

Flu-like symptoms in pregnancy – A case study

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Case

A woman, 35 years of age and gravida 2, para 1 (G2P1), presented at 32 weeks' gestation to a local emergency department in the middle of the influenza season. She had a one-day history of non-productive cough, lethargy, leg cramps, nausea and vomiting. She was afebrile and treated with metoclopramide, paracetamol and intravenous fluids, and subsequently discharged. The next day (day two) she presented to her general practitioner (GP), who performed nasopharyngeal swabs. She re-presented to the emergency department on day three with severe dyspnoea and crepitations in both lungs. Her respiratory rate was 24 breaths/minute, saturating 91% on room air, and she was febrile (38.8°C), tachycardic (113 beats/minute) and hypotensive (98/64 mmHg).

A chest X-ray on day three showed patchy infiltrates consistent with bilateral pneumonia. A follow-up chest X-ray on day four showed extensive bilateral infiltrates consistent with acute respiratory distress syndrome. Arterial blood gases (ABG) showed PaO₂ <60 mmHg, in keeping with type 1 respiratory failure. She was initially commenced on intravenous benzylpenicillin and roxithromycin at her local hospital. When she was transferred to a tertiary hospital, her treatment was changed to cefotaxime and flucloxacillin, following infectious disease consultation. Four days after her initial emergency department presentation, the

nasopharyngeal swabs taken by her GP returned positive for influenza A and she was commenced on oseltamivir 150 mg twice daily via a nasogastric tube.

She required admission to the intensive care unit (ICU), where she also developed hypotension requiring intravenous noradrenaline infusion for inotropic support, significant peripheral oedema requiring frusemide infusion, hypokalaemia, malnutrition requiring nasogastric feeding, and sepsis-related pancytopenia. In addition to maternal clinical decline, fetal cardiotocography showed borderline tachycardia, decreased variability and repetitive unprovoked decelerations, which necessitated delivery of her baby via an emergency caesarean section (category 2) at 34 weeks' gestation.

A male infant was delivered and transferred directly to the neonatal ICU. Agpar (appearance, pulse, grimace, activity, respiration) scores were 6, 7 and 7 at one, five and ten minutes, respectively; mechanical ventilation was required for 20 hours due to respiratory depression.

The woman had received first-trimester care from her GP, followed by regular midwifery-led antenatal care for a low-risk pregnancy. Antenatal records showed that the woman had never received influenza vaccination.

Question 1

How are women who are pregnant affected by influenza?

Question 2

What is the evidence for efficacy and safety of influenza vaccination in women who are pregnant?

Question 3

What is the uptake of influenza vaccination during pregnancy in Australia?

Question 4

How can the uptake of influenza vaccination during pregnancy be increased?

Question 5

How do women who are pregnant access influenza vaccination?

Question 6

How important is early detection and initiation of treatment in pregnant women with influenza?

Answer 1

Women who are pregnant, especially those in their second and third trimesters, are at an increased risk of severe morbidity and mortality from influenza.¹ This is due to:

- increased heart rate, stroke volume and oxygen consumption
 - decreased lung capacity
 - a shift away from cell-mediated immunity towards humoral immunity.
- In an Australian study of 43 women who were pregnant and admitted to hospital with laboratory-confirmed influenza:¹
- 19% were admitted to ICU
 - 10% required vasopressor support

- 40% delivered pre-term
- 19% had a hospital admission of more than seven days.

Answer 2

There is strong evidence that influenza vaccination for women who are pregnant is both efficacious and safe, with no increased incidence of miscarriages, fetal anomalies or neurodevelopmental disorders.² There is also evidence that infants born to mothers vaccinated against influenza during pregnancy, compared with those not vaccinated, had lower rates of laboratory-confirmed influenza (4% versus 10%) and febrile respiratory illness (69% versus 97%) up to 24 months of age.³

The Australian immunisation guidelines recommend that all women who are pregnant be immunised against influenza.

Answer 3

Despite the evidence for vaccination, uptake remains low at approximately 30% of pregnant women in Australia.^{4,5}

Answer 4

One Australian study found that pregnant women who had received information about influenza and vaccination were twice as likely to be vaccinated.⁵ Another study found that 68% of those who were concerned about vaccine safety would consent to the vaccine if their doctor or midwife recommended it.⁴

Answer 5

Although hospitals have a role in providing education and advice about influenza vaccination during pregnancy, the majority of hospital antenatal clinics are not equipped to vaccinate because of a lack of systems infrastructure and facilities such as vaccine refrigeration. Furthermore, obstetricians and midwives perceive that vaccinations are more the responsibility of GPs,⁵ most of whom have vaccine refrigerators at their practices that stock influenza vaccines.

The Australian immunisation guidelines recommend that all women who

are pregnant be immunised against influenza. The vaccine is currently funded for women who are pregnant under the National Immunisation Program.⁶

Answer 6

Testing women who are pregnant for influenza should be done by sending two nasopharyngeal swabs (one nose and one throat) marked 'urgent' to the lab. However, the Centers for Disease Control and Prevention (CDC) recommend that, on the basis of clinical judgement and knowledge of influenza activity in the community, women who are pregnant should receive empirical treatment with neuraminidase inhibitors, ideally within 48 hours of illness onset.⁷ Delays in treatment beyond 48 hours of symptom onset are associated with a fourfold increase in ICU admission or death for women who are pregnant.⁸

Compared with no treatment, neuraminidase inhibitor treatment (irrespective of timing) was associated with a reduction in mortality risk for patients admitted to hospital (adjusted odds ratio [OR]: 0.81; 95% confidence interval [CI]: 0.70–0.93; $P = 0.0024$).⁹ Oseltamivir is a category B1 medication and there is no evidence that it is associated with adverse fetal outcomes.¹⁰

Key points

- Women who are pregnant are at an increased risk of severe morbidity and mortality from influenza.
- The Australian immunisation guidelines recommend that all women who are pregnant be immunised against influenza.
- Vaccine uptake is low (despite being funded), but education and recommendation for vaccination from a maternity care provider hold particular weight in influencing women who are pregnant to receive vaccination.
- Early laboratory testing and empirical treatment with neuraminidase inhibitors are important secondary preventions of complications.

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References

1. Hewagama S, Walker SP, Stuart RL, et al. 2009 H1N1 influenza A and pregnancy outcomes in Victoria, Australia. *Clin Infect Dis* 2010;50(5):686–90.
2. Tamma PD, Ault KA, del Rio C, Steinhoff MC, Halsey NA, Omer SB. Safety of influenza vaccination during pregnancy. *Am J Obstet Gynecol* 2009;201(6):547–52.
3. Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med* 2008;359(15):1555–64.
4. Wiley KE, Massey PE, Cooper SC, et al. Uptake of influenza vaccine by pregnant women: A cross-sectional survey. *Med J Aust* 2013;198(7):373–75.
5. Lu AB, Halim AA, Dendle C, et al. Influenza vaccination uptake amongst pregnant women and maternal care providers is suboptimal. *Vaccine* 2012;30(27):4055–59.
6. Department of Health. The Australian Immunisation Handbook. 10th edn. Woden, ACT: DoH, 2015. Available at www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home [Accessed 18 October 2015].
7. Centers for Disease Control and Prevention. Recommendations for obstetric health care providers related to use of antiviral medications in the treatment and prevention of influenza. Atlanta, GA: CDC, 2015. Available at www.cdc.gov/flu/professionals/antivirals/avrec_ob.htm [Accessed 18 October 2015].
8. Louie J, Acosta M, Jamieson D, Honein M. Severe 2009 H1N1 influenza in pregnant and postpartum women in California. *N Engl J Med* 2010;362(1):27–35.
9. Muthuri SG, Venkatesan S, Myles PR, et al. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: A meta-analysis of individual participant data. *Lancet Respir Med* 2014;2(5):395–404.
10. Xie HY, Yasseen AS 3rd, Xie RH, et al. Infant outcomes among pregnant women who used oseltamivir for treatment of influenza during the H1N1 epidemic. *Am J Obstet Gynecol* 2013;208(4):293.e1–7.

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