SHORT REPORT: HUMAN METAPNEUMOVIRUS IN CHILDREN WITH INFLUENZA-LIKE ILLNESS IN YUCATAN, MEXICO

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Abstract. The present study suggests that human metapneumovirus (hMPV) is an important cause of community-acquired respiratory infections in children. We report the detection of hMPV in a pediatric population with influenza-like illness in the subtropical area of Yucatan in Mexico. Our data also shows that hMPV circulates in the community with other respiratory pathogens.

Human metapneumovirus (hMPV) was described by van den Hoogen and others who isolated the virus from young children with respiratory infections in The Netherlands. Recently, hMPV was reported in Mexico as a cause of respiratory tract infections in hospitalized young children. The Yucatan region of Mexico has a subtropical climate and the epidemiology of common pathogens can differ from that seen in other regions of Mexico with different locations, climates, and epidemic patterns. In this study, we were interested to know the frequency of hMPV in children ≤ 5 years of age in the context of two factors that have been poorly analyzed, the role of hMPV in community-acquired acute respiratory infections and its prevalence in the tropics.

From December 1999 through December 2002, a total of 98 throat swabs from children ≤ 5 years of age were submitted to the respiratory virus laboratory in Merida, Yucatan, Mexico. All samples were negative for influenza A or B viruses by indirect immunofluorescence assay at the time of collection. Ninety throat swabs were analyzed. Original samples were thawed and used for extraction of viral RNA using the QIAamp viral RNA mini kit (Qiagen, Valencia, CA). cDNA was amplified as described by Ellis and others. To amplify a fragment of the hMPV F gene, we used a nested reverse transcription–polymerase chain reaction (RT-PCR) with specific primers to obtain a PCR product of 311 basepairs (Zambon MC, unpublished data) (primer sequences available upon request). The remaining cDNA was frozen at −80°C until subsequent analysis by multiplex RT-PCR to detect other respiratory viruses.

False-negative results were ruled out by using a positive control for hMPV, which in the nested PCR produced a unique and clear band of the appropriate size. False-positive results were ruled out by including water as a negative control every sixth clinical sample. Both positive and negative controls were tested with clinical samples in all experiments. Negative samples for hMPV were ruled out either because of the presence of a band of unexpected size or the absence of bands.

Human metapneumovirus was detected in 18 (20%) of 90 clinical samples from children ≤ 5 years of age with influenza-like illness (ILI). Our investigation showed that hMPV in Yucatan, Mexico is an important cause of community-acquired respiratory tract infections in the pediatric population. In addition to the recent report of hMPV in San Luis Potosi Mexico, our data are not surprising because the Yucatan region has been reported to have the highest rates of acute respiratory tract infections in Mexico. Conversely, Noyola and others studied hospitalized children with well-defined respiratory conditions, who showed a different pattern of respiratory pathogens when compared with our study.

The hMPV-positive patients ranged in age from 13 to 60 months (mean age = 32.6 months), and the virus was detected more frequently in children between 13 and 36 months of age (13%) and in infants more than three years of age (5%). The most common symptoms in hMPV-positive patients included fever (100%), cough (95%), rhinorrhea (75%), headache (54%), and general malaise (33%). There was no statistically significant difference in clinical symptoms between patients positive or negative for hMPV. Nine (50%) of 18 patients were treated with antibiotics at the time that they were seen by a clinician. Another important observation was that 13 (72%) of 18 positive samples were obtained from patients with an onset of symptoms ≤ 24 hours after sample collection. Thus, collection of specimens early in the illness increases the likelihood of detecting hMPV.

Human metapneumovirus was detected from 1999 through 2002. Fifty percent of the positive samples were detected in the summer of 2001 (September) and 2002 (May, June, and August) when the peak of ILI was recorded and also when Yucatan has its greatest rainfall, temperature, and relative humidity. The remaining samples were detected in December 1999, February 2000, and January and March 2001. The pattern of hMPV circulation is similar to what we previously reported for influenza virus. In contrast, Noyola and others reported hMPV only during the winter months, which suggests that differences in location and climate between Yucatan and San Luis Potosi alter the epidemic pattern of hMPV. Our data are consistent with those of a study in Hong Kong that reported the presence of hMPV in the late spring and summer.

The fact that samples were collected from children with ILI suggests possible circulation of several other respiratory viruses at the same time. Although all samples were negative for influenza A and B viruses at the time of collection, we analyze these samples retrospectively by multiplex RT-PCR. We detected mixed infections with hMPV and influenza and other respiratory viruses. Overall, 44 (48%) of 90 samples were positive for one or more respiratory viruses. Coinfections with hMPV and other viruses were detected in seven...
patients (Table 1). Coinfections with hMPV and other respiratory viruses have previously been detected at low rates of 1–3%.8,9 Our study reports a higher rate of 8%. However, this is not surprising because we used a sensitive PCR assay to detect other respiratory viruses.4

Our results show that hMPV cocirculates in the Yucatan region of Mexico with other respiratory pathogens and is as prevalent as influenza virus. The low frequency at which respiratory syncytial virus (RSV) was detected may be explained by the type of clinical sample (throat swabs are not optimal for RSV isolation) and the case definition used to recruit patients. Coinfections were all detected in children more than 30 months of age, except in one infant who was only six months of age.

In conclusion, hMPV showed an incidence rate of 20% in children with ILI in the subtropical region of Yucatan, Mexico. There is a clear peak of circulation of hMPV and other respiratory viruses during the summer months. A more carefully designed survey will give us a better epidemiologic picture of hMPV circulating in this region.

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REFERENCES

<table>
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<tr>
<th>Virus</th>
<th>No. (%) positive</th>
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<tbody>
<tr>
<td>hMPV</td>
<td>11 (12)</td>
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<tr>
<td>hMPV + Influenza H3</td>
<td>5 (5)</td>
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<tr>
<td>HMPV + RSV</td>
<td>2 (2)</td>
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<tr>
<td>Influenza A H3</td>
<td>18 (20)</td>
</tr>
<tr>
<td>RSV A</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Influenza H3 + RSV</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Total</td>
<td>44/90 (48)</td>
</tr>
</tbody>
</table>

* RSV = respiratory syncytial virus.