Comparison of Clinical Features of Pediatric Respiratory Syncytial Virus and Human Metapneumovirus Infections

To the Editor—Respiratory syncytial virus (RSV) has long been known to be an important cause of morbidity and mortality in the young pediatric age group. The more recently identified human metapneumovirus (hMPV) is now increasingly recognized as a cause of acute respiratory tract disease in all age groups,[1,2] with symptomatic disease most often seen in young children, especially those less than 1 year old.[3,4] Infections due to hMPV are an important cause of pediatric hospitalizations,[5,6] but to our knowledge the spectrum of clinical manifestations has not been fully defined.

In this study, we determined the local prevalence of hMPV infection and RSV infection among children aged 0–60 months during the winter seasons from November 2004 through April 2006 and compared the clinical manifestations of the 2 infections in a subset of the study population. We also examined the influence of comorbidities on the clinical course of the diseases.

Studies were performed under a protocol approved by the institutional review board of North Shore University Hospital. Discarded respiratory tract samples (nasopharyngeal aspirates, nasopharyngeal washes, nasopharyngeal swabs in viral transport media [Universal Transport Medium, Diagnostic Hybrids], transtracheal aspirates, and sputum), collected during the period from November 2004 through April 2006 and stored at −70°C, were obtained from 653 children (433 children aged 0–24 months and 220 children aged 25–60 months) who were symptomatic for a respiratory disease. Samples were submitted to the North Shore University Hospital Clinical Virology Laboratory, Manhasset, New York, for routine respiratory virus testing by means of direct immunofluorescence for influenza A, influenza B, parainfluenza 1, 2, and 3, adenovirus, and RSV and by means of R-Mix rapid cell culture (Diagnostic Hybrids). Total nucleic acids were extracted from a 200-μL specimen aliquot by using NucliSENS magnetic silica extraction reagents (bioMérieux) and the NucliSENS miniMAG or NucliSENS easyMAG extraction platforms (bioMérieux). Molecular detection of RSV RNA and hMPV RNA was performed by using NucliSENS analyte-specific reagents (bioMérieux) according to in-house validated protocols and published studies.[7,8]

Standardized case report forms were completed by means of retrospective review of the medical records of a subset of patients who tested positive for RSV, hMPV, or both and for whom medical records were available. Patient demographics, clinical findings, comorbidities, and radiologic results were recorded. Fever was defined as any temperature greater than 38°C. Comorbidity was defined as any other diagnosis that was present at the time of the evaluation, for example, a history of substantial prematurity, reactive airway disease,

TABLE 1. Comparison of Patient Characteristics and Clinical Features in Human Metapneumovirus (hMPV) and Respiratory Syncytial Virus (RSV) Infections

Characteristic	hMPV-infected patients (n = 26)	RSV-infected patients (n = 35)	P
Age			.916
0–24 months	17	23	...
25–60 months	9	12	...
Comorbidities	19	22	.400
Upper respiratory tract infection	8	10	>.99
Lower respiratory tract infection	10	19	.301
Mechanical ventilation	5	4	.477
Fever	13	1	<.001
Cough	16	24	.568
Vomiting	4	9	.367
Diarrhea	1	9	.034
Rash	5	0	.011
Rhinorrhea	2	15	.003
Retractions	4	11	.230
Wheeze	6	8	.984
Crackles	6	12	.343
Pneumonia	9	6	>.99
Chest radiography performed	12	8	.055
Antibiotics prescribed	19	22	.481
Duration of pediatric intensive care unit stay, days, mean	1.3	1.9	.878
Duration of hospital stay, days, mean	3.6	3.5	.855

NOTE. Data are no. (%) of patients, unless otherwise indicated.

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chronic lung disease, congenital heart disease, muscular disease, or malignancy.

Statistical analysis was performed by means of SAS statistical analysis software, version 9.1.3 (SAS Institute). The χ^2 test or Fisher exact test was used to compare parameters. For nonparametric comparisons, that is, length of pediatric intensive care unit stay and length of hospital stay, the Wilcoxon rank sum test was used. A P value of less than .05 was considered to indicate a statistically significant difference.

We collected 653 unique patient specimens during the study period. A combination of all test methods identified 143 specimens (22%) as RSV positive (113 [79%] of 143 RSV-positive specimens were from children aged 0–24 months, and 30 [21%] of 143 RSV-positive specimens were from children aged 24–60 months) and 35 specimens (5%) as hMPV positive (25 [71%] of 35 hMPV-positive specimens were from children aged 0–24 months, and 10 [29%] of 35 hMPV-positive specimens were from children aged 24–60 months). RSV infections peaked in January, and hMPV infections peaked in March and April. Hospitalization was required for 35 (24%) of 143 RSV-infected children, and 4 (11%) of the 35 hospitalized children were admitted to the pediatric intensive care unit. A significantly higher proportion of hMPV-infected children, 20 (57%) of 35, were hospitalized ($P <$ .01), and 4 (20%) of the 20 hospitalized children were admitted to the pediatric intensive care unit.

The clinical comparison of 61 children with RSV infection and/or hMPV infection is presented in the Table. Overall, the clinical manifestations of hMPV infection were similar to those of RSV infection, as in other studies.[6,9,10] However, children with hMPV infection were significantly more likely to present with a fever or with a rash, whereas RSV-infected children were significantly more likely to have diarrhea or rhinorrhea. Rashes were not uniformly described in all medical records. Three children had a nonspecified type of rash on the face, neck, or palms, and 2 children had a maculopapular rash with no location noted. A rash was also described in 16.7% of hMPV-infected patients in a Canadian study[9] and in 12.9% of hMPV-infected children in a Hong Kong study; in the Hong Kong study, the duration of the rash was a few hours to 1 day.[11] RSV-infected and hMPV-infected patients were equally likely to have an underlying comorbidity. Coinfection with hMPV and RSV was extremely uncommon, and there was no evidence that respiratory disease was more severe in coinfected children.

The higher rate of hospitalization in hMPV-infected children may have been due to the lack of a specific diagnosis at the time of presentation, because the routine direct immunofluorescence and R-mix culture did not screen for hMPV (the results of the hMPV molecular testing were not available to the clinician). In the future, the availability of rapid testing for hMPV could reduce unnecessary hospitalization, as well as inappropriate antibiotic use. Additional studies, to evaluate further the clinical and economic effect of rapid diagnosis by means of molecular testing, would be valuable.

There were some limitations to our study. The relatively small number of medical records available for review may have skewed results toward patients who were hospitalized, because those charts were more readily available. In addition, the data that we obtained retrospectively are limited by the subjectivity inherent in information recorded by physicians.

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C. Beneri, DO; C. C. Ginocchio, PhD; R. Manji, BS; S. Sood, MD

From Stony Brook University Medical Center, Stony Brook (C.B.), North Shore University Hospital, Manhasset (C.C.G., S.S.), and North Shore–Long Island Jewish Health System Laboratories, Lake Success (C.C.G., R.M.), New York.

Address reprint requests to Christy Beneri, DO, SUNY Stony Brook, HSC T11 Room 030, Stony Brook, NY 11794 (cbeneri@notes.cc.sunysb.edu).

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