# A Rare Presentation of Maternal H1N1 in the Second Trimester Resulting in Neonatal Cholestasis in a Twin Pregnancy

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**We report a case of twins born to a mother who developed H1N1 during pregnancy. The babies were delivered by normal vaginal delivery at the gestational age of 27+6 days. Apart from there prematurity complications, they developed neonatal cholestasis. All known causes of neonatal cholestasis were ruled out. The main finding was maternal H1N1 and newborn cholestasis.**

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H1N1 is a human influenza A virus; it is a single-stranded RNA virus belonging to the orthomyxoviridae family[1]. There are three types of this virus: A, B and C. Its incubation period is 1 to 5 days and it is mainly transmitted by aerosol route[1].

H1N1 is considered a pandemic disease by the WHO since April 2009 with the first reported case in Mexico in March 2009[2,3]. Only a few cases have been reported from the Middle East[3].

The most common complications of H1N1 affect the respiratory system. Other complications affect the heart, thymus, liver, and spleen, which are rarely reported[4].

The aim of this report is to present a case of twins who developed neonatal cholestasis since birth; they were born to a mother with H1N1 detected during her second trimester.

**THE CASE**

**Case 1**

A twin baby boy was a product of spontaneous conception of dichorionic diamniotic twin pregnancy, born by normal vaginal delivery at 27 + 6 weeks of gestation. Birth weight was 1.130 kg with an Apgar score of 7, 9 and 10 at 1, 5 and 10 minutes, respectively.

The patient was admitted to the Neonatal Intensive Care Unit (NICU) due to prematurity, Respiratory Distress Syndrome (RDS), suspected sepsis and neonatal jaundice.

Initial laboratory investigations were as follows: CBC white cell count of 2.82 x10^9/l, hemoglobin 15 g/dl, platelets of 209 x10^9/l, C-reactive protein 6.9 mg/L, total protein 40.9 g/l, albumin 18.9 g/l, total bilirubin 329.8 umol/l, direct bilirubin 214.34 umol/l, alkaline phosphatase (ALP) 928 u/l, alanine aminotransferase (ALT) 10 u/l, Gamma-Glutamyl Transferase (GGT) 326.5 u/l, aspartate aminotransferase (AST) 30.2 u/l. The blood group was O positive.

The patient was ventilated soon after birth, given Survanta (beractant) and kept on an invasive and non-invasive ventilator until he was weaned off successfully to room air on day 17 of life. The baby was hemodynamically stable since birth; murmur was detected and did not require any inotropic support.

The patient received intravenous antibiotics and parenteral nutrition for suspected sepsis and Necrotizing Enterocolitis (NEC). Antibiotics were stopped after the result of negative blood, urine and cerebrospinal fluid cultures.

The liver enzymes were elevated and high direct bilirubin was more than 50% of the total bilirubin; therefore, the possibility of neonatal cholestasis was contemplated. Tandem Mass Spectrometry (TMS) ruled out metabolic causes for cholestasis. Newborn screening was normal and TORCH screening was negative. Ultrasound of the abdomen initially showed ill-defined hyperechoic area containing air locules in hepatic segment adjacent to the right portal vein. Repeated sonogram one month later was unremarkable; gallbladder was contracted after feeds, which was considered normal. Hepatobiliary Iminodiacetic Acid (HIDA) scan revealed normal hepatocyte uptake function with significant delayed biliary to bowel transit time suggestive of hepatocellular disease. The patient was kept on ursodeoxycholic acid and discharged on it.

**Case 2**

The second twin baby boy was a product of spontaneous conception of dichorionic diamniotic twin pregnancy, born by normal vaginal delivery at 27 + 6 weeks of gestation. Birth weight was 1.150 kg and Apgar score was 7, 9 and 9 at 1, 5 and 10 minutes, respectively.

The patient was admitted to the NICU due to prematurity, RDS, Patent Ductus Arteriosus (PDA), suspected sepsis and neonatal jaundice.

Initial laboratory investigations were as follows: CBC showed white cell count of 2.59 x10^9/l, hemoglobin 17.6 g/dl, platelets

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of 211 x10^9/l, C-reactive protein 4.7 mg/L, total protein 44.5 g/l, albumin 21.6 g/l, total bilirubin 111.6 (increased to 194) umol/l, direct bilirubin 29.3 (increased to 106) umol/l, alkaline phosphatase (ALP) 553 u/l, alanine aminotransferase (ALT) 7 u/l, Gamma-Glutamyl Transferase (GGT) 141 u/l, aspartate aminotransferase (AST) 25.2 u/l. The blood group is O positive.

Chest X-ray was suggestive of RDS, required intubation at the delivery room and received Survanta, remained ventilated for 7 days and subsequently required nasal CPAP then to room air.

The baby had significant PDA and was treated with intravenous paracetamol for five days; echocardiography showed PDA 2 mm in size with a left to right shunt. The patient received intravenous antibiotics and parenteral nutrition for suspected sepsis. Antibiotics were discontinued after negative cultures.

Neonatal cholestasis was suspected in this twin due to the elevated liver enzymes and high direct bilirubin more than 50% of the total bilirubin. TMS was sent to rule out metabolic causes for cholestasis. Newborn screening was reported normal and TORCH screening was negative. Ultrasound of the abdomen revealed sludge in the biliary tract, no triangular cord sign was seen and gall bladder was contracted after feeds, which was considered normal. HIDA scan revealed normal hepatocyte uptake function with significant delayed biliary to bowel transit time suggestive of hepatocellular disease. The patient was kept on ursodeoxycholic acid and discharged.

The mother was a 24-year-old female, gravida 4 para 3 with a previous miscarriage at 8 weeks of gestation. No known medical illness and oral glucose tolerance test was negative. She presented with lower abdominal pain with no per vaginal bleeding or rupture of membranes and had reactive cardiotocography. She received dexamethasone and magnesium sulfate.

During the second trimester of the pregnancy, she was diagnosed with H1N1 and completed a course of Tamiflu (oseltamivir). No history of ingestion of any other medication during pregnancy.

The liver function test started to improve and the direct bilirubin started to decrease with medication during follow-up one month after discharge. Therefore, the most likely cause of neonatal cholestasis for these boys, after excluding all other causes, was maternal H1N1.

## DISCUSSION

The influenza virus is responsible for respiratory problems in the affected individuals; the severity of the disease ranges from mild cough, respiratory distress, headache, fatigue, and fever to severe pneumonia that requires intubation and leads to septic shock and acute organ failure[5].

H1N1 virus rarely affects any other than the respiratory system[1-5]. In Mexico City in 2010, the first two adult cases of H1N1 with liver involvement were reported[1-5].

Fislova et al found that the virus can reach other organs from the lung by a process of transient viremia, as well as the production of cytokine and chemokine[4]. In 2012, a reported case of a 9-year-old child with acute hepatic failure and H1N1 infection was reported in Kuwait[5]. In 2013, a 21-month-old Qatari child was reported to have H1N1 and abnormal liver function test[6].

A review of respiratory viruses in NICU revealed only one case of neonatal mortality due to influenza virus[1]. Another study in Jordan revealed the side-effect of maternal H1N1 during pregnancy on the newborn[7].

## CONCLUSION

**H1N1 during pregnancy is a serious disease; it can affect the mother as well as the newborn.**

**The severity of the disease differs from one infant to another. Even though hepatic involvement is considered rare in children with H1N1, early investigations and initiation of treatment is a must in order to avoid serious complications.**

**Further studies involving neonates and infection during pregnancy is advised. Guidelines to avoid H1N1 complications during pregnancy are necessary.**

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