Influenza during pregnancy and the postpartum period

Pregnant women are at increased risk of severe and complicated influenza, including associated hospitalisation and death, compared to non-pregnant women of reproductive age.\(^1\) Normal physiological alterations in heart rate, lung capacity, and immunological function that occur in pregnancy put pregnant women at increased risk of being more severely affected by certain infections, including influenza.

Postpartum women, who are in transition to normal heart, lung and immune function, are also at increased risk of severe and complicated influenza up to two weeks postpartum (including following pregnancy loss).

Complications of influenza in pregnancy may include severe pneumonia, early labour (premature birth), reduced foetal growth, low birth weight and stillbirth. Premature birth can lead to long-term medical and social consequences. The risk of these complications is higher in the second and third trimesters of pregnancy and is greater for pregnant women with at-risk medical conditions.\(^1\)

These guidelines provide recommendations for managing pregnant, postpartum and breastfeeding women presenting with an influenza-like illness (ILI) or confirmed influenza. Of note, the diagnosis of Influenza should be considered in all patients presenting with ILI regardless of their vaccine status.

\(^1\) Chronic illness requiring regular medical follow-up e.g. chronic heart disease, chronic lung disease, chronic liver disease, chronic kidney disease, chronic neurological disease, diabetes mellitus, haemoglobinopathies, immunosuppression.
Influenza-like illness

Influenza-like illness (ILI) is defined as sudden onset of symptoms

AND at least one of the following four systemic symptoms:
1. fever or feverishness
2. malaise (a general feeling of being unwell)
3. headache
4. myalgia

AND at least one of the following three respiratory symptoms:
1. cough
2. sore throat
3. shortness of breath

Pregnant women should be advised of the signs and symptoms of ILI and encouraged to present early to their GP if they develop ILI or if they develop any respiratory symptoms after close contact with a person who has ILI or laboratory confirmed influenza. They should be assessed, diagnosed and managed on clinical grounds, noting that there are a number of differential diagnoses for people presenting with ILI or respiratory infection. Influenza typically involves symptoms such as fatigue, headache, muscle aches and pains and patients usually have a fever. In addition, this winter (2020/2021) we are experiencing a COVID-19 pandemic and COVID-19 and influenza can be difficult to distinguish from their symptoms alone, and require a laboratory test. This needs to be considered when a clinical assessment is being undertaken. The consequences of being infected with influenza and COVID-19 at the same time are not yet clear but the importance of preventing influenza infection is a certainty, this year more than ever. The most effective way to avoid influenza infection is through vaccination.
Testing/Diagnosis

Nose and throat viral swabs should be taken for all women admitted to hospital with ILI and for women with ILI being considered for hospital admission within the next seven days (whether for ILI or obstetric reason). COVID-19 and influenza can be difficult to distinguish from their symptoms alone, and require a laboratory test.

Prevention

Influenza vaccine

The World Health Organization (WHO) has stated that pregnant women are the highest priority group for seasonal influenza vaccination.²

The seasonal influenza vaccine is strongly recommended for all pregnant women and can be administered at any stage of pregnancy (inactivated influenza vaccine only). Vaccination is also recommended for those considering pregnancy or trying to become pregnant. It takes approximately two weeks after the vaccine has been given to be fully protected. The flu vaccine given during pregnancy has been shown to protect both the mother and her baby (up to 6 months old) from influenza.

See flu vaccine during pregnancy information at

https://www.hse.ie/eng/health/immunisation/infomaterials/

It is estimated that influenza immunisation could prevent 1-2 hospitalisations per 1,000 pregnant women. There is evidence that influenza vaccination reduces the rate of stillbirth by over 50% ². The inactivated quadrivalent influenza vaccine which will be used in Ireland for the 2020/2021 influenza season is not a live vaccine and is considered very safe in pregnancy.

**Treatment**

Scientific evidence attests to improved outcomes in pregnant women who receive early treatment with antiviral medication, including reduced likelihood of ICU admission and death. Antiviral treatment is recommended for pregnant women or women up to two weeks postpartum (including following pregnancy loss) with suspected or confirmed influenza, and can be taken during any trimester of pregnancy.

During the influenza season, treatment should not be delayed while awaiting laboratory test results. Empiric antiviral treatment should be started as soon as possible, ideally within 48 hours of symptom onset, as studies demonstrate that early initiation of treatment is more likely to confer benefit. However, some studies of hospitalised patients with influenza, including an analysis of hospitalised pregnant women, suggest benefit of antiviral treatment even when started more than 48 hours after symptom onset.

Multiple observational studies have shown that antiviral treatment with oral oseltamivir or inhaled zanamivir is safe during pregnancy and does not increase the risk of adverse pregnancy outcomes. Oseltamivir remains the first line option for the vast majority of pregnant women with influenza and is generally well tolerated, although side effects can occur. There are no data suggesting that tolerability differs between pregnant and non-pregnant women.

Standard dose and duration of treatment with oseltamivir is 75mg orally twice daily for 5 days. Hospitalised patients with severe or complicated influenza may require a longer duration of treatment, extension of treatment will be based on clinical assessment.

For further guidance for the use of antivirals in pregnancy see Annex A of the “Guidance on the use of antiviral agents for the treatment and prophylaxis of influenza” on the HPSC website.
Chemoprophylaxis

Post-exposure antiviral chemoprophylaxis can be considered for pregnant women and women who are up to two weeks postpartum who have had close contact\(^3\) with someone likely to have been infectious with influenza. Clinical judgement should be exercised in individual cases to determine if the benefit outweighs the risk. Previous influenza vaccination does not preclude the use of post exposure prophylaxis. Pregnant women and women who are up to two weeks postpartum who are given post-exposure chemoprophylaxis should be informed that the chemoprophylaxis lowers but does not eliminate the risk of influenza and that protection stops when the medication course is stopped\(^3\). Those receiving chemoprophylaxis should seek advice from their doctor if they develop respiratory symptoms that might indicate influenza.

An alternative approach for pregnant and postpartum women (up to two weeks postpartum) who have had close contact with a patient with laboratory confirmed influenza is to provide information on the early signs and symptoms of ILI and influenza, and advise them to contact their doctor immediately for evaluation and possible early treatment if clinical signs or symptoms develop following a risk assessment.\(^3\)

Oseltamivir is considered the drug of choice for influenza chemoprophylaxis in pregnant women. Standard dose and duration of oseltamivir chemoprophylaxis is 75mg orally once daily for 10 days. For further guidance see “Guidance on the use of antiviral agents for the treatment and prophylaxis of influenza” on the HPSC website.

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\(^3\) Close contact is defined as having cared for or lived with a person who has confirmed, probable or suspect influenza or having been in a setting where there is a high likelihood of contact with respiratory droplets and/or body fluids of such a person, including having talked face-to-face with them.
Pre-Delivery

- Prior to delivery, a hospitalised pregnant woman with ILI/influenza should be managed in accordance with the infection prevention control guidelines for patients with suspected or confirmed influenza in healthcare settings. Standard and droplet precautions, with additional precautions for aerosol generating procedures (AGPs) should be employed. This includes patient placement in a single room, cough etiquette including wearing a facemask if being transported outside of their room and additional personal protective equipment (PPE) for staff. Facilities should refer to the guidelines for more detailed information.

- Healthcare staff entering rooms of pregnant women with suspected or confirmed influenza should adhere to standard and droplet precautions, including wearing a facemask, performing hand hygiene, wearing gloves for any contact with potentially infectious material and wearing a gown for any activity where contact with the patients’ body fluids may occur.\(^{(5)}\)

- International recommendations in relation to the duration of droplet precautions for cases of influenza vary from country to country. As a general rule, the duration of isolation precautions for hospitalised patients with viral respiratory illness should be continued for 24 hours after resolution of fever and respiratory symptoms. In the case of Influenza appropriate infection prevention and control precautions should be maintained for 5 days after onset of symptoms. Patients on droplet precautions should be discharged from hospital when clinically indicated, NOT based on the period of potential infectiousness or recommended duration of droplet precautions.

- Patients should be asked to restrict visitors in so far as is possible. Family members and other visitors should be informed of the risks of influenza virus transmission and instructed to adhere to respiratory hygiene and cough etiquette, hand hygiene, and use of PPE according to current HPSC policy.\(^{(5)}\)

Delivery

- Patients with suspected or confirmed influenza who are in labour and/or in the delivery suite should remain on droplet precautions. Mothers should not be asked to wear a mask during labour and birth. Healthcare staff in the delivery suite
should adhere to Standard and Droplet Precautions including practicing hand hygiene before and after handling the newborn.

- If delivery is by planned induction or elective caesarean section, consider deferral, if appropriate. This decision should be taken at senior level weighing up obstetric indication for delivery with risk to mother and baby of delivery while unwell.

**Postpartum**

- Infection control precautions for mothers with ILL/influenza should continue as above.
- Breast feeding should be strongly encouraged.
- Appropriate efforts should be made to reduce the likelihood of the baby becoming infected, while minimising the effect on the mother-baby relationship. These include:
  - Treating the mother to reduce the risk of transmission.
  - The mother and baby should sleep at least 1 metre apart (3 feet), in separate beds in the same room (at least while in hospital). When breast feeding, bathing, caring for, cuddling, or otherwise being within 1 metre of the baby, the mother should wear a surgical mask and clean her hands thoroughly with alcohol hand rub or soap and water before interacting with the baby.
  - The mother should avoid coughing and practice **cough etiquette** near the baby.
  - If expressing breast milk using a pump, this should be cleaned as per the manufacturer’s instructions.
  - While these measures can be ceased when the mother is no longer infectious, continued good hygiene should be encouraged at all times.
  - These measures should also apply to any carer or family member with influenza.
  - Mothers requiring hospital care should not be prematurely discharged because they have influenza.
  - If discharged while still infectious, mothers should be provided with a sufficient supply of surgical masks to take home.
Post exposure prophylaxis for neonates born to mothers with laboratory confirmed influenza

A particular clinical challenge arises with regard to the neonate if a pregnant woman develops laboratory confirmed seasonal influenza shortly before the onset of labour. The potential mode of transmission to the neonate in such a scenario is via direct contact with the infected respiratory secretions of the mother rather than via breastmilk. The Summary of Product Characteristics (SPC) for Tamiflu® (oseltamivir) oral suspension states that the medicine can be used for post-exposure prevention of influenza in infants aged over 1 year; therefore oseltamivir prophylaxis for infants aged less than 1 year would be an off-label use. Treatment of seasonal influenza in children, including full term neonates, is however, specified in the SPC for capsules and Tamiflu® (oseltamivir) 6mg/ml powder for oral suspension. Relenza® (zanamivir) inhalation powder is not licensed for treatment or prophylaxis in children less than 5 years of age.

There are three potential options which may be considered by mothers and clinicians in relation to neonates born to mothers with laboratory confirmed influenza

1. Oseltamivir oral suspension for post-exposure prophylaxis in the neonate, as an off-label use. As prophylaxis reduces but does not eliminate the risk of infection, infants should be closely monitored for signs and symptoms of Influenza.

2. Physical separation of the symptomatic mother and asymptomatic neonate until 5 days after symptom onset. Disadvantages for the neonate would include the effect on the mother baby relationship and not being able to benefit from breastfeeding-related transfer of immune factors and nutrients. These considerations should be included in the discussion with the mother. Women should be encouraged to express breastmilk so that
the neonate can receive
the benefits of breastmilk, and to maintain the mother’s milk supply in
order that breastfeeding can continue once mother and baby are reunited.
More detailed advice on use of oseltamivir in breastfeeding should be
sought from the SPC.
3. No prophylaxis for the neonate and no separation of neonate and
mother. This will require careful monitoring for symptoms of influenza, a
discussion in advance with the mother about prompt antiviral treatment of
the neonate, and advance arrangements for rapidly accessing oseltamivir
oral suspension if required (as this is more readily available via hospital
pharmacies than community pharmacies). There should also be
consideration of laboratory testing of a symptomatic neonate, as per
existing local arrangements.

Decisions regarding the most appropriate course of action should be made on a
case-by-case basis and are likely to involve detailed discussion between the
mother and physician regarding the relative advantages and disadvantages of
each potential option. This advice does not constitute a specific endorsement of
the routine use of oseltamivir oral suspension for prophylaxis in neonates, but
recognises that this may occur as an off-label use in specific circumstances.

**Neonatal Unit**
- Symptomatic mothers, care givers, and family members should not enter the
  neonatal unit.
- Appropriate signage should be displayed at the entrance to the neonatal unit
to discourage visitors with ILI from entering.
- If a newborn infant of a mother with suspected or confirmed influenza is
  housed in the hospital nursery instead of the mother’s room, infants without
  symptoms of influenza can be cared for by a non-ill person using standard
  precautions and should be closely observed for signs of infection.
- A newborn that develops symptoms should be placed on droplet and contact
  precautions and assessed by a paediatrician.
Visitors
As a general rule, visitors are prohibited from attending the labour unit as they are a possible source of influenza infection for patients. In certain cases, they may be allowed but they should be limited to persons who are necessary for the patient's emotional wellbeing and clinical care. If they are allowed then the following is recommended:

- Visitors should be instructed to limit their movement within the facility.
- Appropriate signage to discourage those visitors with ILI from entering the hospital should be placed prominently at hospital entrances.
- Facilities should provide instruction, before visitors enter patients' rooms, on hand hygiene, limiting surfaces touched, and use of PPE while in the patient's room.

Discharge
- Influenza vaccination should be considered for the postpartum woman (if unvaccinated) as well as any unvaccinated family members aged 6 months and older and caregivers who will be in contact with the newborn.\(^{(5)}\)
- The postpartum woman and baby should be discharged from hospital as soon as it is safe to do so.
- The postpartum woman should be given remaining course of antivirals and advised to complete them.
- Ensure that the GP and home care team are informed of the discharge and influenza status of the postpartum woman and newborn baby.
- Ensure the postpartum woman has information on:
  - Influenza and knows that it is important to contact the GP/hospital promptly if the newborn baby develops ILI symptoms.
  - Avoiding contact, as far as possible, with any individuals in the home who develop ILI to minimise exposure to herself and the newborn baby.
  - Hand hygiene and respiratory etiquette when having contact with the newborn baby.
  - Endeavouring, if possible, to have vaccinated, non-ill adults provide
care to the newborn at home if the mother develops ILI symptoms until the mother’s illness resolves.

References


