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Clinical Features and Predictors of Severity in Children Hospitalized With Human Metapneumovirus

A Multicenter Italian Study

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Background: Human metapneumovirus (hMPV) is an important cause of pediatric lower respiratory tract infection. We describe the epidemiology and clinical severity of hMPV-associated pediatric hospitalizations in Italy in the post–coronavirus disease 2019 period and identify predictors of pediatric intensive care unit (PICU) admission and prolonged hospitalization.

Methods: We conducted a multicenter observational study across 11 tertiary care centers in Italy. Children hospitalized for ≥48 hours with laboratory-confirmed hMPV infection between January 2023 and June 2025 were included. Clinical features were analyzed overall and compared across co-infection categories and age groups. Associations with prolonged hospitalization (>7 days) and PICU admission were evaluated using logistic regression models.

Results: A total of 312 children were hospitalized with hMPV infection (median age 14 months, interquartile range 5–36); 86.2% were <5 years, and 44.6% were infants <1 year. Oxygen supplementation was required in 67.5% of cases, and 10.6% were admitted to the PICU. Co-detected pathogens were identified in 47.1% of cases, without significant differences in severity or outcomes. Infants experienced more severe respiratory involvement, whereas older children more frequently had underlying comorbidities, radiologic consolidation and received antibiotics. In adjusted models, comorbidities, moderate-to-severe respiratory distress, dehydration and higher base excess were independently associated with prolonged hospitalization and PICU admission.

Conclusions: In the post–coronavirus disease 2019 period, hMPV remains a clinically relevant cause of pediatric hospitalization, particularly among infants and children with underlying medical conditions. Simple bedside assessment of respiratory distress and hydration status may support early risk stratification and inform diagnostic-driven clinical management, including antimicrobial stewardship.

Key Words: human metapneumovirus, children, respiratory infection, hospitalization, severity

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Human metapneumovirus (hMPV) is an enveloped, negative-sense single-stranded RNA virus classified within the family *Pneumoviridae*, first identified in 2001 as a cause of pediatric respiratory tract disease.[1,2] The infection predominantly affects young children, with the highest incidence and clinical impact observed in those younger than 5 years, particularly during the first year of life. In temperate regions, hMPV circulation typically peaks in late winter and spring.[3,4] Globally, hMPV was estimated to account for more than 500,000 hospitalizations for acute lower respiratory tract infection (LRTI) in children under 5 years, with infants bearing the greatest share of severe disease.[5]

In the post–coronavirus disease 2019 (COVID-19) period, respiratory virus epidemiology has undergone substantial changes, including shifts in seasonal circulation patterns and a marked expansion in the use of multiplex molecular diagnostic panels. These factors have increased the detection of hMPV across both community and hospital settings, contributing to renewed clinical attention to this pathogen.[6]

Despite its well-established role in pediatric LRTI, there are currently no licensed vaccines or specific therapies for hMPV.[2,3] Although preventive strategies are under development, a clearer understanding of the clinical spectrum and predictors of severe disease is essential to inform risk stratification, clinical management and future prevention.[7,8]

However, contemporary multicenter data describing the epidemiology, clinical severity and predictors of adverse outcomes in children hospitalized with hMPV infection remain limited.[9] Therefore, this multicenter study aimed to characterize the epidemiology and clinical features of hMPV-associated pediatric hospitalizations in Italy during the post-COVID-19 period and to identify clinical and laboratory predictors of severe outcomes, including pediatric intensive care unit (PICU) admission and prolonged hospitalization.

MATERIALS AND METHODS

Study Design and Setting

This multicenter observational study was conducted within the INF-ACT (One Health Basic and Translational Actions Addressing Unmet Needs on Emerging Infectious Diseases) pediatric surveillance system, established as part of a European Union–funded National Recovery and Resilience Plan project. The INF-ACT initiative supports coordinated surveillance and translational research on emerging infectious diseases, including respiratory viral infections.[10]

Cases were identified retrospectively through the INF-ACT pediatric network, which includes 11 tertiary care pediatric centers distributed across Italy, covering northern, central and southern regions. The list of participating centers and the number of enrolled patients per site are provided in Table, Supplemental Digital Content 1, https://links.lww.com/INF/G642.

Participants

Children hospitalized for at least 48 hours with laboratory-confirmed hMPV infection between January 2023 and June 2025 were eligible for inclusion. Only the first hospitalization episode per patient during the study period was considered.

Microbiologic Testing

At all participating centers, nasopharyngeal swabs were routinely obtained at hospital admission in children presenting with symptoms consistent with acute respiratory tract infection. Respiratory samples were analyzed using multiplex real-time polymerase chain reaction panels capable of detecting hMPV together with other common respiratory viruses, according to local laboratory protocols.

Bacterial cultures were performed on respiratory specimens (eg, expectorated/aspirated sputum and bronchoalveolar lavage fluid) and/or blood samples when clinically indicated and when appropriate specimens were available.

Data Collection and Clinical Definitions

Demographic, clinical, laboratory, imaging and outcome data were extracted retrospectively from electronic medical records using a standardized data collection form. Collected variables included age, sex, comorbidities, clinical presentation, laboratory and radiologic findings, treatments administered, need for respiratory support, PICU admission and length of hospital stay.

Respiratory distress at presentation was assessed using the Clinical Respiratory Score (CRS), which assigns 0–2 points across 6 parameters (respiratory rate, wheezing, accessory muscle use, mental status, oxygen saturation and skin color [normal/pale/cyanotic]), yielding a total score ranging from 0 to 12. Respiratory distress was categorized as none-to-mild (CRS ≤3) and moderate-to-severe (CRS 4–12).

Hyponatremia was defined as serum sodium <135 mmol/L, based on the first available measurement at admission.

Chest imaging (chest radiography and/or lung ultrasound) was performed at the discretion of the treating physician. Imaging findings were abstracted from official radiology reports and categorized accordingly for analysis.

All data were deidentified locally at each participating center before transfer and were subsequently merged and managed at the coordinating center (Fondazione IRCCS Policlinico San Matteo, Pavia).

The study protocol was reviewed and approved by the Ethics Committee of the coordinating center (n.616/2023) and by the local Ethics Committees of participating institutions. Written informed consent for participation and use of clinical data was obtained from parents or legal guardians, with assent obtained from children when appropriate according to age and local regulations. The study was conducted in accordance with the Declaration of Helsinki and applicable data protection regulations, including the General Data Protection Regulation.

Statistical Analysis

Patient characteristics were summarized using descriptive statistics. Continuous variables are reported as medians with interquartile range (IQR), and categorical variables as frequencies and percentages. Comparisons between groups were performed using the Mann–Whitney *U* test or Kruskal–Wallis test for continuous variables, and the Pearson χ^2 test or Fisher exact test for categorical variables, as appropriate.

Univariate logistic regression analyses were conducted to explore associations between candidate clinical variables and study outcomes. The primary outcomes were admission to the PICU and prolonged hospitalization, defined as a length of hospital stay greater than 7 days, corresponding to the median duration among study participants.

Variables significantly associated with each outcome at univariate analysis were entered into separate mixed-effects logistic regression models. Models were adjusted for age, with study center included as a random effect to account for between-center variability.

Due to missing data, denominators varied across variables; percentages were calculated on available observations. Missing data were not imputed. The number of missing observations is reported for each variable in Table 1. Complete-case analysis was applied within each regression model.

Results are presented as crude odds ratios (cORs) and adjusted odds ratios (aORs) with corresponding 95% confidence intervals (95% CIs) and *P* values. All statistical tests were 2-sided, and a *P* value of <0.05 was considered statistically significant. Statistical analyses were performed using Jamovi (version 2.4.11).

RESULTS

A total of 312 children hospitalized with laboratory-confirmed hMPV infection were included in the analysis. Using mutually exclusive co-infection categories, 165 children (52.9%)

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TABLE 1. Baseline Characteristics, Clinical Presentation, Investigations, Treatment, Outcomes and Missing Data Among Hospitalized Children With hMPV Infection

Characteristics		Missing, n	Total (n=312)	HMPV alone (n=165)
Sociodemographics	Age, months	0	14 (5-36)	13 (4-36)
	Sex (female)	0	138 (44.2)	67 (40.6)
	Urban	117	149 (76.4)	83 (81.4)
	Siblings	146	112 (69.3)	60 (67.4)
	Community	109	93 (45.8)	45 (42.5)
Medical history	Any underlying comorbidity	1	98 (31.5)	50 (30.5)
	Immunosuppression	0	15 (4.8)	8 (4.8)
	Personal history of atopy	84	20 (8.8)	9 (7.6)
	Family history of atopy	120	24 (12.5)	7 (6.9)
	RSV immunoprophylaxis	128	44 (23.9)	29 (29.6)
	Influenza vaccine	154	21 (13.3)	8 (9.9)
	SARS-CoV-2 vaccine	133	18 (10.1)	7 (7.5)
	Antibiotics before admission	100	58 (27.4)	25 (22.5)
Clinical presentation	Fever	1	246 (79.1)	124 (75.2)
	Fever peak, °C	86	38.7 (38.3–39.0)	38.7 (38.5–39.4)
	Fever duration, d	74	4 (2–5)	4 (3–5)
	Cough	0	260 (83.3)	141 (85.5)
	Cough duration, d	159	7 (4–10)	7 (5–10)
	Rhinitis	3	152 (49.2)	90 (54.9)
	Wheezing	80	82 (35.3)	44 (36.1)
	Pharyngitis	80	32 (13.8)	12 (9.8)
	Conjunctivitis	1	17 (5.5)	10 (6.1)
	Diarrhea	1	28 (9.0)	12 (7.3)
	Vomiting	1	41 (13.2)	21 (12.8)
	Poor appetite	10	166 (55.0)	88 (54.7)
	Fatigue	89	63 (28.3)	31 (26.7)
	Neurological symptoms	1	27 (8.7)	10 (6.1)
	Moderate-severe CRS	118	68 (35.1)	34 (32.4)
	Dehydration	176	15 (11.0)	10 (13.7)
	Altered mental status	2	36 (11.6)	16 (9.8)
	Appearance (pallor/cyanosis)	0	49 (15.7)	25 (15.2)
Laboratory findings	WBC count, $\times 10^9$/L	13	10.9 (8.4–15.7)	10.9 (8.2–14.5)
	NLR	20	1.6 (0.8–3.0)	1.4 (0.8–2.6)
	CRP, mg/L	11	17.5 (5.1–55.3)	16.6 (3.6–48.4)
	PCT, ng/mL	142	0.2 (0.1–0.9)	0.2 (0.1–0.6)
	ALT, U/L	68	19 (14–26)	20 (15–27)
	AST, U/L	110	37 (29–49)	40 (29–50)
	LDH, U/L	199	350 (294–449)	360 (303–452)
	CK, U/L	212	75 (49–121)	76 (49–132)
	Albumin, g/dL	207	4.3 (3.9–4.5)	4.2 (3.8–4.5)
	HCO_3^-, mmol/L	203	23.8 (21.7–25.4)	23.6 (21.7–25.1)
	BE, mmol/L	228	−1.0 (−3.1 to 1.2)	−1.1 (−3.0 to 0.4)
	Hyponatremia	41	47 (17.3)	21 (14.2)
Chest imaging*	Not performed	0	106 (34.0)	61 (37.0)
	Normal	0	19 (6.1)	12 (7.3)
	Interstitial abnormalities	0	41 (13.1)	18 (10.9)
	Consolidation	0	137 (43.9)	70 (42.4)
	Pleural effusion	0	9 (2.9)	4 (2.4)
Management	Fluids	2	211 (68.1)	115 (69.7)
	Antibiotics	3	201 (65.0)	90 (55.2)
	Antivirals	80	3 (1.3)	2 (1.6)
	Bronchodilators	2	166 (53.5)	87 (53.0)
	Corticosteroids, inhaled	8	126 (41.4)	56 (35.0)
	Corticosteroids, systemic	8	143 (47.0)	74 (46.0)
Outcomes	Respiratory support	1	210 (67.5)	114 (69.1)
	High-flow oxygen	48	96 (36.4)	54 (38.8)
	Admission to PICU	0	33 (10.6)	14 (8.5)
	Death	0	1 (0.3)	0 (0)
	Length of hospitalization, days	12	7 (5–9)	6 (5–9)

*Chest imaging includes chest X-ray and/or ultrasound; imaging findings were abstracted from radiology reports.

ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; BE, base excess; CK, creatine kinase; LDH, lactate dehydrogenase; WBC, white blood cell.

Data are presented as median (IQR) for continuous variables and n (%) for categorical variables. The number of missing observations is reported for each variable in the total cohort. Percentages were calculated using available nonmissing observations; denominators may vary across variables.

had hMPV-only infection, while 147 (47.1%) had co-detected pathogens: 12 with respiratory syncytial virus (RSV), 88 with other respiratory viruses and 47 with bacterial co-infection. Among bacterial detections, the most frequently identified pathogens were *Streptococcus pneumoniae* (n = 14) and *Haemophilus influenzae* (n = 14). Atypical bacteria included *Mycoplasma pneumoniae* (n = 5) and *Chlamydophila pneumoniae* (n = 3). Other detected organisms were *Moraxella catarrhalis* (n = 5), *Bordetella pertussis* (n = 4) and *Pseudomonas aeruginosa* (n = 4). *Candida albicans* was isolated from bronchoalveolar lavage fluid in 2 cases.

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Baseline Characteristics and Seasonality

The median age of the study population was 14 months (IQR 5–36). Most hospitalizations occurred in children younger than 5 years (86.2%), with infants younger than 1 year accounting for 44.6% of cases. Overall, 174 patients were male (55.8%), and 98 children (31.5%) had at least 1 underlying comorbidity (Table 1).

Hospital admissions displayed a marked seasonal pattern, with most cases occurring between February and April and peaking in March. Admissions declined toward the summer months, with only sporadic cases observed outside the December–June period (Fig. 1). A similar seasonal pattern was observed across geographic areas, with northern regions showing a slightly delayed peak in April (Figure, Supplemental Digital Content 2, https://links.lww.com/INF/G643).

Clinical Presentation, Investigations, Treatment and Outcomes

Fever (79.1%) and cough (83.3%) were the most common presenting symptoms, followed by poor appetite (55.0%) and rhinitis (49.2%). Wheezing was documented in 82 children (35.3%). Among patients with available data, moderate-to-severe respiratory distress (CRS 4–12) was observed in 68 children (35.1%) (Table 1). The number of missing observations for each variable is reported in Table 1. Blood gas–related parameters were available in a subset of patients: bicarbonate was available in 109 children and base excess in 84 children. C-reactive protein (CRP) was available in 301 children, whereas procalcitonin (PCT) was available in 170 children.

Dehydration was recorded in 15 children (11.0% of those with available data). Chest imaging was not performed in 34.0% of cases. Consolidation was the most frequent radiologic finding (43.9% of the overall cohort), whereas pleural effusion was uncommon (2.9% of all patients).

Antibiotics were administered to 201 children (65.0%). Children who received antibiotic therapy had significantly higher inflammatory markers than those who did not receive antibiotics. Median CRP was 26.4 mg/L (IQR 7.3–71.1) among antibiotic-treated children compared with 7.3 mg/L (IQR 2.3–21.6) among those who did not receive antibiotics. Similarly, median PCT was 0.3 ng/mL (IQR 0.1–1.6) versus 0.1 ng/mL (IQR 0.05–0.3), respectively. Both differences were statistically significant ($P < 0.01$). Among antibiotic-treated children, information on the specific agent or combination was available for 200 antibiotic prescriptions. The most frequently used agents were ceftriaxone (n = 63) and amoxicillin–clavulanate (n = 62), followed by macrolides, including clarithromycin (n = 23) and azithromycin (n = 18), often in combination with beta-lactams. Amoxicillin alone (n = 11), ampicillin–sulbactam (n = 14) and ampicillin (n = 4) were less commonly used. Broad-spectrum antibiotics, including piperacillin–tazobactam, other third-generation cephalosporins, meropenem, vancomycin and linezolid, were administered less frequently. Bronchodilators and systemic corticosteroids were also frequently used. Overall, 210 children (67.5%) required oxygen supplementation, 96 (36.4%) received high-flow oxygen therapy and 33 (10.6%) were admitted to the PICU. The median length of hospital stay was 7 days (IQR 5–9). One in-hospital death occurred during the study period.

Selected cases with severe or atypical extrapulmonary manifestations included hepatitis, anemia requiring red blood cell transfusion, cardiorespiratory arrest requiring advanced organ support, neurologic manifestations beyond febrile seizures and 1 fatal case with multiorgan failure. These rare events are reported in aggregate to preserve patient confidentiality.

Comparison by Co-infection Category

Pharyngitis and moderate-to-severe distress were more frequent among children with bacterial co-infection (pharyngitis 33.3%, $P = 0.02$; moderate-to-severe CRS 59.2%, $P = 0.02$) (Table 2). RSV co-infection was not associated with worse clinical outcomes; however, it was associated with a higher prevalence of hyponatremia (50.0% in RSV co-infected vs. 16.5% in non-RSV co-infected children, $P = 0.03$). Data on RSV immunoprophylaxis were incomplete. Among the 12 patients with RSV co-infection, information was available for six, with only 1 having received nirsevimab.

Overall, clinical presentation, laboratory inflammatory markers, need for respiratory support, PICU admission and length of hospital stay were broadly comparable across co-infection categories. Similar patterns were observed in the subgroup of patients admitted to the PICU, except for higher neutrophil-to-lymphocyte ratios (NLR) among those with bacterial co-infection (Table, Supplemental Digital Content 3, https://links.lww.com/INF/G644).

Comparison by Age Group

Infants younger than 1 year (n = 139) had more frequent wheezing, had a higher prevalence of moderate-to-severe respiratory distress, and required respiratory support more often than older

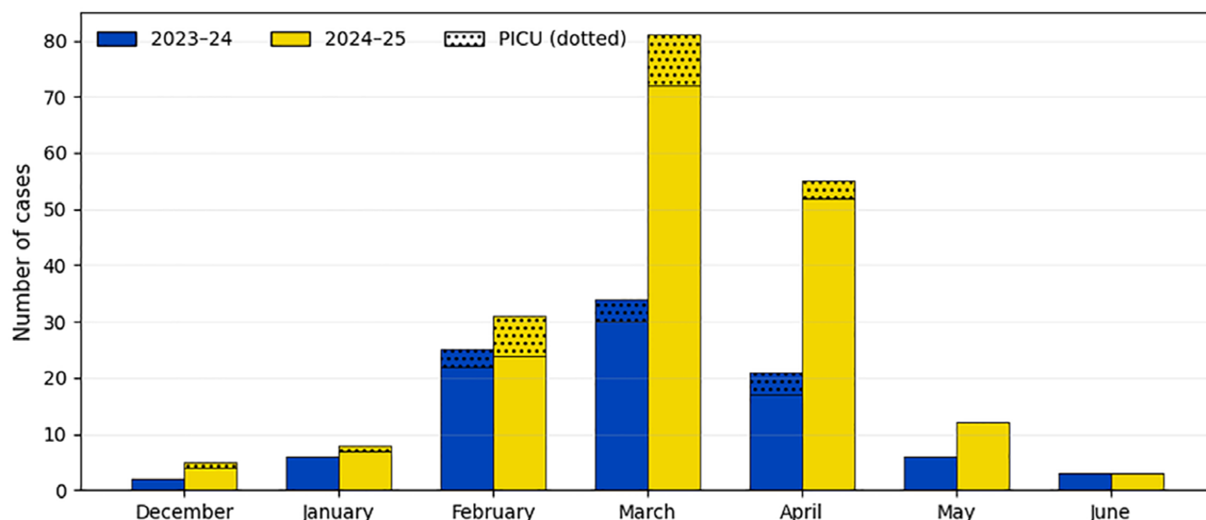

FIGURE 1. Monthly distribution of hMPV-associated hospital admissions (January 2023–June 2025).

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TABLE 2. Comparison of Clinical Characteristics and Outcomes by Mutually Exclusive Co-infection Category

	hMPV-only Infection (n = 165)	Co-infection With RSV (n = 12)	Other Viral Co-infection (n = 88)	Bacterial Co-infection (n = 47)	*P* Value
Age, mo	13 (4–36)	15 (4–36)	16 (6–37)	13 (5–40)	0.48
Comorbidity	50 (30.5)	4 (33.3)	29 (33.0)	15 (31.9)	0.97
Fever	124 (75.2)	9 (75.0)	73 (83.9)	40 (85.1)	0.27
Pharyngitis	12 (9.8)	0 (0.0)	10 (11.3)	10 (33.3)	**0.02**
Wheezing	44 (36.1)	1 (16.7)	26 (35.1)	11 (36.7)	0.89
Moderate-severe CRS	34 (32.4)	1 (10.0)	17 (32.7)	16 (59.2)	**0.02**
NLR	1.4 (0.8–2.6)	2.5 (1.1–3.6)	1.7 (1.1–3.3)	1.7 (0.9–4.1)	0.24
CRP, mg/L	16.6 (3.6–48.4)	15.5 (3.2–50.2)	21.4 (7.1–62.9)	16.5 (7.1–52.6)	0.64
PCT, ng/mL	0.2 (0.1–0.6)	0.2 (0.1–0.9)	0.2 (0.1–1.8)	0.1 (0.1–1.2)	0.50
Hyponatremia	21 (14.2)	4 (50.0)	12 (17.1)	10 (22.2)	0.06
Consolidation	74 (44.8)	7 (58.3)	40 (45.4)	25 (53.1)	0.63
Antibiotic	90 (55.2)	7 (58.3)	58 (66.7)	46 (97.9)	**<0.01**
Respiratory support	114 (69.1)	6 (50.0)	58 (66.7)	32 (68.1)	0.66
Admission to PICU	14 (8.5)	1 (8.3)	10 (11.5)	8 (17.0)	0.36
Hospitalization >7 days	68 (41.2)	5 (41.7)	35 (39.8)	21 (44.7)	0.96

Data are presented as median (IQR) or n (%). Percentages are calculated on available (nonmissing) observations.
Bold values indicate statistically significant results ($P < 0.05$).

TABLE 3. Comparison of Demographic, Clinical, Laboratory, Imaging, Treatment and Outcome Variables by Age Group

	<1 Yr (n = 139)	≥1 Yr (n = 173)	*P* Value
Comorbidity	16 (11.5)	82 (47.7)	**<0.01**
Fever	95 (68.3)	151 (87.8)	**<0.01**
Pharyngitis	5 (4.8)	27 (21.1)	**<0.01**
Wheezing	44 (42.7)	38 (29.5)	**0.04**
Moderate-to-severe CRS	39 (48.1)	29 (25.7)	**<0.01**
NLR	1.0 (0.6–1.7)	2.3 (1.4–4.8)	**<0.01**
CRP, mg/L	13.7 (3.3–32.6)	24.8 (6.4–72.2)	**<0.01**
PCT, ng/mL	0.1 (0.1–0.4)	0.3 (0.1–1.8)	**0.02**
Hyponatremia	21 (17.6)	26 (17.1)	0.91
Consolidation	43 (30.9)	103 (59.5)	**<0.01**
Bacterial co-infection	20 (14.4)	27 (15.7)	0.75
Antibiotic	68 (49.6)	133 (77.3)	**<0.01**
Respiratory support	108 (77.7)	102 (59.3)	**<0.01**
Admission to PICU	13 (9.4)	20 (11.6)	0.52
Hospitalization >7 d	58 (41.7)	71 (41.0)	0.90

Data are presented as median (IQR) or n (%). Percentages are calculated on available (nonmissing) observations.
Bold values indicate statistically significant results ($P < 0.05$).

children (77.7% vs. 59.3%; $P < 0.01$). In contrast, children 1 year old and older (n = 173) more commonly had underlying comorbidities (47.7% vs. 11.5%; $P < 0.01$), higher inflammatory markers (NLR, CRP and PCT; all $P \leq 0.02$) and radiographic consolidation (59.5% vs. 30.9%; $P < 0.01$). Antibiotic use was also more frequent in older children (77.3% vs. 49.6%; $P < 0.01$) (Table 3).

Rates of PICU admission did not differ significantly between age groups ($P = 0.52$).

Predictors of Severe Outcomes

In adjusted mixed-effects logistic regression models, moderate-to-severe respiratory distress (CRS 4–12) and dehydration were independently associated with both prolonged hospitalization and PICU admission (Table 4). Specifically, moderate-to-severe CRS was associated with prolonged hospitalization (aOR 3.96, 95% CI: 1.97–7.96) and PICU admission (aOR 14.95, 95% CI: 3.78–59.13). Dehydration was associated with prolonged hospitalization (aOR 3.54, 95% CI: 1.34–9.35) and PICU admission (aOR 6.49, 95% CI: 2.12–19.82).

Higher base excess values were independently associated with both prolonged hospitalization (aOR 1.39, 95% CI: 1.15–1.68) and PICU admission (aOR 1.22, 95% CI: 1.03–1.45). Fatigue and radiologic consolidation (with or without pleural effusion) were independently associated with PICU admission (fatigue: aOR 3.05, 95% CI: 1.14–8.18; consolidation: aOR 6.28, 95% CI: 2.48–15.93), but not with prolonged hospitalization.

Underlying comorbidities were also independently associated with an increased risk of prolonged hospitalization (aOR 2.97, 95% CI: 1.72–5.15) and PICU admission (aOR 2.71, 95% CI: 1.23–5.98).

DISCUSSION

In this large multicenter cohort of children hospitalized with laboratory-confirmed hMPV infection across Italy during the post-COVID-19 era, we documented a substantial clinical burden, with more than two-thirds of patients requiring oxygen supplementation and approximately 1 in 10 requiring PICU admission. These findings reinforce that hMPV is a clinically relevant cause of pediatric LRTI requiring hospitalization, particularly in early childhood.[11]

Hospital admissions clustered in the late winter and early spring, consistent with prepandemic observations from temperate Northern Hemisphere settings and with large prospective surveillance data from the United States showing hMPV circulation peaking later than RSV and exhibiting greater interannual variability.[5,12] In the post-COVID-19 period, changes in respiratory virus circulation and the widespread use of multiplex molecular diagnostics have likely contributed to increased detection of hMPV.[7]

The age distribution observed in our cohort is consistent with the established epidemiology of hMPV, with most hospitalizations occurring in children younger than 5 years and nearly half in infants younger than 1 year. Infants showed more severe respiratory involvement, including higher rates of wheezing, moderate-to-severe respiratory distress and need for respiratory support.[13–15] These findings are biologically plausible and consistent with prior studies identifying young age as a determinant of severe hMPV disease.[16] At the same time, our data complement recent large-scale prospective evidence showing that, compared with RSV, children hospitalized with hMPV tend to be older and more likely to have underlying medical conditions.[12] This age–comorbidity interplay highlights distinct clinical phenotypes of hMPV infection across pediatric age groups and suggests that risk stratification strategies should not be limited to infancy alone.

Clinically, fever and cough predominated, while wheezing and moderate-to-severe respiratory distress were common, particularly in younger children. The association between hMPV infection

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TABLE 4. Predictors of Prolonged Hospitalization and PICU Admission in Children Hospitalized With hMPV Infection

	cOR (95% CI)	*P* Value	aOR (95% CI)	*P* Value
Prolonged hospitalization				
Any underlying comorbidity	2.72 (1.67–4.45)	**<0.001**	2.97 (1.72–5.15)	**<0.001**
Fatigue	2.18 (1.20–3.94)	**0.010**	1.66 (0.80–3.47)	0.174
Moderate-to-severe CRS	3.29 (1.78–6.11)	**<0.001**	3.96 (1.97–7.96)	**<0.001**
Dehydration	3.02 (1.24–7.36)	**0.015**	3.54 (1.34–9.35)	**0.011**
HCO_3^-	1.19 (1.04–1.36)	**0.011**	1.21 (1.04–1.39)	**0.012**
BE	1.41 (1.17–1.71)	**<0.001**	1.39 (1.15–1.68)	**<0.001**
Consolidation ± pleural effusion	1.50 (0.95–2.36)	0.079	1.51 (0.94–2.42)	0.088
PICU admission				
Comorbidity	2.57 (1.24–5.34)	**0.011**	2.71 (1.23–5.98)	**0.014**
Fatigue	3.50 (1.47–8.31)	**0.005**	3.05 (1.14–8.18)	**0.027**
Moderate-to-severe CRS	11.60 (3.22–41.76)	**<0.001**	14.95 (3.78–59.13)	**<0.001**
Dehydration	5.03 (1.91–13.19)	**0.001**	6.49 (2.12–19.82)	**0.001**
HCO_3^-	1.18 (1.01–1.37)	**0.036**	1.19 (1.01–1.39)	**0.041**
BE	1.23 (1.04–1.45)	**0.014**	1.22 (1.03–1.45)	**0.024**
Consolidation ± pleural effusion	6.01 (2.41–15.03)	**<0.001**	6.28 (2.48–15.93)	**<0.001**

BE indicates base excess; cOR, crude odds ratio.
Each adjusted model included the candidate predictor shown in the row and age in months as fixed effects, with study site included as a random effect.
Bold values indicate statistically significant results ($P < 0.05$).

and wheezing in early childhood is well described, with multiple studies reporting frequent hMPV detection among infants hospitalized for wheezing illnesses and ongoing uncertainty regarding long-term respiratory sequelae such as recurrent wheeze or asthma.[17–20] Our findings further support including hMPV in the differential diagnosis of infants presenting with acute wheeze during the respiratory virus season.

Radiologic findings were largely nonspecific. Consolidation was common, whereas pleural effusion was rare, consistent with previous pediatric cohorts.[21,22] Importantly, in older children, the combination of consolidation and elevated inflammatory markers may mimic bacterial pneumonia and contribute to diagnostic uncertainty and high antibiotic exposure.

Almost half of patients had a co-detected pathogen, but overall severity and outcomes were broadly comparable across mutually exclusive co-infection categories. Bacterial co-infection was associated with higher rates of pharyngitis and moderate-to-severe respiratory distress, while viral co-infections, including RSV, were not associated with worse outcomes.[4,11] The absence of a clear severity signal associated with RSV co-infection in our cohort should be interpreted with caution, given the limited number of RSV co-infected cases and incomplete information on RSV immunoprophylaxis with long-acting monoclonal antibodies, such as nirsevimab.[23] Nevertheless, the progressive implementation of universal RSV immunoprophylaxis may contribute to reshaping the epidemiology of severe respiratory infections in early childhood, with hMPV potentially assuming a relatively greater role in age groups previously dominated by RSV.

We observed an association between RSV co-infection and hyponatremia. Although mechanistic inference is not possible, hyponatremia is a recognized complication of acute infections and may reflect dehydration and/or SIADH-like physiology, supporting early electrolyte assessment in children with severe respiratory presentations or multiple pathogen detection.[24]

Among children admitted to the PICU, those with bacterial co-infection showed higher NLR values, a finding that may at least partly reflect their older age, as higher NLR values are expected in older children. The overall similarity in disease severity and clinical presentation between children with hMPV alone and those with viral co-detections suggests that hMPV itself plays a central role in driving severe lower respiratory tract illness, while co-detected respiratory viruses may frequently represent coincidental findings rather than true contributors to disease severity.

Underlying medical conditions, including immunocompromised status, have consistently been identified as risk factors for severe and prolonged hMPV infection. In our cohort, comorbidities were associated with an approximately 2-fold increased risk of both prolonged hospitalization and PICU admission. They were more common among older children, whereas most infants were previously healthy. These findings are consistent with large prepandemic pediatric cohorts showing that most children ≥2 years of age hospitalized with RSV or hMPV had comorbidities, and that children hospitalized with hMPV tend to be older and more medically complex than those with RSV. In our cohort, among children admitted to the PICU, comorbidities were more frequent in children with bacterial co-infection. Overall, these findings support prioritizing children with underlying conditions as a key target group for future preventive strategies, potentially extending beyond infancy to include older pediatric age groups.

A key contribution of this study is the identification of simple, bedside predictors of severe outcomes. Moderate-to-severe respiratory distress assessed by the CRS and dehydration were independently associated with both prolonged hospitalization and PICU admission, while fatigue and consolidation identified children at higher risk for intensive care. These readily available clinical parameters may support early risk stratification and triage decisions in routine care.[9,25]

The association between higher base excess and adverse outcomes should be interpreted cautiously.

Rather than reflecting a virus-specific effect, it likely captures systemic physiologic stress and compensatory metabolic responses, for instance, related to dehydration and/or evolving acid–base derangements. Nevertheless, it may serve as an objective adjunct to clinical assessment in selected patients.

Antibiotic exposure was frequent, despite the predominantly viral etiology. Children receiving antibiotics had higher CRP and PCT values, suggesting that antibiotic prescribing was likely influenced by inflammatory markers, radiologic findings, disease severity and concern for bacterial co-infection. However, because this was an observational retrospective study and the timing of antibiotic initiation relative to laboratory testing was not uniformly assessed, these findings should be interpreted descriptively. Similar patterns have been reported in other hMPV cohorts and underscore

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the need for diagnostic-driven antimicrobial stewardship.[4,11] Integrating multiplex molecular results with objective severity markers and predefined reassessment or discontinuation criteria may help reduce unnecessary antibiotic use, particularly in older children presenting with bacterial pneumonia–like phenotypes.

Although hMPV is predominantly a respiratory pathogen, rare severe or atypical manifestations were observed in this cohort, including hepatic, hematologic, neurologic manifestations and life-threatening systemic complications. These observations are consistent with sporadic reports in the literature and highlight the need for clinical vigilance in severe or atypical presentations.[26–28]

Strengths of this study include its multicenter design, broad geographic representation across Italy and focus on the post-COVID-19 period. As such, our findings add novel and timely evidence to the existing literature, which is largely based on prepandemic cohorts.

This study has several limitations. First, its retrospective design relies on routinely collected clinical data, resulting in missing information for some variables, particularly laboratory and blood gas parameters. The number of missing observations is therefore reported for each variable, and complete-case analysis was applied within each regression model. Second, bacterial testing was not standardized and was more frequently performed in children with more severe disease, potentially introducing ascertainment and misclassification bias. Third, several subgroup comparisons and univariable analyses were performed without formal adjustment for multiple comparisons. Therefore, some statistically significant associations may reflect chance findings, and these results should be interpreted as exploratory and hypothesis-generating. Fourth, the analysis was limited to hospitalized children; therefore, our findings reflect only the more severe end of the disease spectrum and likely represent the "tip of the iceberg," as we lacked data on nonhospitalized children, milder cases managed in the community and asymptomatic infections. As a result, the overall burden and full clinical spectrum of hMPV infection in the pediatric population may be underestimated. Finally, viral load, genotype and long-term respiratory outcomes were not assessed.

In conclusion, this multicenter study shows that hMPV infection is associated with substantial clinical burden among hospitalized children, particularly infants and children with underlying comorbidities. However, because the study included only hospitalized cases and lacked a population denominator or comparator pathogen group, it was not designed to estimate the overall burden of hMPV disease in the pediatric population. Our findings highlight that simple bedside indicators, including respiratory distress and hydration status, may help identify children at risk for severe outcomes. Further studies using formal predictive performance analyses are needed to compare these clinical markers with pathogen-based, laboratory-based or combined risk stratification approaches. If validated in future studies, these pragmatic clinical markers may support earlier risk stratification, guide management decisions, and inform future preventive strategies targeting both infants and medically vulnerable older children.

REFERENCES

1. van den Hoogen BG, de Jong JC, Groen J, et al. A newly discovered human pneumovirus isolated from young children with respiratory tract disease. *Nat Med*. 2001;7:719–724.
2. Vinci A, Lee PJ, Krilov LR. Human metapneumovirus infection. *Pediatr Rev*. 2018;39:623–624.
3. Garg A, Singh R, Gupta D, et al. Human metapneumovirus (HMPV): current insights and future perspectives. *Przegl Epidemiol*. 2025;79:178–186.
4. Yang S, Lu S, Guo Y, et al. Human metapneumovirus in children with acute lower respiratory infections: effects on clinical and disease severity. *BMC Pediatr*. 2025;25:709.
5. Wang X, Li Y, Deloria-Knoll M, et al; Respiratory Virus Global Epidemiology Network. Global burden of acute lower respiratory infection associated with human metapneumovirus in children under 5 years in 2018: a systematic review and modelling study. *Lancet Glob Health*. 2021;9:e33–e43.
6. Abdulkader RS, Vijay N, Potdar V, et al; Virus Research and Diagnostic Laboratory Network and the Model for Integrated Influenza Surveillance in Tamil Nadu. Epidemiology of human metapneumovirus (HMPV) in India: a cross-sectional study. *Lancet Reg Health Southeast Asia*. 2025;41:100667.
7. Mohammadi K, Faramarzi S, Yaribash S, et al. Human metapneumovirus (hMPV) in 2025: emerging trends and insights from community and hospital-based respiratory panel analyses-a comprehensive review. *Virol J*. 2025;22:150.
8. Bakkers MJG, Ritschel T, Tiemessen M, et al. Efficacious human metapneumovirus vaccine based on AI-guided engineering of a closed prefusion trimer. *Nat Commun*. 2024;15:6270.
9. Yoon Y, Park E, Choi JS, et al. Risk factors for pediatric intensive care unit admission in children with human metapneumovirus infections. *Infect Chemother*. 2025;57:358–367.
10. Moracas C, Poeta M, Grieco F, et al. Bacterial-like inflammatory response in children with adenovirus leads to inappropriate antibiotic use: a multicenter cohort study. *Infection*. 2025;53:935–946.
11. Howard LM, Edwards KM, Zhu Y, et al. Clinical features of human metapneumovirus-associated community-acquired pneumonia hospitalizations. *Clin Infect Dis*. 2021;72:108–117.
12. Goldstein LA, Michaels MG, Salthouse A, et al. Human metapneumovirus and respiratory syncytial virus in children: a comparative analysis. *Pediatrics*. 2025;156:e2024070218.
13. Chen L, Miao C, Chen Y, et al. Age-specific risk factors of severe pneumonia among pediatric patients hospitalized with community-acquired pneumonia. *Ital J Pediatr*. 2021;47:100.
14. Simon AK, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age. *Proc Biol Sci*. 2015;282:20143085.
15. Poeta M, Moracas C, Albano C, et al. Pertussis outbreak in neonates and young infants across Italy, January to May 2024: implications for vaccination strategies. *Euro Surveill*. 2024;29:2400301.
16. Papenburg J, Hamelin ME, Ouhoummane N, et al. Comparison of risk factors for human metapneumovirus and respiratory syncytial virus disease severity in young children. *J Infect Dis*. 2012;206:178–189.
17. Esper F, Martinello RA, Boucher D, et al. A 1-year experience with human metapneumovirus in children aged <5 years. *J Infect Dis*. 2004;189:1388–1396.
18. Heymann PW, Carper HT, Murphy DD, et al. Viral infections in relation to age, atopy, and season of admission among children hospitalized for wheezing. *J Allergy Clin Immunol*. 2004;114:239–247.
19. Williams JV, Tollefson SJ, Heymann PW, et al. Human metapneumovirus infection in children hospitalized for wheezing. *J Allergy Clin Immunol*. 2005;115:1311–1312.
20. Coverstone AM, Wang L, Sumino K. Beyond respiratory syncytial virus and rhinovirus in the pathogenesis and exacerbation of asthma: the role of metapneumovirus, bocavirus and influenza virus. *Immunol Allergy Clin North Am*. 2019;39:391–401.
21. Hilmes MA, Daniel Dunnavant F, Singh SP, et al. Chest radiographic features of human metapneumovirus infection in pediatric patients. *Pediatr Radiol*. 2017;47:1745–1750.
22. Guier-Bonilla L, Yock-Corrales A, Vargas-Acuña MT, et al. Hospitalizations due to acute respiratory tract infections caused by human metapneumovirus in Costa Rican children. *Bol Med Hosp Infant Mex*. 2025;82:238–244.
23. Semple MG, Cowell A, Dove W, et al. Dual infection of infants by human metapneumovirus and human respiratory syncytial virus is strongly associated with severe bronchiolitis. *J Infect Dis*. 2005;191:382–386.
24. Królicka AL, Kruczkowska A, Krajewska M, et al. Hyponatremia in infectious diseases—a literature review. *Int J Environ Res Public Health*. 2020;17:5320.
25. Caracciolo S, Minini C, Colombrita D, et al. Human metapneumovirus infection in young children hospitalized with acute respiratory tract disease: virologic and clinical features. *Pediatr Infect Dis J*. 2008;27:406–412.
26. Vehapoglu A, Turel O, Uygur Sahin T, et al. Clinical significance of human metapneumovirus in refractory status epilepticus and encephalitis: case report and review of the literature. *Case Rep Neurol Med*. 2015;2015:131780.
27. Mori A, Kawano Y, Hara S, et al. A nationwide survey of human metapneumovirus-associated encephalitis/encephalopathy in Japan. *Brain Dev*. 2023;45:197–204.
28. Hennawi HA, Khan A, Shpilman A, et al. Acute myocarditis secondary to human metapneumovirus: a case series and mini-review. *Glob Cardiol Sci Pract*. 2024;2024:e202452.

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