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### Case Report

#### Life threatening severe Influenza A Virus (H1N1) infection in Pregnancy

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**ABSTRACT:** H1N1 influenza is an emerging threat that is life threatening to pregnant women in the third trimester. Pregnant women are a high-risk group for morbidity and mortality from influenza (H1N1). During the current pandemic of H1N1 influenza, few cases of H1N1 have been reported in pregnancy. We report a case of H1N1 influenza in a 23-year old female with 28 weeks of gestation, who developed acute respiratory distress syndrome, required mechanical ventilation and eventually recovered.

**KEY WORDS:** *H1N1; Acute Respiratory Distress Syndrome; Pregnancy; Influenza*

#### INTRODUCTION

The first reports of the 2009 H1N1 virus were confirmed in California by the Centre for Disease Control and Prevention (CDC) in April 2009. During seasonal influenza epidemics, pregnant women constitute a high-risk group for disease-related morbidity and mortality. There are reports of an increased risk of miscarriage, birth defect and preterm delivery when pregnancy is associated with influenza infection. However, much less is known about pregnancy and novel influenza A (H1N1).<sup>1</sup> The effects of influenza during pregnancy have been noted in previous pandemics, particularly the increased mortality in pregnant women compared with the general population.<sup>2</sup>

#### CASE REPORT

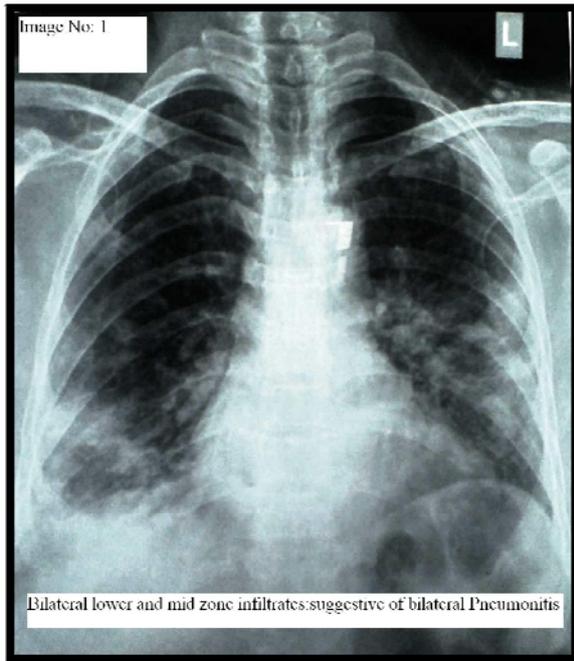
A 23-year old lady primigravida with 28 weeks of gestation presented with rhinorrhoea, breathlessness, vomiting, cough with scanty yellow coloured sputum and fevers for two days. Past medical history was significant for patent ductus arteriosus (PDA) ligation two year ago. She was evaluated in the emergency room. Her pulse rate was 130/min, respiratory rate 34/min, blood pressure 102/72 mm of Hg, and temperature 102°F.

Her oxygen saturation (SpO<sub>2</sub>) ranged from 70% to 75%.

On physical examination, she had bilateral rhonchi and crepitations in her lungs. She had tachycardia with gallop rhythm on auscultation. After initial evaluation she was shifted to intensive care unit for further management.

On investigation her hemoglobin was 10.5 gram %, white blood count (WBC) was 8700 cmm and platelet count was within normal limits. Her chest radiogram revealed bilateral middle and lower lobe infiltrates consistent with pneumonia (**Figure 1**). Arterial blood gas analysis (ABG) was suggestive of respiratory acidosis with PO<sub>2</sub> 34 mmHg. Renal functions tests, liver function tests, blood sugar level and serum electrolytes were within normal limits. Two dimensional transthoracic echocardiogram was suggestive of mild pulmonary hypertension (30 mmHg) calculated by TR jet with mild tricuspid regurgitation and trivial mitral regurgitation. Left ventricular systolic and diastolic function was normal with overall ejection fraction of 60%.

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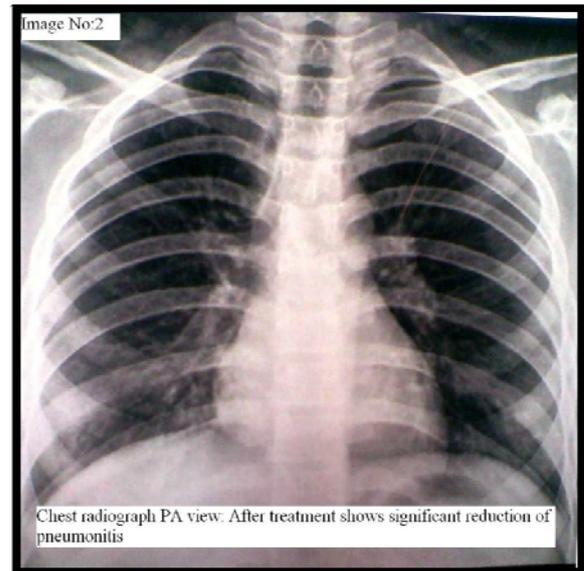


**Figure 1: Bilateral lower and mid zone infiltrates suggestive of bilateral pneumonia**

In view of the clinical scenario, we sent nasopharyngeal and throat swabs for H1N1 testing to National Institute of Virology (NIV), Pune. When the patient was admitted, she was started on Ceftriaxone and Azithromycin as an empirical antibacterial cover. After 4 hours of admission to intensive care unit, the patient developed acute respiratory distress syndrome (ARDS). She had difficulty breathing, respiratory rate of 44/min and temperature of 103<sup>0</sup> F. Her oxygen saturation (SpO<sub>2</sub>) declined to 60%. Considering short history of respiratory symptoms with bilateral pulmonary infiltrates with ARDS, she was empirically started on Oseltamivir 75 mg twice a day. She was intubated and put on artificial ventilator. After 24 hours of ventilation, she showed some improvement in the form of improving oxygenation (SpO<sub>2</sub>) up to 82% and reduction in tachycardia (pulse rate 96/min).

After two days, we got the report of nasopharyngeal swab which was positive for H1N1 [Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) assay]. On the third day of admission the gynecologist diagnosed intrauterine death (IUD) on ultrasound examination and proceeded with normal delivery. In the post delivery period the patient's oxygenation status showed some improvement but she was still requiring high FiO<sub>2</sub> to maintain proper oxygenation. Over the next four days the patient's condition remained critical. After 5 days of admission patient was weaned from ventilator and extubated. Repeat chest radiograph on 5<sup>th</sup> day of admission shows partial reduction in the infiltrates and on 17<sup>th</sup> day there was near total

resolution of radiographic findings compared to 1<sup>st</sup> day (**Figure 2**). Patient was discharged on 18<sup>th</sup> day from hospital in ambulatory state, but unfortunately we were not able to save the baby.



**Figure 2: Chest radiograph PA view: After treatment shows near total resolution of bilateral pneumonia**

## DISCUSSION

The effects of influenza during pregnancy have been noted in previous pandemics, particularly the increased mortality in pregnant women compared with the general population. The effect of alterations in maternal immunity is a predisposition to more severe manifestations of infections due to influenza. A number of changes occur in a pregnant woman's immune system to allow tolerance to paternally derived fetal antigens. Some suppression of cell-mediated immunity occurs, and maternal lymphocytes demonstrate a diminished proliferative response to soluble antigens and to allergenic lymphocytes. Decreased numbers of T-helper cells have been documented, either because of an absolute decrease in numbers or because of a reduction in the CD4-to-CD8 ratio.<sup>3,4</sup> The patient in this report rapidly progressed to ARDS. Along with pregnancy our patient had past history of PDA ligation with residual pulmonary hypertension (30 mmHg) which was the confounding risk factor for developing H1N1 infection and progress to ARDS and respiratory failure. Similar cases were reported by Fridman D et al with high mortality as out of two patients one developed acute respiratory distress syndrome, required intubation, and eventually died.<sup>2</sup> Webb et al in their study of 722 patients noted that 66 patients (9.1%) admitted to the ICU with 2009 H1N1 influenza were pregnant women<sup>3</sup>. Janice K et al<sup>4</sup> in their study of 102

pregnant patients with H1N1, reported that 8% died, with H1N1 influenza-specific maternal mortality ratio of 4.3.

Sharma V et al<sup>5</sup> in their study reported that deaths from H1N1 appeared to occur primarily in individuals with underlying risk factors, such as pregnancy, underlying chronic respiratory illness, diabetes, obesity, etc. Similarly the patient in this case report has pregnancy as risk factor to develop complications of H1N1. Patients with H1N1 viral infection present with acute respiratory symptoms - dry cough, sore throat, nasal congestion and fever. The CDC recommends that clinicians should send nasopharyngeal swabs for rapid detection of antigens for influenzas A and B in patients with fever and respiratory symptoms.<sup>3</sup> If an unsubtypeable influenza A virus infection is found, the specimen should be sent to a state public health laboratory for additional testing to identify H1N1 virus using the real-time PCR technique which is currently recommended for laboratory confirmation of H1N1 viral infection<sup>6</sup>.

Antiviral therapy is often delayed for pregnant patients; it should be reinforced that antiviral therapy should be started as soon as possible based only on clinical presentation of fever and sore throat or cough without waiting for results of laboratory testing, unless another cause of symptoms is reasonably suspected. It is preferable to start antiviral therapy within 48 hours of the first influenza-related symptoms and continue for 5 days. H1N1 virus is sensitive to both oseltamivir (75 mg twice a day) and zanamivir (two 5mg inhalations twice a day). Due to systemic absorption and more experience with oseltamivir, it is the preferred medication. The benefit of treating the influenza outweighs any theoretical risk for the fetus. It is recommended to treat severe cases of H1N1 infection in a hospital, using respiratory support with supplemental oxygen and mechanical ventilation as required.<sup>7</sup> Antibiotic supplementation should be guided by the presence of pneumonia depending on the patterns of resistance in the region. Since pneumococcal pneumonia is frequently a secondary invader, pregnant women who are in risk groups should also be vaccinated against that organism.

Current CDC recommendation suggests that pregnant women who had contact with someone suspected of infection with novel H1N1 influenza virus should receive prophylactic treatment with either oseltamivir (75 mg daily) or zanamivir (two 5 mg inhalations daily) for 10 days. The CDC states that zanamivir is preferable due to its low systemic absorption, but because of its inhaled route of administration, respiratory complications must be considered.<sup>8</sup>

The advisory committee on immunization safety recommends that pregnant women be included in primary targeted groups for vaccination.<sup>9</sup>

Vaccination is also recommended for household contacts of pregnant women; however, chemoprophylaxis is not indicated for otherwise healthy people exposed to influenza. Early empiric treatment should be started if symptoms arise.<sup>8</sup> Currently all subtyped influenza A viruses reported to CDC (99% of all specimens sent to CDC) are H1N1.<sup>10</sup> Obstetricians should be prepared to diagnose and rapidly treat H1N1 and, now with the availability of H1N1 vaccine, to be proactive with vaccination programs to blunt the spread of the infection.

## CONCLUSION

Early diagnosis, early antiviral treatment and efficient intensive care management will definitely reduce overall morbidity and mortality associated with H1N1 infection. H1N1 influenza in pregnancy can be associated with severe complications. H1N1 influenza is especially dangerous to pregnant women. Pregnancy is a risk factor for critical illness related to 2009 H1N1 influenza, which causes maternal and neonatal morbidity and mortality. In the present case report along with pregnancy as risk factor for developing complications associated with H1N1 infection, the past history of PDA ligation with associated residual pulmonary hypertension could be a confounding factor.

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