

BRIEF COMMUNICATION

COVID-19 VACCINATION AND PREGNANCY: A PATIENT'S DILEMMA.

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Introduction

COVID-19 pandemic has crippled the health and socioeconomic systems of many countries since it began approximately 18 months ago. Without an established treatment, COVID-19 vaccination is seen as a crucial pharmacological tool to stop the current pandemic. However, many remain skeptical about the safety of these vaccines. The concerns are especially relevant for vaccination of pregnant women because pregnant women were not included in the initial phase III clinical trials of the COVID-19 vaccines.^[1, 2]

In Malaysia, the National COVID-19 immunisation Programme started on 24th Feb 2021, aiming to vaccinate at least 80% of Malaysian adults by Feb 2022 to induce herd immunity. At present, three vaccines have been approved by the Malaysian National Pharmaceutical Regulatory Agency (NPRA) and deployed. These are i) Pfizer-BioNTech (mRNA vaccine), ii) Sinovac (Inactivated virus vaccine) and Oxford-AstraZeneca (viral vector vaccine).

Using current evidence and recommendations of the relevant authorities, this scenario-based article aims to answer the queries of a Malaysian woman regarding COVID-19 vaccination and pregnancy.

Case Scenario

Maria, a 45-year-old lady, sees her family physician for pre-pregnancy counselling. She just got married 3 months ago and is trying to conceive for the first time. She also enquires whether she should register for COVID-19 vaccination.

She is a senior office clerk at a local secondary school. The nature of her job is mainly dealing with documents and teachers in the school office but occasionally she will need to meet with parents of the students and officials from the district education office.

She and her husband stay with her parents who are in their 70s. Her parents are diabetics on insulin therapy and she will often bring them to the clinic for follow up and medication refill. She has no significant past medical history except for occasional episodes of urticarial rash due to seafood intake since she was young. The rash gets resolved with oral antihistamine from the clinic and she had never been admitted to the hospital for that. The last episode of allergy was about two years ago. No history of allergy to any medication or previous scheduled vaccination.

Questions:

- a) Should Maria get vaccinated now?
- b) Will it harm Maria and her baby if she gets vaccinated when she is pregnant?
- c) Can Maria get vaccinated since she has allergic reaction to seafood?
- d) If Maria is vaccinated now, how soon can she plan for pregnancy?
- e) Will Maria's baby be protected from if she gets vaccinated now?

Answers & Discussion

- a) COVID-19 vaccines have been shown to be effective in protecting against COVID-19 infection and may prevent severe COVID-19 disease.^[3-5] All women above 18 years old who are vulnerable are strongly advised to complete their COVID-19 vaccination before getting pregnant.^[3,4] In this case, Maria belongs to the vulnerable group because of her advanced maternal age and regular exposure to people who are at risk of contracting the disease. She should register promptly for vaccination to get vaccinated as soon as the vaccine is accessible to her.

Various studies have reported that pregnant mothers who contracted Covid-19 infection had increased risk of severe pneumonia, pulmonary embolism, iatrogenic prematurity, stillbirth and maternal mortality.^[6-8] Consequently, the need for intensive care (ICU) admission, mechanical ventilation and ventilatory support are greater, particularly with infection by the newer strains of virus.^[2,7,8] Therefore, vaccinating pregnant mother and women of reproductive age with identifiable risk factors such as increasing age, diabetes, obesity and cardiovascular conditions not only improves maternal morbidity and mortality, it will also reduce the risk of fetal morbidity.^[3,4]

Minimising the risk to the foetus is especially important for Maria as this would be a precious pregnancy. Conceiving her first baby at an advanced maternal age of 45 with family history of first-degree relatives with diabetes mellitus put Maria at much higher risk of getting complications of pregnancy such as gestational diabetes mellitus, pre-eclampsia, miscarriage, and birth defect.^[9] Her pregnancy will surely be further complicated if she contracted COVID-19.

Maria should also be advised to get her parents and husband vaccinated against COVID-19. This will indirectly reduce her chance of contracting the illness during pregnancy. Furthermore, her elderly parents are diabetic, making them vulnerable to severe complication from Covid-19 infection.^[10,11]

- b) Vaccination of pregnant mothers with the Pfizer-BioNTech (mRNA vaccine) and Sinovac (Inactivated virus vaccine) COVID-19 vaccines are probably safe based on observational data and current scientific information.^[4,12] However, pregnant women should not be offered the AstraZeneca COVID-19 vaccine due to concerns regarding vaccine-Induced prothrombotic immune thrombocytopenia (VIPIT) following vaccination.^[13]

Effects on Foetus:

Foetal malformation have not been reported after vaccination during pregnancy.^[12] This is based on the results of the Development and Reproductive Toxicity (DART) studies on animals for mRNA vaccines and observational data from the ongoing v-safe pregnancy registry of CDC (Centre of Disease Control and Prevention) USA.⁴ Furthermore, mRNA vaccines are not live vaccines and will not cause infection in the mother or foetus.^[14] It does not enter the nucleus of the cells and thus do not alter human DNA and cause genetic changes.^[4]

However, it is best to avoid vaccination during the first 12 weeks of gestation when organogenesis occur because the effect of exogenous RNA on the host genome in the placenta cannot be completely excluded.^[12] In addition, vaccine reactogenicity such as fever could increase the risk of neural tube defects and other congenital abnormalities.^[15] Therefore, fever following vaccination should be treated with acetaminophen which is safe in pregnancy and does not affect the immunologic response.^[3,12]

The Sinovac/Coronavac vaccine from China is an inactivated vaccine. Inactivated virus or bacteria vaccines and toxoids have been administered to pregnant mothers for decades without known harm to the foetus or mother.^[3,14]

As for the AstraZeneca COVID-19 vaccine which uses viral vector vaccine technology is not a live vaccine. A recent study done for vaccines with viral vector technology for Ebola, did not show any safety concerns.^[16] However, the Joint Committee on Vaccination and Immunisation (JCVI), UK recommended that Pfizer-BioNTech or Moderna mRNA vaccines be offered to pregnant women.^[17] This is based on the fact that unlike AstraZeneca vaccine, there is robust real-world data from the United States that have shown any safety concerns among the 90,000 pregnant women vaccinated with the mRNA vaccines.

Effects on pregnant mothers:

The safety profiles of the vaccines for pregnant mothers are similar to non-pregnant women.⁴ As of 9th Feb 2021, observation data from the ongoing v-safe pregnancy registry of CDC (Centre of Disease Control and Prevention) USA which consist of over 1,800 pregnant mothers who inadvertently received the mRNA vaccines showed that side effects and pregnancy outcome were similar whether a woman is pregnant or not.⁴ Other studies did not identify any safety threat among common population for the four vaccines that had been rolled out, including mRNA (Pfizer and Moderna), viral vector (AstraZeneca) vaccine and inactivated virus vaccine (Sinovac).¹⁸

Common adverse effects identified are pain at the injection site, fatigue, fever, headache and bodyache which will mostly resolve within a few days.^{19,20} These represent the normal body reaction to the vaccine to develop protective antibodies.⁴

Serious adverse effects are rare. These include anaphylaxis for mRNA vaccines which happened in 4.7 cases per million doses administered for mRNA(Pfizer) vaccine and 2.5 cases per million doses administered for mRNA(Moderna) vaccine.^{4,20} Recently in mid-March 2021, the viral vector vaccine from AstraZeneca was reported to be associated with vaccine-induced prothrombotic immune thrombocytopenia VIPIT, a life threatening adverse effect.¹³ At the moment, this vaccine from AstraZeneca should probably be withheld from pregnant women until further evidence is available, as pregnancy itself imposes higher risk of venous thromboembolism.²¹

- c) Persons who had severe allergic reaction i.e. anaphylaxis (severe angioedema, bronchospasm and/or hypotension) to drugs, vaccines, food, insect stings or unknown triggers, or persons with a previous allergic reaction to a previous dose of COVID- 19 vaccine or any of its components, or persons

with acute febrile illness are contraindicated to the vaccine.³

Persons with atopy (eczema, asthma, allergic rhinitis) and those with family history of anaphylaxis can be vaccinated. Persons with multiple allergies should be vaccinated in a hospital setting.³ and those who had a history of allergic reaction to vaccination (not amounting to an anaphylaxis) should be assessed by specialists to decide if they could be allergic to the components of the vaccine.³

Since Maria does not have any contraindication, she can be vaccinated with COMIRNATY (Pfizer-Biontech) vaccine. After getting the vaccine, she will need to be monitored for at least 30 minutes at the vaccination centre.³

- d) No scientific evidence to date indicates that the COVID-19 vaccine can affect fertility either for males or females.⁵ Pregnancy need not be delayed after vaccination²² except for those who received certain fertility therapy.²³

Routine pregnancy screening prior to vaccination is not necessary.² In the event that she gets pregnant after receiving the first dose, she may choose to delay the second dose until after 14 weeks of gestation.³

Although one dose of COVID- 19 vaccination gives good protection against infection, the efficiency of it in providing adequate protection throughout the pregnancy is questionable.¹⁷ Therefore, it is recommended that both doses of vaccine be completed before becoming pregnant for maximum coverage and protection throughout pregnancy.¹⁷

- e) Although recent systematic review of mostly case reports and retrospective studies showed low possibility of natural passive immunity in infants born to previously infected

mothers,²⁴ there is no strong evidence to show that COVID 19 vaccination in mother can provide passive immunity to the infant. There is only 1 non-peer reviewed case report so far on passive immunity in an infant born to a mother who had been vaccinated with Moderna's vaccine.²⁵

Conclusion

Current evidences and recommendations by various professional bodies support COVID-19 vaccination in pregnant mother especially those who are at a higher risk. Although the benefits of the vaccine are promising, acknowledgement of the risks and benefits of the vaccine for the pregnant women, the foetus and the newborn should be included in the discussion with our patients. Evidence from specific studies of COVID-19 vaccines on pregnant women and longitudinal studies are required to establish the safety of various COVID-19 vaccines in pregnancy.

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