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ORIGINAL ARTICLE

Human Metapneumovirus Infection is Associated with Severe Respiratory Disease in Preschool Children with History of Prematurity

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asthma;
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Background: Human metapneumovirus (HMPV) is a recently discovered respiratory pathogen of the family Paramyxoviridae, the same family as that of respiratory syncytial virus (RSV). Premature children are at high risk of severe RSV infections, however, it is unclear whether HMPV infection is more severe in hospitalized children with a history of severe prematurity.
Methods: We conducted a retrospective analysis of the clinical respiratory presentation of all polymerase chain reaction-confirmed HMPV infections in preschool-age children (≤5 years) with and without history of severe prematurity (<32 weeks gestation). Respiratory distress scores were developed to examine the clinical severity of HMPV infections. Demographic and clinical variables were obtained from reviewing electronic medical records.
Results: A total of 571 preschool children were identified using polymerase chain reaction-confirmed viral respiratory tract infection during the study period. HMPV was identified as a causative organism in 63 cases (11%). Fifty–eight ($n = 58$) preschool-age children with HMPV

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infection were included in this study after excluding those with significant comorbidities. Our data demonstrated that 32.7% of children admitted with HMPV had a history of severe prematurity. Preschool children with a history of prematurity had more severe HMPV disease as illustrated by longer hospitalizations, new or increased need for supplemental O_2, and higher severity scores independently of age, ethnicity, and history of asthma.
Conclusion: Our study suggests that HMPV infection causes significant disease burden among preschool children with a history of prematurity leading to severe respiratory infections and increasing health care resource utilization due to prolonged hospitalizations.

1. Introduction

Respiratory tract infections are the second leading cause of death among children who are aged < 5 years worldwide.[1] Human metapneumovirus (HMPV), a relatively new respiratory pathogen of the family Paramyxoviridae—the same family as that of respiratory syncytial virus (RSV)—was discovered only a decade ago,[2] however, it is now recognized as a frequent cause of acute lower respiratory tract infections in the pediatric population.[1,4–6] Most children who are <5 years old have already been infected with HMPV,[3] with the overall prevalence of acute HMPV infection in the pediatric population ranging from 5–25% with some variation across different regions and age groups.[5,7–12] It has been estimated that approximately 27,000 HMPV-related hospitalizations will occur per year in the future among preschool children in the US.[13] This estimation is alarming and emphasizes the need to investigate the epidemiology and pathogenesis of HMPV in children.

HMPV shares the same clinical respiratory signs and symptoms as RSV, including cough, wheezing, rales, hypoxemia, and respiratory distress in high-risk groups.[5,14–16] HMPV lower respiratory tract infections contribute to 5–15% of all hospitalizations in infants and young children.[17,18] Despite the importance of this pathogen in the pediatric population, no treatment or prevention strategies have been developed,[19,20] which may reflect the lack of understanding of the risk factors that increase the morbidity and mortality of HMPV infection in children.[19,20] Interestingly, prematurity has recently been suggested to be an important risk factor for severe HMPV infection.[20–22] Young children with a history of prematurity are at an increased risk of hospitalization and frequent outpatient visits due to HMPV bronchiolitis and pneumonia,[20–23] epidemiologies that resemble the phylogenetically and clinically related pathogen RSV.[21] Other risk factors associated with severe HMPV infection include immunosuppression, young age, and existence of underlying comorbidities, such as asthma, congenital heart diseases, neuromuscular disorders, and other chronic pulmonary conditions.[23–25]

Although the aforementioned risk factors have been reported, there are limited data about the clinical presentation of severe HMPV infection in hospitalized premature children. Moreover, the link between the severity of HMPV respiratory infections and the history of prematurity in hospitalized children still needs to be better defined. Accordingly, the aim of this cross-sectional study was to examine the clinical severity of HMPV infection in hospitalized children aged ≤ 5 years with and without a history of severe prematurity (<32 weeks gestation), using respiratory parameters derived from standardized bronchiolitis scores validated by our group,[26,27] and health care utilization (i.e, length of admission).

2. Materials and methods

2.1. Study participants

We conducted a retrospective cross-sectional analysis of a cohort of preschool children aged ≤ 5 years who were admitted with HMPV infection, which was confirmed using polymerase chain reaction (PCR) analysis, at Children's National Medical Center (CNMC) between January 2013 and February 2014. Viral PCRs were performed on patients who presented to the hospital with suspected viral respiratory tract infection at the discretion of the clinician. We only included children with positive PCR for HMPV and excluded individuals with mixed viral infections.

Patients with significant comorbidities such as cardiorespiratory conditions (other than asthma and prematurity), genetic syndromes, and immunosuppression were excluded from the study. This study was approved by the Institutional Review Board at CNMC.

2.2. Clinical and demographic variables

Clinical and demographic variables were obtained by reviewing electronic medical records (EMR) at CNMC. Demographic variables comprised gestational age in weeks, age, sex, and ethnicity. Other clinical variables included tachypnea, retractions, abnormal breath sounds (wheezing), asthma diagnosis, oxyhemoglobin saturation values by pulse oximetry (SaO_2), supplemental oxygen (O_2) requirement relative to the patient's baseline, length of hospitalization, and the need for admission to the pediatric intensive care unit (PICU). In our institution, PICU admission criteria include worsening hypoxemia or hypercapnia, worsening respiratory distress, continuing requirement for >50% O_2, hemodynamic instability, and apnea. In addition, in the setting of viral respiratory tract infection PICU admission is also required for the following: (1) initiation of