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Case Report

J Clin Gynecol Obstet. 2019;8(4):107-110

# A Report of Two Cases of Human Metapneumovirus Infection in Pregnancy Involving Superimposed Bacterial Pneumonia and Severe Respiratory Illness

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## Abstract

Human metapneumovirus (HMPV) is a cause of mild to severe respiratory viral infection. There are few descriptions of infection with HMPV in pregnancy. We present two cases of HMPV infection occurring in pregnancy, including a case of superimposed bacterial pneumonia in a pregnant woman after HMPV infection. In the first case, a 40-year-old woman at 29 weeks of gestation developed an asthma exacerbation in association with a positive respiratory pathogen panel (RPP) for HMPV infection. She was admitted to the intensive care unit (ICU) for progressive respiratory failure. In the second case, a 36-year-old woman at 31 weeks of gestation developed respiratory distress in association with a positive RPP for HMPV. A subsequent sputum culture was positive for beta-lactamase producing *Haemophilus influenzae* raising concern for superimposed bacterial pneumonia. HMPV can be an important cause of severe respiratory illness in pregnant women and may predispose pregnant women to superimposed bacterial pneumonia.

**Keywords:** Metapneumovirus; Pregnancy; Pneumonia; Bacterial

## Introduction

Human metapneumovirus (HMPV) is an enveloped, negative sense ribonucleic acid (RNA) virus in the Pneumoviridae family discovered in 2001 to be a cause of respiratory illness in children [1]. It shares a similar structure and clinical presentation to respiratory syncytial virus (RSV). Treatment is currently with supportive care. HMPV polymerase chain reaction (PCR) testing has been found to be positive in 17.2% of pregnant women without asthma but with upper respiratory infection (URI) [2].

In a literature search on PubMed of "human metapneumovirus AND pregnant" and "human metapneumovirus AND pregnancy", we identified two case reports of severe HMPV infection in pregnant women in the USA, and one descriptive report of 25 pregnant women infected with mild HMPV infection in rural Nepal. In a case by Haas et al (2012), a 24-year-old woman at 30 weeks of gestation developed respiratory failure requiring intensive care unit (ICU) admission secondary to HMPV pneumonia [3]. The case by Fuchs et al (2017) describes an 18-year-old patient at 36 weeks of gestation admitted to an intensive care unit (ICU) for acute respiratory distress syndrome, which was treated with extracorporeal membrane oxygenation (ECMO) [4]. Although none of the women infected with HMPV in Lenahan's 2017 report from Nepal had severe respiratory illness, these women were more likely to give birth to children who were small for gestational age compared to women who were not infected with HMPV during pregnancy [5].

To better characterize the potential clinical course of HMPV in pregnancy, we present two additional cases of HMPV infection in pregnant women. The second case details the first description of superimposed bacterial pneumonia in a pregnant woman infected with HMPV.

## Case Reports

### Case 1

A 40-year-old woman (G10P2072) at 29 weeks and 5 days of gestation with a history of mild intermittent asthma presented to the Emergency Department of Women and Infants Hospital (WIH) of Rhode Island due to shortness of breath. Her prenatal care was remarkable only for daily enoxaparin injections due to multiple prior miscarriages despite a negative thrombophilia panel. On presentation, she reported fever, productive cough, and body aches, but denied chest pain, sore throat, nausea, vomiting, and diarrhea. She was afebrile (36.8 °C) and normotensive (123/76 mm Hg). Her pulse was 107 beats per minute (bpm) and respiratory rate was 20 breaths per minute. Her physical examination was normal including bilateral clear lung sounds. A chest X-ray (CXR), respiratory pathogen panel (RPP), and rapid flu test were all negative.

Manuscript submitted September 13, 2019, accepted December 2, 2019

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doi: https://doi.org/10.14740/jcgo573

Fetal monitoring revealed a normal baseline heart rate with moderate variability, positive accelerations, and no decelerations. She was discharged home with daily *per os* (PO) 30 mg prednisone as a steroid burst for presumed asthma exacerbation.

She returned to triage 2 days later with worsening symptoms, and was then found to have bilateral wheezing, a pulse of 120 bpm and a respiratory rate of 32 breaths per minute. Fetal monitoring was unremarkable. She remained afebrile (37 °C). Her white blood cell count was 11.2 × $10^3$ / µL. A repeat CXR showed left basilar atelectasis and bilateral trace pleural effusions. She received an ipratropium/albuterol nebulizer treatment, and was started on albuterol, and PO prednisone was increased to 50 mg daily. She required increasing amounts of oxygen up to 45 L 100% $O_2$ high flow nasal cannula in order to maintain $O_2$ saturation > 95%. Due to concerns for further respiratory decompensation, she was transferred to the ICU. A repeat RPP was positive only for HMPV. On day 2 of ICU admission, she was started on bi-level positive airway pressure (BiPap) due to increased work of breathing. On day 3, she spiked a fever to 38.6 °C and CXR showed right lower lobe (RLL) airspace disease concerning for superimposed pneumonia. She was started on vancomycin and piperacillin-tazobactam. Sputum cultures returned on day 5 and demonstrated normal respiratory flora. Vancomycin was discontinued on day 4 after her methicillin-resistant *Staphylococcus aureus* (MRSA) screen by nasal swab was negative. Additionally, due to worsening cough and increased oxygen requirement, she was diuresed with furosemide out of concern for pulmonary edema. She continued to remain afebrile and had overall improving respiratory status throughout her ICU stay. A repeat CXR on day 7 showed low lung volumes with atelectasis but no pleural effusions or consolidations. She was transferred out of the ICU on day 9. She continued to require 1 - 3 L nasal cannula until day 16 when her $O_2$ saturation on room air was > 95%, and she was discharged home. At 38 weeks and 6 days of gestation, she went into spontaneous labor, and had an uncomplicated vaginal delivery of a 3,600 g female infant.

## Case 2

A 36-year-old (G4P2102) at 31 weeks of gestation presented to the WIH Emergency Department for evaluation of fever and sore throat. She was followed for her prenatal care by the high-risk clinic due to multiple ongoing medical conditions (Table 1), but had otherwise routine prenatal care. On presentation, she denied cough or shortness of breath at that time and had an ambulatory $O_2$ saturation of 98-99%. She was diagnosed with group A streptococcal pharyngitis and discharged with a 10-day course of amoxicillin. Four days later she returned complaining of nonproductive cough and shortness of breath. She was afebrile (36.8 °C) and normotensive (112/62 mm Hg). Her pulse was 76 bpm, respiratory rate was 18 breaths per minute, and $O_2$ saturation was 93% on room air. On exam, she had bilateral diffuse expiratory wheezes and diminished lung sounds at the bases. A fetal nonstress test revealed variable decelerations. She was placed on oxygen via nasal cannula, and after a

**Table 1.** Summary of Individual Case Report of HMPV Infection in Pregnancy

| Study | Age | OB history | Weeks of gestation at HMPV infection | PMH | Month of infection | Complications | Length of hospital stay | Delivery GA (method) | Fetal weight |
|---|---|---|---|---|---|---|---|---|---|
| Haas et al, 2012 [3] | 24 | G1P0 | 30 w 0 d | None | January | ICU | N/A | 36 w (N/A) | N/A |
| Fuchs et al, 2017 [4] | 18 | G1P0 | 36 w 2 d | Asthma, obesity | Late March | ECMO | 10 d | 36 w 4 d (PCD) | 2,530 g |
| Current case 1 | 40 | G10P2072 | 29 w 5 d | Asthma | Late March | ICU | 16 d | 38 w 6 d (SVD) | 3,600 g |
| Current case 2 | 36 | G4P2102 | 31 w 0 d | Tobacco use, seizures, Charcot-Marie-Tooth, history of opioid dependence, bipolar disorder | Late March | Superimposed bacterial pneumonia with *Haemophilus influenzae* | 8 d | 39 w 0 d (RCD) | 3,230 g |

OB: obstetrics; G: gravida; P: para; w: week; d: day; HMPV: human metapneumovirus; PMH: past medical history; ICU: intensive care unit; ECMO: extracorporeal membrane oxygenation; PCD: primary cesarean delivery; SVD: spontaneous vaginal delivery; RCD: repeat cesarean delivery; N/A: not applicable; GA: gestational age.

period of prolonged monitoring, no further decelerations were noted. A CXR showed that the lungs were well inflated and clear with no evidence of pneumonia, pulmonary edema, pleural effusion, or pneumothorax. She was admitted for hypoxia secondary to a URI. An RPP was positive only for human metapneumovirus. Respiratory therapy administered albuterol nebulizer treatments. Over the ensuing days, she continued to have an oxygen requirement of 1 - 2 L to maintain oxygen saturation above 95%, and on exam she had scattered rhonchi and diminished air movement. On hospital day 3, she developed a productive cough with white sputum and crackles in the left lung base. A repeat CXR was unchanged. A sputum culture was positive for *Haemophilus influenzae* that was beta lactamase positive and resistant to amoxicillin, which the patient was still taking for streptococcal pharyngitis. Amoxicillin was replaced with ceftriaxone. Over the following days, she had gradual clinical improvement, and was discharged on hospital day 8 with a 7-day course of cefdinir. She went on to have an elective repeat cesarean delivery of a 3,230 g female infant at 39 weeks of gestation.

## Discussion

HMPV is a common cause of URIs in children, but its manifestations in pregnant women have only recently been described. In pregnant individuals, HMPV is the second most common cause of PCR-positive URIs after human rhinovirus [2]. Our cases add to the existing literature by describing HMPV in pregnant women with existing asthma and superimposed bacterial pneumonia (Table 1, [3, 4]).

The patients we report were tested for HMPV using the GenMark Dx ePlex respiratory pathogen panel, a multiplex nucleic acid amplification test (GenMark Diagnostics, Inc., Carlsbad, CA). In a multicenter prospective comparison of the ePlex RPP and PCR, the ePlex RPP was found to have a positive percent agreement of 94.7% and a negative percent agreement of 99.7% for HMPV [6]. Additionally, estimated background carriage rates for HMPV are low. In one study of swabs of 2,685 asymptomatic individuals, only three (0.11%) tested positive for HMPV by PCR [7]. In a second study, none of 158 asymptomatic subjects had a positive PCR for HMPV [8]. Thus, it seems quite likely that both patients we describe were truly infected with HMPV and that their respiratory illness was a result.

The first case supports the conclusion of the case by Fuchs et al [4] that HMPV infection in a pregnant woman with asthma can lead to progressive respiratory failure requiring ICU level of care and ultimately ECMO. HMPV has been shown to be associated with nearly one quarter of URI among pregnant women with asthma [2].

Our second case demonstrates the risk of superimposed bacterial pneumonia with beta-lactamase-producing *Haemophilus influenzae* in a pregnant woman infected with HMPV. Bacterial and viral pneumonia with ongoing HMPV infection have previously been described in non-pregnant patients, particularly in children [9-11]. As this is the first case to present superimposed bacterial pneumonia in HMPV in pregnancy, it is unclear whether pregnant women with HMPV have increased risk of pneumonia compared to non-pregnant individuals.

What is notable about our cases and the two existing cases is that all four occurred in the third trimester, potentially highlighting increased susceptibility to HMPV at that time during the pregnancy. Additionally, all four cases occurred during the winter or early spring, consistent with the typical seasonality of HMPV, which peaks in incidence slightly later than RSV and influenza.

While both of the patients we describe delivered infants at term of normal birth weights, following up on the outcomes of pregnancy in patients with HMPV is important in future research. As seen in Lenahan's study, there may be an increased risk of SGA infants among pregnant women infected with HMPV [5]. There is additional evidence that children born to women with asthma who had a URI during pregnancy, including due to HMPV, have an increased risk of infant wheezing compared to children born to women with asthma who did not have a URI during pregnancy [12].

Currently, treatment for HMPV infection is only supportive, and there is no vaccination for HMPV. Although there has been *in vitro* research and *in vivo* case reports that ribavirin and intravenous (IV) immunoglobulin may be effective against HMPV, this would not be a viable option for treating pregnant women due to the teratogenicity of ribavirin [13]. Research to develop an HMPV vaccine is ongoing however only one candidate, a live attenuated vaccine, has progressed to a phase I clinical trial, and was shown to be over-attenuated in humans [14].

### Conclusions

HMPV is an important cause of viral infections in pregnant women. Infections can range from mild URI symptoms to severe respiratory failure. Our cases further highlight the role of HMPV as a cause of severe respiratory failure in a pregnant woman with asthma, and as a risk factor for superimposed bacterial pneumonia. We recommend that practitioners consider HMPV infection in the differential diagnosis of pregnant women presenting in the third trimester with respiratory illness. Our cases additionally highlight the importance of heightened vigilance for superimposed pneumonia in pregnant women with confirmed HMPV infection as well as early, aggressive treatment with antibiotics if pneumonia is suspected. Finally, considering the potential for severe respiratory illness in pregnant women due to HMPV, further research is needed into antiviral therapies and vaccination that are effective and safe in pregnancy.

## Acknowledgments

Thanks to our patients who allowed us to write up their cases.

## Financial Disclosure

None to declare.

## Conflict of Interest

None to declare.

## Informed Consent

Both patients described have approved of our publication of their cases.

## Author Contributions

J. Emont and K. Chung wrote each of the cases, the introduction, and discussion sections. D. Rouse provided editing and writing contributions to all sections of the manuscript.

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