# Human 2009 influenza A (H1N1) virus infection in a premature infant born to an H1N1-infected mother: placental transmission?

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**SUMMARY: Çetinkaya M, Özkan H, Çelebi S, Köksal N, Hacımustafaoğlu M. Human 2009 influenza A (H1N1) virus infection in a premature infant born to an H1N1-infected mother: placental transmission? Turk J Pediatr 2011; 53: 441-444.**

**Human infection with H1N1 virus reached pandemic status by the spring of 2009. Consequently, the rates of morbidity and mortality related with H1N1 2009 infections have been reported to be higher in pregnant women. H1N1 viremia is rare in the mother, and the risk for transmission of H1N1 2009 influenza from mother to fetus is unknown. To our knowledge, the literature contains only one previous report of a premature infant with H1N1 2009 infection whose mother also had H1N1 2009 infection. Here, we report an H1N1 pandemic influenza 2009-positive female premature infant born at 32 weeks of gestation whose mother had a confirmed H1N1 2009 infection by real-time reverse transcriptase polymerase chain reaction (rRT-PCR). This case suggests that H1N1 2009 virus might be transmitted across the placenta, and therefore, all infants born to an H1N1 2009-positive mother must be evaluated for possible H1N1 2009 infection.**

***Key words: H1N1 2009, influenza A, newborn, pregnant women, transplacental transmission.***

Human infection with 2009 pandemic influenza A (H1N1) virus (commonly known as swine flu) first emerged in April 2009[1]. In May 2009, the virus had spread to other areas of the world and the World Health Organization (WHO) declared a pandemic alert on 11 June 2009[2]. According to recent reports, the Centers for Disease Control and Prevention (CDC) estimates that 22 million people have been infected with H1N1; 98,000 H1N1-related hospitalizations and 3,900 H1N1-related deaths occurred between April and 17 October 2009 in the United States[3].

Pregnant women have a 4- to 5-fold increased rate of serious illness and hospitalization due to influenza[4,5]. To our knowledge, no infections have been reported in infants born to women with H1N1 2009 infection[4], and further, the risk for transmission of novel H1N1 2009 influenza from mother to fetus is unknown[4,6]. To our knowledge, only one premature infant with H1N1 2009 infection whose mother became ill with H1N1 2009 virus during the perinatal period has been reported in the literature previously[7].

Here, we report an H1N1-positive female premature infant born at 32 weeks of gestation whose mother was also infected with H1N1.

## Case Report

In November 2009, a female infant was born by cesarean section at 32 weeks' gestation to a 22-year-old mother with Apgar 1-4-7 at 1, 5 and 10 minutes (min), respectively. The mother had a history of cough, fever, cyanosis, nausea, and vomiting, which started 5 days prior to the delivery. After treatment with amoxicillin/clavulanic acid and paracetamol for 4 days, she presented to our hospital due to deterioration in her general health condition. On admission,

she had dyspnea, cyanosis, a temperature of 38°C, pulse of 122/min, and respiratory rate of 36 breaths/min with an oxygen saturation of 88%. Her white blood cell (WBC) was 6700/mm$^3$ and she had a platelet count of 120,000/mm$^3$. Her initial C-reactive protein (CRP) was negative. Chest radiography showed bilateral diffuse infiltrates. She started receiving ceftriaxone, erythromycin and oseltamivir. However, because of respiratory distress within the first 6 hours, she was intubated and then transferred to an isolated room in an adult Intensive Care Unit. She delivered the premature infant by cesarean section within 24 hours of admission and oseltamivir treatment. After delivery, the mother responded well to antibiotic and oseltamivir and she was extubated on the 7th day of hospitalization. She was discharged 17 days after delivery. The mother's nasal swab sample obtained during hospitalization was tested in the laboratory of the Turkish Ministry of Health with real-time reverse transcriptase polymerase chain reaction (rRT-PCR), a rapid diagnostic test for H1N1, and was found positive. She stated that no influenza vaccination was performed during pregnancy. The placenta was paraffin-sectioned and stained with hematoxylin-eosin (H&E) and was evaluated by a pathologist. Neutrophils, calcification, hyperemia, and hemorrhagic infarct in the placenta were detected under light microscopy.

The delivery was performed in an isolated operation room. The infant had no spontaneous breathing at delivery; thus, positive pressure ventilation was performed and she was intubated due to respiratory distress. Her birth weight was 2050 g (50-90 p), birth length 45 cm (50-90 p) and head circumference 32.5 cm (50-90 p). Physical examination revealed respiratory distress, tachypnea (60 breath/min), cyanosis, and intercostal and subcostal retractions with prematurity findings. She was given one dose of surfactant since air bronchograms were seen in her anteroposterior chest radiography. Ampicillin and gentamicin were also started for possible neonatal sepsis. She was closely monitored for signs and symptoms of influenza in an isolated sterile room in the Neonatal Intensive Care Unit (NICU). No air bronchograms or other findings such as pneumonia were determined in her second chest radiography that was taken 6 hours later; therefore, no other therapies such as a second dose of surfactant or oseltamivir were given. The infection control procedures developed for novel H1N1 infection were applied. Her initial complete blood count at birth was not significantly abnormal, revealing WBC 8220/mm$^3$, hemoglobin 15.9 g/dl and platelet count 322000/mm$^3$. Her CRP level at birth was negative. She was extubated on the second day of life, and oxygen therapy was stopped on the third day of life. She was given ampicillin plus gentamicin for 7 days. No organism was isolated from her blood culture. Since no signs of sepsis or H1N1 2009 infection were detected, she was discharged from the hospital with suggestion of close monitoring for influenza signs. The infant's nasal swab sample was collected immediately after birth and sent for analysis to the same laboratory in order to screen for H1N1 2009 infection. The test result, which was available 48 hours later, was positive for H1N1 2009 infection.

## Discussion

Here, we report a premature infant with H1N1 2009 infection born to an H1N1-positive mother. To the best of our knowledge, this is only the second report of H1N1 2009 infection in a premature infant due to possible transplacental transmission of novel H1N1 2009 virus.

Dulyachai et al.[7] first reported a female infant born at 31 weeks of gestation who had respiratory distress. They stated that the mother had H1N1 2009 virus infection 7 days before delivery. In addition to routine premature care, she was given oseltamivir, as her throat swab specimen was found to be positive for H1N1 2009 infection by real-time PCR. She was also started on cefotaxime for minimal pulmonary infiltrations. Although she was discharged at 28 days of life during the follow-up, the mother died from respiratory failure 7 days after delivery. Our case had similar characteristics as she was also born to an H1N1-infected mother, had respiratory distress and responded well to oseltamivir therapy. Dulyachai et al.[7] suggested that the patient was likely infected *in utero* as she was never exposed to her mother. Similarly, our patient was never exposed to her mother as she was delivered by cesarean section in an isolated sterile isolation room. No H1N1

2009-positive infant was followed up in our NICU in the same period. There was also no H1N1 2009-positive healthcare staff in the NICU. All these data together might suggest a possible placental transmission of the H1N1 2009 infection.

Pregnancy has been reported to be a risk factor for increased rates of illness and death due to both pandemic and seasonal influenza[4]. This increased risk is believed to be associated with several physiologic changes that occur during pregnancy[8]. Pregnancy-related complications of novel H1N1 2009 infection include non-reassuring fetal testing (most commonly fetal tachycardia) and febrile morbidity[9]. A primary life-threatening complication that results in severe illness or death is the development of pneumonia and acute respiratory distress syndrome requiring mechanical ventilation[10]. In agreement with the literature, in our case, the mother had severe pneumonia requiring mechanical ventilation and intravenous antibiotic treatment.

The effect of maternal influenza on the fetus has not yet been fully understood. It is believed that viremia is infrequently seen during influenza, and therefore, placental transmission of the virus might be extremely rare[8, 11]. Human influenza virus primarily infects and causes disease in the respiratory tract. However, human influenza virus infection is also associated with disease in other organs. Influenza virus spreads via blood to other tissues and replicates there[12]. In our patient's mother, systemic infection was evidenced by the viremia, which is rarely reported in humans with influenza[13]. Even if the influenza virus does not have a direct effect on the fetus, fever that often accompanies influenza infection is thought to be associated with adverse fetal effects, especially neural tube defects[8].

During the previous pandemics of 1918 and 1957, remarkably high rates of spontaneous pregnancy loss, preterm delivery and fetal death were reported, especially among women with pneumonia[8]. In good accord with these observations, our case was a premature infant, suggesting that the infection causes preterm delivery. A previous animal study suggested that Hsw1N1, the swine influenza, could be transmitted transplacentally[14]. In addition, it was reported in humans that avian influenza A (H5N1), the highly pathogenic strain of influenza virus, might be transmitted across the placenta; viral genomic sequences of the virus were identified in the placental cytotrophoblasts and the fetal respiratory tract of a pregnant woman infected with H5N1[15,16]. To date, there has been only one previous case that might suggest the possible placental transmission of novel H1N1 2009 virus in humans.

Although apnea, tachypnea, dyspnea, central cyanosis, dehydration, altered mental status, and extreme irritability have been reported as symptoms of more severe disease in young infants[17], no specific findings for newborns have been reported. Our case had respiratory distress characterized by tachypnea, dyspnea and requirement of mechanical ventilation. However, it was not possible to distinguish whether these findings were indeed associated with surfactant deficiency or with H1N1 influenza infection. The rRT-PCR test, which is recommended in the United States as a reliable technique for accurate and rapid diagnosis of H1N1 2009 infection[9,17], was ordered immediately. Respiratory distress syndrome occurs in 25% of preterm infants born ≥30 weeks of gestation[18]. Although respiratory distress may be associated with prematurity, the effect of maternal H1N1 infection on neonatal respiratory distress is unknown. Since the infants' symptoms resolved within 24 hours, which coincided with the availability of the PCR test result, and the infant responded well to surfactant and antibiotic therapy, oseltamivir was not given. No other complications of novel H1N1 virus infection developed in the infant during the follow-up in the NICU.

In conclusion, our case suggests a vertical transmission of novel H1N1 2009 virus. To the best of our knowledge, this is only the second report of H1N1 2009 infection in a premature infant due to possible transplacental transmission of novel H1N1 2009 virus. Therefore, all pregnant women should be monitored for premature delivery, and all infants born to H1N1-positive mothers should be evaluated for H1N1 2009 infection. Future studies including a greater number of infants are required in order to support our finding of possible vertical transmission of H1N1 virus and the effects of maternal H1N1 2009 infection on neonatal outcomes.

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