old, 31.2% were between two and five years old, and 43.8% were older than five years old. When assessed by virus type, the lethality rate by RSV, influenza H3N2, and SARS-CoV-2 were 47.8%, 23.7%, and 10.1%, respectively. Significant differences in lethality were observed between RSV and SARS-CoV-2 (p< 0.001) and between influenza H3N2 and SARS-CoV-2 (p= 0.028). However, no differences were observed between RSV and influenza H3N2 (p = 0.052). Among children infected with RSV and presenting a high lethality rate, 82.6% were younger than five years old, 65.2% were living in the countryside, 56.5% were hospitalized with SpO_2< 95%, and 52.2% required invasive mechanical ventilation.

As shown in **Table 2**, the multivariate analysis identified the following independent factors associated with death: invasive mechanical ventilation (RR = 6.81; 95%CI: 2.52 to 18.39), comorbidity (RR = 2.25; 95%CI: 1.13 to 4.46), infection by RSV (RR = 2.38; 95%CI: 1.12 to 5.04), and cough (RR = 0.50; 95%CI: 0.25 to 0.96). According to the Hosmer-Lemeshow classification, the discriminatory capacity of the model for death

was excellent (ROC = 0.857; 95%CI: 0.789 to 0.925). Calibration was satisfactory according to the Hosmer-Lemeshow (p = 0.675) and Stukel (p = 0.382) tests.

Table 2 - Raw and adjusted relative risks for death in children hospitalized with respiratory viruses infection from May 2020 to May 2022, Amapá, Brazil.

Variable	Death		Univariate analysis		Multivariate analysis	
	Yes	No				
	N (%)	N (%)	RR (95%CI)	p-value	aRR (95%CI)	p-value
Age (years)				0.854		
0 to 2	8 (12.7)	55 (87.3)	0.81 (0.36 to 1.81)			
2 to 5	10 (13.5)	64 (86.5)	0.86 (0.40 to 1.82)			
5 to 12	14 (15.7)	75 (84.3)	1.0			
Gender				0.550		
Male	18 (15.5)	98 (84.5)	1.22 (0.64 to 2.33)			
Female	14 (12.7)	96 (87.3)	1.0			
Ethnicity				0.542		
Brown	23 (13.5)	147 (86.5)	0.79 (0.38 to 1.66)			
Not brown	8 (17.0)	39 (83.0)	1.0			
Location				0.516		
Capital	15 (12.7)	103 (87.3)	0.81 (0.42 to 1.54)			
Countryside	17 (15.7)	91 (84.3)	1.0			
Residential area				0.044		
Urban	21 (11.5)	162 (88.5)	0.47 (0.23 to 0.98)			
Rural	8 (24.2)	25 (75.8)	1.0			
Number of symptoms				0.855		
One to three	12 (13.2)	79 (86.8)	1.0			
Four to six	19 (15.2)	106 (84.8)	1.15 (0.59 to 2.26)			
Seven to nine	1 (10.0)	9 (90.0)	0.76 (0.11 to 5.26)			
Fever				0.721		
Yes	24 (13.7)	151 (86.3)	0.87 (0.42 to 1.83)			
No	8 (15.7)	43 (84.3)	1.0			
Dyspnea				0.010		
Yes	27 (19.3)	113 (80.7)	3.32 (1.32 to 8.30)			
No	5 (5.8)	81 (94.2)	1.0			
SpO_2< 95%				< 0.001		
Yes	18 (27.3)	48 (72.7)	3.12 (1.65 to 5.90)			
No	14 (8.8)	146 (91.3)	1.0			
Comorbidity				0.082		**< 0.020**
Yes	8 (23.5)	26 (76.5)	1.88 (0.92 to 3.84)		2.25 (1.13 to 4.46)	
No	24 (12.5)	168 (87.5)	1.0		1.0	
Vaccine against influenza				0.067		
Yes	1 (2.6)	37 (97.4)	0.16 (0.02 to 1.14)			
No	26 (16.6)	131 (83.4)	1.0			
ICU admission				< 0.001		
Yes	26 (29.5)	62 (70.5)	6.80 (2.91 to 15.87)			
No	6 (4.3)	132 (95.7)	1.0			
Mechanical ventilation				< 0.001		**< 0.001**
IMV	20 (38.5)	32 (61.5)	10.08 (3.98 to 25.49)		6.81 (2.52 to 18.39)	
NIMV	6 (14.3)	36 (85.7)	3.74 (1.20 to 11.67)		2.56 (0.86 to 7.61)	
None	5 (3.8)	126 (96.2)	1.0		1.0	
Virus				< 0.001		**< 0.001**
Influenza H3N2	9 (23.7)	29 (76,3)	2.33 (1.06 to 5.11)		1.3 (0.64 to 2.86)	
RSV	11 (47.8)	12 (52.2)	4.70 (2.37 to 9.35)		2.38 (1.12 to 5.04)	
SARS-CoV-2	12 (10.2)	106 (89.8)	1.0		1.0	
Other viruses	0 (0.0)	47 (100.0)	0.00 (0.00 to 0.00)			
Cough				0.048		**0.039**
Yes	23 (12.2)	166 (87.8)	0.50 (0.25 to 0.99)		0.50 (0.25 to 0.96)	
No	9 (24.3)	28 (75.7)	1.0		1.0	

Data expressed in absolute and relative frequencies. 95% CI = 95% confidence interval. RR = relative risk; aRR = adjusted relative risk; SpO_2 = peripheral oxygen saturation; ICU = intensive care unit; IMV = invasive mechanical ventilation; NIMV = non-invasive mechanical ventilation; Influenza H3N2 = influenza A virus; RSV = respiratory syncytial virus; SARS-Cov-2 = severe acute respiratory syndrome 2 Coronavirus. **Source:** Nogueira FGSB, et al., 2026.

ICU admission (RR = 4.14; 95%CI: 2.78 to 6.17) and infection with RSV (RR = 1.66; 95%CI: 1.24 to 227) and influenza H3N2 (RR = 1.59; 95%CI = 1.13 to 2.23) were identified as independent risk factors for the need for mechanical ventilation (**Table 3**). The discriminative analysis of the model was considered excellent according to the Hosmer-Lemeshow classification (ROC = 0.859; 95%CI: 0.807 to 0.910), while the calibration was satisfactory (p = 0.391, Hosmer-Lemeshow; and p = 0.375, Stukel test).

Table 3 - Raw and adjusted relative risks for the need for mechanical ventilation in 226 children hospitalized with respiratory virus infection from May 2020 to May 2022, Amapá, Brazil.

	Mechanical ventilation		Univariate analysis		Multivariate analysis	
	Yes	No				
Variable	**N (%)**	**N (%)**	**RR (95%CI)**	**p-value**	**aRR (95%CI)**	**p-value**
Age (years)				0.217		
0 to 2	27 (42.9)	36 (57.1)	0.90 (0.63 to 1.29)			
2 to 5	25 (33.8)	49 (66.2)	0.71 (0.48 to 1.04)			
5 to 12	42 (47.7)	46 (52.3)	1.0			
Gender				0.175		
Male	43 (37.4)	72 (62.6)	0.81 (0.59 to 1.10)			
Female	51 (46.4)	59 (53.6)	1.0			
Ethnicity				0.773		
Brown	68 (40.2)	101 (59.8)	0.95 (0.65 to 1.38)			
Not brown	20 (42.6)	27 (57.4)	1.0			
Location				0.402		
Capital	52 (44.4)	65 (55.6)	1.14 (0.84 to 1.56)			
Countryside	42 (38.9)	66 (61.1)	1.0			
Residential area				0.027		
Urban	71 (39.0)	111 (61.0)	0.68 (0.48 to 0.96)			
Rural	19 (57.6)	14 (42.4)	1.0			
Number of symptoms				0.290		
One to three	33 (36.7)	57 (63.3)	1.0			
Four to six	58 (46.4)	67 (53.6)	1.27 (0.91 to 1.76)			
Seven to nine	3 (30.0)	7 (70.0)	0.82 (0.30 to 2.20)			
Fever				0.215		
Yes	69 (39.7)	105 (60.3)	0.81 (0.58 to 1.13)			
No	25 (49.0)	26 (51.0)	1.0			
Dyspnea				< 0.001		
Yes	72 (51.4)	68 (48.6)	1.99 (1.34 to 2.95)			
No	22 (25.9)	63 (74.1)	1.0			
SpO_2< 95%				< 0.001		
Yes	45 (68.2)	21 (31.8)	2.21 (1.66 to 2.94)			
No	49 (30.8)	110 (69.2)	1.0			
Comorbidity				0.761		
Yes	15 (44.1)	19 (55.9)	1.07 (0.70 to 1.62)			
No	79 (41.4)	112 (58.6)	1.0			
Vaccine against influenza				0.016		
Yes	7 (18.4)	31 (81.6)	0.43 (0.21 to 0.85)			
No	68 (43.3)	89 (56.7)	1.0			
ICU admission				< 0.001		
Yes	70 (80.5)	17 (19.5)	4.63 (3.17 to 6.76)		4.14 (2.78 to 6.17)	**< 0.001**
No	24 (17.4)	114 (82.6)	1.0		1.0	
Virus				< 0.001		**< 0.006**
Influenza H3N2	23 (62.2)	14 (37.8)	2.04 (1.41 to 2.95)		1.59 (1.13 to 2.23)	
RSV	20 (87.0)	3 (13.0)	2.85 (2.08 to 3.91)		1.68 (1.24 to 2.27)	
SARS-CoV-2	36 (30.5)	82 (69.5)	1.0		1.0	
Other	15 (31.9)	32 (68.1)	1.05 (0.63 to 1.72)		1.23 (0.86 to 1.76)	
Cough						
Yes	79 (41.8)	110 (58.2)	1.0 (0.66 to 1.53)	0.988		
No	15 (41.7)	21 (58.3)	1.0			

Data shown as absolute and relative frequencies. RR = relative risk; aRR = adjusted relative risk; 95% CI = 95% confidence interval; SpO_2 = peripheral oxygen saturation; ICU= intensive care unit; Influenza H3N2 = influenza A virus; RSV = respiratory syncytial virus; SARS-Cov-2 = severe acute respiratory syndrome 2 coronavirus.
Source: Nogueira FGSB, et al., 2026.

The independent risk factors for prolonged hospitalization time included SpO2 < 95% upon hospital admission (RR = 1.47; 95%CI: 1.33 to 5.64) and infection by other respiratory viruses (RR = 1.86; 95%CI: 1.36 to 2.53) and by influenza H3N2 virus (RR = 1.67; 95%CI: 1.22 to 2.27) compared with SARS-CoV-2 (**Table 4**).

The discriminatory capacity of the model for prolonged hospitalization time was considered acceptable (ROC = 0.705; 95%CI: 0.624 to 0.756, Hosmer-Lemeshow test). Calibration was satisfactory according to Hosmer-Lemeshow (p = 0.388) and Stukel (p = 0.622) tests.

Table 4 - Raw and adjusted relative risks for hospitalization time in 226 children hospitalized with respiratory virus infection from May 2020 to May 2022, Amapá, Brazil.

Variable	Hospitalization time (days)		Univariate analysis		Multivariate analysis	
	Yes (≥ 6)	No (< 6)				
	N (%)	N (%)	RR (95%CI)	p-value	aRR (95%CI)	p-value
Age (years)				0.610		
0 to 2	36 (57.1)	27 (42.9)	1.00 (0.75 to 1.32)			
2 to 5	37 (50.0)	37 (50.0)	0.87 (0.65 to 1.17)			
5 to 12	51 (57.3)	38 (42.7)	1.0			
Gender				0.531		
Male	66 (56.9)	50 (43.1)	1.08 (0.85 to 1.37)			
Female	58 (52.7)	52 (47.3)	1.0			
Ethnicity				0.679		
Brown	92 (54.1)	78 (45.9)	0.94 (0.71 to 1.25)			
Not brown	27 (57.4)	20 (42.6)	1.0			
Location				0.548		
Capital	67 (56.8)	51 (43.2)	1.0			
Countryside	57 (52.8)	51 (47.2)	0.93 (0.73 to 1.18)			
Residential area				0.617		
Urban	97 (53.0)	86 (47.0)	1.0			
Rural	19 (57.6)	14 (42.4)	1.09 (0.79 to 1.50)			
Number of symptoms				0.086		
One to three	42 (46.2)	49 (53.8)	1.0			
Four to six	75 (60.0)	50 (40.0)	1.30 (1.00 to 1.69)			
Seven to nine	7 (70.0)	3 (30.0)	1.52 (0.95 to 2.41)			
Fever				0.313		
Yes	93 (53.1)	82 (46.9)	0.87 (0.67 to 1.14)			
No	31 (60.8)	20 (39.2)	1.0			
Dyspnea				0.059		
Yes	110 (58.2)	79 (41.8)	1.29 (0.99 to 1.68)			
No	14 (37.8)	23 (62/2)	1.0			
SpO_2< 95%				< 0.001		**< 0.001**
Yes	84 (60.0)	56 (40.0)	1.58 (1.27 to 1.97)		1.47 (1.33 to 5.64)	
No	40 (46.5)	46 (53.5)	1.0		1.0	
Comorbidity				0.351		
Yes	49 (74.2)	17 (25.8)	1.15 (0.86 to 1.55)			
No	75 (46.9)	85 (53.1)	1.0			
Vaccine against influenza				0.271		
Yes	21 (61.8)	13 (38.2)	0.81 (0.55 to 1.8)			
No	103 (53.6)	89 (46.4)	1.0			
ICU admission				0.006		
Yes	17 (44.7)	21 (55.3)	1.38 (1.09 to 1.74)			
No	87 (55.4)	70 (44.6)	1.0			
Mechanical ventilation				0.002		
IMV	38 (73.1)	14 (26.9)	1.54 (1.21 to 1.97)			
NIMV	24 (57.1)	18 (42.9)	1.21 (0.88 to 1.66)			
None	62 (47.3)	69 (52.7)	1.0			
Virus				< 0.001		**< 0.003**
Influenza H3N2	58 (65.9)	30 (34.1)	1.74 (1.31 to 2.31)		1.67 (1.22 to 2.27)	
RSV	66 (47.8)	72 (52.2)	1.44 (0.97 to 2.12)		1.22 (0.81 to 1.85)	
SARS-CoV-2			1.0		1.0	
Other	28 (73.7)	10 (26.3)	1.61 (1.20 to 2.14)		1.86 (1.36 to 2.53)	
Cough	14 (60.9)	9 (39.1)		0.050		
Yes	50 (42.4)	68 (57.6)	1.54 (1.00 to 2.37)			
No	32 (68.1)	15 (31.9)	1.0			

Data expressed as absolute and relative frequencies. RR = relative risk; aRR = adjusted relative risk; 95% CI = 95% confidence interval; ICU = intensive care unit; IMV = invasive mechanical ventilation; NIMV = non-invasive mechanical ventilation; influenza H3N2= influenza A virus; RSV= respiratory syncytial virus; SARS-Cov-2 = severe acute respiratory syndrome 2 Coronavirus. **Source:** Nogueira FGSB, et al., 2026.

DISCUSSION

This retrospective cohort investigated the independent risk factors for poor outcomes among 226 children hospitalized with SARI in the state of Amapá (North region, Brazil). Invasive mechanical ventilation, comorbidities, and infection by RSV were associated with death, whereas cough was a protective factor. For mechanical ventilation, the risk factors were ICU admission and infection by RSV and H3N2 influenza. The independent risk factors for prolonged hospitalization time were SpO2 < 95% upon admission, infection by other respiratory viruses, and influenza H3N2. Thus, the present study confirmed the hypothesis that respiratory viruses were independent risk factors for poor outcomes in children hospitalized with SARI.

The lethality rate found in the present study was high compared with other studies conducted in Brazil (1% to 9.6%) and low- and middle-income countries (1%) (DIAS CS, et al., 2024; SOBRINHO FLDV, et al., 2021; SONG X, et al., 2020; MENEZES RC, et al., 2024; SOUZA BL, et al., 2021; PUCARELLI-LEBREIRO G, et al., 2022). The 14.2% lethality rate observed in this study may be related to the quality and accessibility of public healthcare services, including the availability of pediatric ICU beds, compared to other Brazilian regions (DIAS CS, et al., 2024; OLIVEIRA EA, et al., 2021; FABRIN C, et al., 2023; ROCHA R, et al., 2021).

A Brazilian study evaluated 11,613 patients under 20 years old with COVID-19 and observed a lethality rate of 7.2%; 31% of the patients did not require ICU admission (OLIVEIRA EA, et al., 2021). According to the authors, the proportion of children who died without ICU support was 36% in the Northeast and North regions compared with 23% in the Southeast and South regions, reflecting the regional and intra-regional economic discrepancies (OLIVEIRA EA, et al., 2021). In the multivariate analysis, they also observed a risk of death 2- and 1.5-fold higher in the Northeast and North regions, respectively (OLIVEIRA EA, et al., 2021).

The lethality of respiratory viruses and their etiology are concerning. We observed that SARI caused by RSV was an independent factor for death compared with other viruses, including SARS-CoV-2. In contrast, other Brazilian studies observed a higher mortality risk of SARI induced by SARS-CoV-2 among children under 18 years old and hospitalized by AVRI compared with seasonal viruses (DIAS CS, et al., 2024; SOUSA BL, et al., 2020). The findings of the present study could be related to three factors: the higher RSV load leading to severe disease; two-thirds of patients with SARI caused by RSV were living in the countryside and possibly had lower accessibility to healthcare services; and 56.5% of cases presented SpO2 < 95% upon hospitalization, reflecting the higher severity of the disease.

Similar to our findings, several studies identified the presence of comorbidity as an independent risk factor for mortality (DIAS CS, et al., 2024; SENA GR, et al., 2021; SOUSA BL, et al., 2020). Children with comorbidities may present anatomic, physiologic, and immunologic alterations that increase their susceptibility to morbidity and lethality (MOREIRA AL, et al., 2023; XU C, et al., 2023). In this sense, the active surveillance of children with comorbidities and strategies to improve vaccination adherence for preventable diseases is needed to target early diagnosis and immediate treatment (XU C, et al., 2023). This approach is particularly important for the state of Amapá, where vaccination coverage against influenza in 2022 was 19.5% and 51.1% for the overall population and children aged up to four years, respectively; vaccination coverage in Brazilian children during the same time period was 71.2% (BRASIL, 2022).

Contrary to our findings, other studies identified age less than two years and teenagers (12 to 18 years old) as independent risk factors for death (TRUSINSKA D, et al., 2024; SENA GR, et al., 2021; OLIVEIRA EA, et al., 2021; GOMES NT, et al., 2021). In our study, only one-quarter of the children were under two years old, possibly because data were collected during the COVID-19 pandemic, which may have led to home confinement or death before reaching tertiary health services. On the other hand, SpO2 < 95% upon hospitalization was not an independent risk factor for death. A review study performed in low- and middle-income regions highlighted a higher risk of death in children with SpO2 < 95%, with variations among locations and populations. The mortality was 2-fold higher in children with SpO2 between 94% and 95% compared with those between 98% and 100%, 3-fold higher when SpO2 was 92% to 93%, 4-fold higher at 90% to 91%, and 6-fold higher at 88% to 89%. Thus, hypoxemia must be recognized as an important sign of danger in clinical guidelines (GRAHAM HR, et al., 2024).

Cough was observed as a protective factor, reducing mortality by approximately 50%. A retrospective cohort performed with 60,657 Brazilian children under 19 years old hospitalized with AVRI showed that SARS-CoV-2 infection presented a lower probability of cough (MENEZES RC, et al., 2024). Cough is an innate primitive reflex that protects against foreign materials in the airways, and its etiology may be related to a wide clinical variety, including AVRI (SHARMA S, et al., 2025). In this sense, the comorbidities observed in our cohort (e.g., neurological diseases and asthma) and the need for ventilatory support may have influenced the protective role of cough in the presence of events impairing lung function. Future retrospective cohort studies are required to investigate cough as a protective factor for mortality in children with SARI.

ICU admission and infection by RSV and influenza H3N2 were risk factors for the need for mechanical ventilation. AVRI may evolve to more severe conditions (e.g., impaired gas exchange and acute respiratory failure), cause hypoxemia, and require mechanical ventilation (NUNZIATA F, et al., 2023; GRAHAM HR, et al., 2024; OLIVEIRA EA, et al., 2021; GOMES NT, et al., 2021).

Similar to our results, a retrospective cohort performed in the United States analyzed the need for mechanical ventilation (invasive, non-invasive, and high-flow nasal cannula) in 847 children hospitalized with AVRI due to SARS-CoV-2, RSV, and influenza. The results indicated a risk of ICU admission 2-fold higher in children with influenza, while the risk for mechanical ventilation was 2-fold higher in children with RSV compared with SARS-CoV-2. In contrast to our findings, the authors reported an increased risk of requiring invasive mechanical ventilation among children with SARS-CoV-2, suggesting the capacity of this virus to cause severe disease (RAO S, et al., 2023; HEDBERG P, 2022).

Another study showed that the need for invasive mechanical ventilation in children hospitalized with SARS-CoV-2 in Mexico was not significantly different compared with those with influenza infection (LARIS-GONZÁLEZ A, et al., 2021). Infections by RSV and influenza in children may increase the activation of the innate immune system, which could lead to more severe symptoms than those observed in the SARS-CoV-2 infection (MIFSUDE EJ, et al., 2021; REN GL, et al., 2021).

Regarding the independent risk factors for prolonged hospitalization time (> 6 days), the multivariate analysis showed that SpO2 < 95% upon admission and infection with influenza H3N2 and other respiratory viruses extended hospitalization time by 1.5, 1.57, and 1.6 days, respectively. On the other hand, vaccination against influenza reduced the chances of prolonged hospitalization time by 30%. Studies assessing this outcome in children are scarce, encompass different periods, and involve multiple respiratory viruses (HEDBERG P, et al., 2022; HAVDAL LB, 2022).

In clinical practice, particularly in epidemics and endemics, prolonging hospitalization time by at least half a day may reduce the number of beds available for children with severe illnesses. Contrary to our findings, the study performed in the United States showed that RSV infection increased the risk for prolonged hospitalization time (> 4 days) by 40% compared with SARS-CoV-2 (RAO S, et al., 2023).

This study has some limitations. We evaluated the internal validity of the adjusted models for death, need for mechanical ventilation, and prolonged hospitalization time and observed excellent discrimination and calibration values for death and mechanical ventilation. However, the model for prolonged hospitalization time presented a good calibration but only acceptable discrimination. Thus, external calibration is needed to confirm the estimations observed in these models. Furthermore, the lack of studies with similar designs hindered the comparison of data related to internal validity.

The SIVEP-GRIPE is responsible for recording sentinel surveillance data on influenza-like illness, hospitalized cases, and deaths from SARI. Despite this, new algorithms can be developed and tested in real time at the time of case notification in the surveillance system for application in clinical practice. Adjustments, such as training operators and increasing the availability of supplies to expedite the release of laboratory tests for respiratory viruses, are also needed to improve the system and enhance the completeness of records and data quality. This study included children with SARI due to respiratory viruses (confirmed by RT-PCR) during the COVID-19 pandemic and also demonstrated that RSV and influenza H3N2 were associated with poor outcomes. Understanding the impacts of respiratory viruses may improve public health strategies

to manage epidemics and optimize the care of severe patients from diagnosis to post-hospital discharge. Furthermore, few studies investigated the independent risks and protective factors for poor outcomes in hospitalized children from low- and middle-income countries. These contexts are unique due to high lethality rates and the limited access to healthcare services and economic resources.

CONCLUSION

These fundings confirm the hypothesis that respiratory viruses were independent risk factors for poor outcomes among children hospitalized with SARI. The independent factors associated with death were mechanical ventilation, comorbidity, infection by RSV, and cough. In contrast, the risk factors for mechanical ventilation were ICU admission, infection by RSV, and influenza H3N2 virus. This study found that the adjusted models investigated for mortality and mechanical ventilation in children with acute viral respiratory infections demonstrated excellent discrimination and calibration, enabling the estimation of outcomes with a high degree of certainty in the studied population.

REFERENCES

1. AGARWAL A, et al. Clinical Profile, Intensive Care Needs and Predictors of Outcome Among Children Admitted with Non-COVID Severe Acute Respiratory Illness (SARI) During the Pandemic. Indian J Pediatr. 2024;91:329–336.
2. BRASIL. Ministério da Saúde. Proporção de óbitos de crianças de até 4 anos de idade por causas claramente evitáveis; 2022 [cited 2024 July 2]. Available at: https://observatoriocrianca.org.br.
3. BRASIL. Ministério da Saúde. Cobertura de vacinas por imunobiológicos sobre menores de um ano de idade e de menores de quatro anos de idade; 2022 [cited 2024 July 2]. Available at: https://observatoriocrianca.org.br/imunobiologicos.
4. BRASIL. Ministério da Saúde. Bancos de dados epidemiológicos de SRAG, da rede de vigilância da Influenza e outros vírus respiratórios; 2023 [cited 2024 January]. Available at: https://opendatasus.saude.gov.br/dataset/srag-2021-a-2024.
5. BRASIL. IBGE. Instituto Brasileiro de Geografia e Estatística, 2024 [cited 2024 July]. Available at: https://cidades.ibge.gov.br.
6. BRASIL. Ministério da Saúde. Protocolo de Manejo Clínico Para o Novo Coronavírus (2019-NCoV), 2020 [cited 2024 July 2]. Available at: https://portalarquivos2.saude.gov.br/images/pdf/2020/fevereiro/11/protocolo-manejo-coronavirus.pdf.
7. DALLMEYER LK, et al. Epidemiology of respiratory viruses among children during the SARS-CoV-2 pandemic: A systematic review and meta-analysis. Int J Infect Di. 2024;138:10–18.
8. DAVID W, et al. Applied Logistic Regression. 3rd ed. United States of America: Wiley. Chapter 5, Assessing the fit of model; p. 153–177. 2013.
9. DEL VALLE R, et al. Comparison of pneumonia features in children caused by SARS-CoV-2 and other viral respiratory pathogens. Pediatr Pulmonol. 2022;57:2374–2382.
10. DIAS CS, et al. Outcomes of SARS-CoV-2 and Seasonal Viruses Among Children Hospitalized in Brazil. Pediatrics. 2024;153(2):e2023064326.
11. FABRIN C, et al. Desigualdade socioeconômica na letalidade e no cuidado hospitalar de crianças e adolescentes internados por COVID-19 no Brasil. Rev Bras Epidemiol. 2023;26:e230015.
12. FARZI R, et al. Prevalence of Influenza Viruses A and B, Adenovirus, Respiratory Syncytial Virus, and Human Metapneumonia Viruses among Children with Acute Respiratory Tract Infection. Adv Virol. 2024; eCollection;1–9.
13. GARNELO L, et al. Barriers to access and organization of primary health care services for rural riverside populations in the Amazon. Int J Equity Health. 2020;19:1–14.
14. GARNELO L, et al. Acesso e cobertura da Atenção Primária à Saúde para populações rurais e urbanas na região norte do Brasil. Saúde Debate. 2018;42:81–99.
15. GOMES NT, et al. Coorte retrospectiva de crianças e adolescentes hospitalizados por COVID-19 no Brasil do início da pandemia a 1º de agosto de 2020. Rev Bras Epidemiol. 2021;24:E210026.
16. GRAHAM HR, et al. Hypoxaemia and risk of death among children: rethinking oxygen saturation, risk-stratification, and the role of pulse oximetry in primary care. Lancet Glob Health. 2024;12(8):e1359–e1364.

17. HAVDAL LB, et al. Risk factors associated with severe disease in respiratory syncytial virus-infected children under 5 years of age. Front Pediatr. 2022;10:1–12.
18. HEDBERG P, et al. Clinical phenotypes and outcomes of SARS-CoV-2, influenza, RSV and seven other respiratory viruses: a retrospective study using complete hospital data. Thorax. 2022;77(2):154–163.
19. LARIS-GONZÁLEZ A, et al. Influenza vs. COVID-19: Comparison of Clinical Characteristics and Outcomes in Pediatric Patients in Mexico City. Front Pediatr. 2021;9:676611.
20. LI Y, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. Lancet. 2022;399:2047–2064.
21. MENEZES RC, et al. Severe viral lower respiratory tract infections in Brazilian children: Clinical features of a national cohort. J Infect Public Health. 2024;17:1–9.
22. MIFSUD EJ, et al. Innate Immune Responses to Influenza Virus Infections in the Upper Respiratory Tract. Viruses. 2021;13(10):2090.
23. MOREIRA AL, et al. Profile analysis of emerging respiratory virus in children. Eur J Clin Microbiol Infect Dis. 2023;42:873–882.
24. NUNZIATA F, et al. Clinical Presentation and Severity of SARS-CoV-2 Infection Compared to Respiratory Syncytial Virus and Other Viral Respiratory Infections in Children Less than Two Years of Age. Viruses. 2023;15:717.
25. OLIVEIRA EA, et al. Clinical characteristics and risk factors for death among hospitalised children and adolescents with COVID-19 in Brazil: an analysis of a nationwide database. Lancet Child Adolesc Health. 2021;5:559–568.
26. OLSEN SJ, et al. Changes in Influenza and Other Respiratory Virus Activity During the COVID-19 Pandemic – United States, 2020–2021. MMWR Morb Mortal Wkly Rep. 2021;70:1013–1019.
27. PUCARELLI-LEBREIRO G, et al. Clinical Manifestations and Complications of Children With COVID-19 Compared to Other Respiratory Viral Infections: A Cohort Inpatient Study From Rio de Janeiro, Brazil. Front Pediatr. 2022;10:934648.
28. RAO S, et al. Respiratory Syncytial Virus, Influenza, and Coronavirus Disease 2019 Hospitalizations in Children in Colorado During the 2021–2022 Respiratory Virus Season. J Pediatr. 2023;260:113491.
29. REN GL, et al. Comparison of acute pneumonia caused by SARS-CoV-2 and other respiratory viruses in children: a retrospective multi-center cohort study during COVID-19 outbreak. Mil Med Res. 2021;8:1–14.
30. ROCHA R, et al. Effect of socioeconomic inequalities and vulnerabilities on health-system preparedness and response to COVID-19 in Brazil: a comprehensive analysis. Lancet Glob Health. 2021;9(6):e782–e792.
31. SENA GR, et al. Clinical Characteristics and Mortality Profile of COVID-19 Patients Aged less than 20 years Old in Pernambuco – Brazil. Am J Trop Med Hyg. 2021;104:1507–1512.
32. SHARMA S, et al. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493221/.
33. SOBRINHO FLDV, et al. Epidemiology and factors associated with the severity of viral acute lower respiratory infection in children hospitalized in Manaus, Amazonas, in 2017–2018: An observational study. Medicine. 2021;100(18):e25799.
34. SONG X, et al. Comparison of Clinical Features of COVID-19 vs Seasonal Influenza A and B in US Children. JAMA Netw Open. 2020;3:1–8.
35. SOUSA BL, et al. Differences among Severe Cases of SARS-CoV-2, Influenza, and Other Respiratory Viral Infections in Pediatric Patients: Symptoms, Outcomes and Preexisting Comorbidities. Clinics (Sao Paulo). 2020;9(6):e782–e792.
36. SOUSA BL, et al. Non-communicable diseases, sociodemographic vulnerability and the risk of mortality in hospitalised children and adolescents with COVID-19 in Brazil: a syndemic descriptive analysis. BMJ Open. 2021;11(9):e050724.
37. SUN YP, et al. Epidemiological Features, Risk Factors, and Disease Burden of Respiratory Viruses among Hospitalized Children with Acute Respiratory Tract Infections in Xiamen, China. Jpn J Infect Dis. 2022;75:537–542.
38. TAYLOR S, et al. Respiratory viruses and influenza-like illness: Epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. J Infect. 2017;74:29–41.
39. TRUSINSKA D, et al. Risk Factors for Poor Outcomes in Children Hospitalized with Virus-associated Acute Lower Respiratory Infections: A Systematic Review and Meta-analysis. Pediatr Infect Dis J. 2024;43:467–476.
40. XU C, et al. Clinical features and risk factors analysis for poor outcomes of severe community-acquired pneumonia in children: a nomogram prediction model. Front Pediatr. 2023;11:e1194186.