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Original Article

Sole infection by human metapneumovirus among children with radiographically diagnosed community-acquired pneumonia in a tropical region

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Background Limited information is available on the role of human metapneumovirus (HMPV) as the unique pathogen among children hospitalized for community-acquired pneumonia (CAP) in a tropical region.

Objective We aimed to describe HMPV infection among children with CAP investigating bacterial and viral co-infections.

Patients and methods A prospective study was carried out in Salvador, North-East Brazil. Overall, 268 children aged <5 years hospitalized for CAP were enrolled. Human metapneumovirus RNA was detected in nasopharyngeal aspirates (NPA) by reverse transcription polymerase chain reaction. Sixteen other bacterial and viral pathogens were investigated by an expanded panel of laboratory methods. Chest X-ray taken on admission was read by an independent paediatric radiologist unaware of clinical information or the established aetiology.

Results Human metapneumovirus RNA was detected in NPAs of 11 (4.1%) children, of which 4 (36%) had sole HMPV infection. The disease was significantly shorter among patients with sole HMPV infection in comparison with patients with mixed infection (4 ± 1 versus 7 ± 2 days, $P = 0.03$). Three of those four patients had alveolar infiltrates.

Conclusion Sole HMPV infection was detected in children with CAP in Salvador, North-East Brazil. HMPV may play a role in the childhood CAP burden.

Keywords Acute respiratory infection, lower tract respiratory infection, new respiratory virus, respiratory viral infection.

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Introduction

Human metapneumovirus (HMPV) was first described in 2001[1] and is a significant respiratory pathogen, particularly among children.[2] Nonetheless, limited information is available on the role of HMPV as the unique pathogen among children hospitalized for radiographically diagnosed community-acquired pneumonia (CAP) in a tropical region. We have recently published the results on the aetiology of Brazilian children hospitalized with CAP.[3] Nevertheless, HMPV has not been investigated in this sample yet.

We aimed to describe HMPV infection among children hospitalized with CAP, identifying bacterial and viral co-infections.

Methods and patients

From September/2003 to May/2005, every child aged ≤5 years hospitalized with CAP in the Paediatric Centre Professor Hosannah de Oliveira, Salvador, North-East Brazil, was prospectively evaluated after written informed consent. The initial diagnosis was made by the paediatrician on duty based on the report of respiratory complaints and pulmonary infiltrates or pleural effusion in a chest X-ray (CXR) taken on admission. CXR was later read by a paediatric radiologist blinded to clinical and aetiological information.

On admission, nasopharyngeal aspirates (NPA) and blood were collected. The NPA and serum samples were kept at −70 and −20°C, respectively, until testing. All

samples were shipped at −70°C to Finland by airplane. Human metapneumovirus RNA was detected by reverse transcription (RT)-PCR in NPA. The HMPV investigation was carried out at the University Central Hospital Laboratory Division, Helsinki, Finland. Infections caused by influenza A and B viruses, respiratory syncytial virus, parainfluenza virus types 1, 2 and 3, adenovirus, rhinoviruses, enterovirus, *Streptococcus pneumoniae*, nontypable *Haemophlus influenzae, Moraxella catarrhalis, Chlamydia pneumoniae, Chlamydia trachomatis, Mycoplasma pneumoniae and Simkania negevensis* were also searched for and the methods for their detection, and the results were published.[3]

Fever was defined as axillary temperature >37.5°C[4] and tachypnoea as RR ≥50 breaths/min in children aged 2–11 months and RR ≥ 40 breaths/min in children from 12 months of age onwards.[5]

For categorical variables, the results are presented as proportions and the Fisher's exact test was used to identify associations. For continuous variables, summary measures are reported and comparison was performed by the Student's t or Mann–Whitney *U* tests as appropriate. The study protocol was approved by the Ethics Committee of the Federal University of Bahia.

Results

Of 268 children studied, 11 (4.1%) were positive for HMPV RNA and 4 (36%) had sole HMPV infection. Table 1 presents the aetiological agents of the seven cases with co-infections. Human metapneumovirus infection frequency varied from 0% to 25% per month ($P = 0.08$). Overall, the median age of HMPV infected cases was 7 months (mean 12 ± 11; range, 1–39) and there were 7 (64%) males. The median duration of disease was 6 days (range, 3–9), and the most frequent findings were cough (100%), fever, difficulty breathing, chest indrawing and crackles (91% each), tachypnoea (89%), chest retraction (82%), wheezing (73%) and vomiting (64%). Three (27%) were transferred to another hospital. The median length of hospitalization for those discharged was 7 days (range, 2–29), and all patients recovered. Pneumonia was radiographically confirmed in the final evaluation in nine cases, while one CXR was normal and one non-readable. The radiographic findings were alveolar ($n = 8$) or interstitial ($n = 1$) pulmonary infiltrates, hyperinflation ($n = 2$) and atelectasis ($n = 1$). The disease was significantly shorter among patients with sole HMPV infection in comparison with patients with mixed infection (4 ± 1 versus 7 ± 2 days, $P = 0.03$). Significant differences were not found when comparing the other characteristics between those groups (data not shown). Three of four patients with sole HMPV infection had alveolar infiltrates, and one had a normal CXR.

Table 1. Co-infections among patients with HMPV infection and community-acquired pneumonia

Co-infections	HMPV cases
Rhinovirus	2
Chlamydia trachomatis	1
Adenovirus	1
Enterovirus	1
Rhinovirus + RSV	1
Streptococcus pneumoniae + Rhinovirus + RSV	1

HMPV, human metapneumovirus.

Discussion

Of 11 (4.1%) cases detected, 4 (1.5%) had probable sole HMPV infection. Taking into account that three of these four cases showed alveolar infiltrates, HPMV is a potential causative agent of childhood CAP in the tropical region. In an Israeli study of children with CAP and alveolar infiltrate, HMPV was the single pathogen in 6.5% of cases but bacterial infection was not investigated.[6] Human metapneumovirus was detected as the unique pathogen in 2.4% of children with respiratory disease in Rio de Janeiro, a subtropical region of Brazil; however, those authors neither searched for bacterial agents nor took CXR to confirm CAP.[7] In an Italian research, 5 (4.9%) children with CAP had HMPV infection, being single in two and mixed (viral–bacterial) in three[8]; the two single pathogen cases presented alveolar or interstitial infiltrate. On the contrary, six children with CAP in Taipei presented HMPV always along with other pathogens; in each case, a bacterial infection was diagnosed and other viral infection was detected in 2; the frequency of HMPV in that study was 5.2%.[9] In a Japanese series of children with acute respiratory tract infection, pneumonia attributable to HMPV was detected in 2.6% but concomitant bacterial infection was not searched for.[10] In Egyptian adults with lower respiratory tract infection, HMPV was detected in 13.6% of 88 patients, 4.5% in co-infection with *S. pneumoniae* and 9.1% as the only pathogen.[11] Our data add evidence that HMPV may be a true causative agent of childhood CAP.

It is important to emphasize the strict criteria used to diagnose CAP. Every included case had available CXR that was read by the paediatrician on duty on admission. Afterwards, a further CXR reading was performed by a paediatric radiologist blinded to clinical or aetiological information. Both readings followed the World Health Organization standardization for the diagnosis of pneumonia.[12]

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Patients with sole infection had significantly shorter disease. The impact of co-infections on disease severity has been reported.[13] Our findings add information on the impact of co-infections on the length of disease before hospitalization. Human metapneumovirus affected young children as the majority were infants. The development of preventive measures for this virus is challenging, and the affected age strata must be taken into account.

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Conflicts of interest

M Lappalainen has received reimbursement for attending a symposium organized by Abbott and Roche Diagnostics, and also received a fee for speaking from Abbott and Roche Diagnostics.

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