REAL ISSUES FOR

# FOR COVID-19 VACCINE IMMUNIZATION

## & Pregnancy, Breastfeeding Mothers

By MyICID & ICR, NIH MY

# Real Issues for COVID-19 Vaccine Immunization & Pregnancy, Breastfeeding Mothers

Cheng Hoon Chew, Yan Yee Yip, Jiveswara Vijiakumar, Norzaihan binti Hassan, Muniswaran Ganeshan, Noel Thomas Ross, Kah Chuan Lim, Benedict Lim Heng Sim, Anusha Shunmugarajoo, Kalaiarasu M. Peariasamy

*Foreword by* Shamala Devi A/P Karalasingam

**Live Webinar Series on COVID-19 Vaccine**

Jointly organized by Malaysian Society of Infection Control and Infectious Diseases (MyICID) & Institute for Clinical Research (ICR), National Institutes of Health (NIH) Malaysia

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**REAL ISSUES FOR COVID-19 VACCINE IMMUNIZATION & PREGNANCY, BREASTFEEDING MOTHERS**

First Edition, 2021.

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# Foreword

Coronavirus can make anyone seriously ill. The most vulnerable people to get Covid-19 are the healthcare professionals and pregnant mothers. Recently published research in BMJ suggests that pregnant women are less likely to experience symptoms but if they develop severe disease, they are more likely to be admitted to the intensive care or will require ventilation as compared to non-pregnant women. Vaccine has been proven to significantly reduce hospitalizations, complications and deaths.

This book contained a lightly edited transcript from the live webinar series on COVID-19 vaccine: COVID-19 Vaccination in Pregnancy & Lessons Learnt From Phase 1 Roll-Out of Vaccines on 5th of May 2021. The panellists for this webinar were Dr. Muniswaran Ganeshan, a Maternal Fetal Medicine Consultant, Dr. Norzaihan binti Hassan, a Family Medicine Consultant and Datuk Dr. Noel Thomas Ross the Head of Acute Medicine and Consultant Physician who chaired the session. The transcript was prepared by Mr. Jiveswara Vijiakumar, Ms. Yip Yan Yee and Dr. Chew Cheng Hoon from Institute for Clinical Research, NIH Malaysia. This is intended to share within healthcare professionals, not for the public.

The objective of the COVID-19 webinar series was to disseminate knowledge and current evidence on COVID-19 management, vaccination and infection control practices to medical practitioners. This is also a Continuing Professional Development (CPD) activity for all Health Care Providers and allied health personnel in Malaysia. This weekly live webinar was jointly organized by Malaysian Society of Infection Control and Infectious Diseases (MyICID) & Institute for Clinical Research (ICR), National Institutes of Health (NIH) Malaysia.

**DR. SHAMALA DEVI A/P KARALASINGAM**
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# “Lessons Learnt From Phase I Roll Out of COVID-19 Vaccines” by Dr. Norzaihan binti Hassan

Thank you, Datuk Dr. Thomas. Assalamualaikum and good afternoon to all viewers. The title of my presentation is “Lessons Learnt from Phase I Roll out of COVID-19 Vaccines”. My presentation is divided into four parts: introduction, our experience in planning for Phase I vaccination, how we set up the mass vaccination, the challenges and ways to overcome them.

## Introduction

We started the vaccination programme on 28 of February 2021 with a group of vaccinators. There are four vaccine storage centres in Kelantan, which are located at the districts of Kota Bharu, Pasir Mas, Kuala Krai, and Gua Musang. The vaccine storage centre is also known as *Pusat Simpanan Vaksin* or PSV. In Kota Bharu’s vaccination centres, *Pusat Pemberian Vaksin* (PPV) are located at the clinics and hospitals.

## Planning for Phase I

We needed to provide a suitable place for ultra low temperature freezer (ULTF). (The Comirnaty, the Pfizer-BioNTech mRNA-based COVID-19 vaccine needs to be stored in ULTF). We also streamlined the electricity supply to avoid any power supply problem to the fridge. We had a few meetings with our Tenaga Nasional Berhad team and engineers to ensure that there will be no internal or external fault in the power supply to the fridge. To ensure the safety of vaccines, a mobile police station and a closed-circuit television (CCTV) has been installed in strategic locations in our vaccine storage centre (PSV).

### Preparation: Manpower

The vaccinators consist of medical specialists, medical officers, paramedics, and nurses. They have their own responsibilities. The medical officers are responsible for handling medical problems of the vaccine recipients. The paramedics will manage the vaccination process like filling up the Vaccine Administration System (MyVAS). They are also the navigator in the process of vaccination. We chose nurses from school health teams and those working in the

maternal and child health team to administer the COVID-19 vaccine because they are already skilled in administering vaccine.

For client monitoring, we selected medical officers who are already trained in emergency care to handle any immediate side effects or anaphylaxis, if it occurs. For backup, the consent taking task was given to the pharmacists.

## Preparation: Training

For the training aspect, we briefed the vaccinators on information about the COVID-19 vaccines which focusing on efficacy, side effects, contraindication and the frequently asked questions. This will help them to address concerns from vaccine recipients and to obtain consent for vaccination. We have also conducted simulation with role-play on how to handle the vaccination process, scenario where the vaccine recipients developed side effects or anaphylaxis. We also conduct cross audits between PPV using the checklist that was provided. Staff have been given training webinars on how to manage MyVAS database and MySejahtera. If there is any unexpected system interruption, the staff will do the task manually and corrections will be sent to KKM MySejahtera team.

## Preparation: Equipment

For the Pfizer-BioNTech mRNA-based COVID-19 vaccine administration, we need a specially designed low-dead volume (LDV) syringes. Besides this, we prepared anaphylactic kits and resuscitation kits at the vaccination centres to treat vaccine recipients who may experience any side effects such as anaphylaxis, even though this is rare.

## Checklist For Vaccine Recipients

Before vaccine recipients (from Phase I immunization programme) come to the vaccination centre, we informed the Person-in-Charge of the respective agencies to ensure that the vaccine recipients will wear appropriate attire so that it would be easy for the vaccinator to administer the vaccine. Vaccine recipients should bring along their identity card (IC), updated their details in MySejahtera app to ensure that their name in MySejahtera is the same as their IC. For those coming for the second dose vaccine, they should bring their vaccine card.

### Client Flow Chart

Firstly, they would go to the triage station at the PPV to check in. Secondly, they will listen to the briefing in form of pre-recorded video with slides about the vaccination process. Next, they will go to the vaccine consent station where the medical officers and pharmacists will take consent from the vaccine recipients. Then, they will go to myVAS registration station, followed by the vaccination station. Next, they will go to the observation area where they will be observed for 15 to 30 minutes. After that, our staff will issue a vaccine card. For those who received their second dose, they will receive a digital vaccine certificate in MySejahtera app.

## Set Up Mass Vaccination

Now, I will share our experience on how we set up a mass vaccination in the phase I roll out of COVID-19 vaccination. During this phase, we have vaccinated range from 500 to nearly 1000 per day in our mass vaccination.

### Manpower: Mobilization of Staff

For the mass vaccination, we need to have sufficient manpower to implement it. In order to do so, we have to mobilize staff from clinics or other departments. We received help from the district health office as well as from the dental division. For instance, dental officers helped in data entry in MyVAS system while the dental assistants helped in filling up the details on the vaccine cards. Other staff are needed to usher the vaccine recipients to follow the process. They would also help in data management.

### Logistic

As for logistic purpose, we felt that having one hall in one floor is easier compared to having a location that has several floors with no lifts or elevators. This is because it will be quite difficult to transfer vaccine recipients to a clinic or hospital if they developed serious side effects that need further intervention in the clinic or hospital.

### Briefing

Staff schedule is also important to ensure adequate staffing at all times. There should be a contingency plan if there are any unexpected changes. The Person in Charge of each agency needs to be responsible for the line listing (list of vaccine recipients) given, and they need to be briefed to ensure the program will run smoothly. This is the example that we have made for the floor plan in the hall (**Figure 1**).

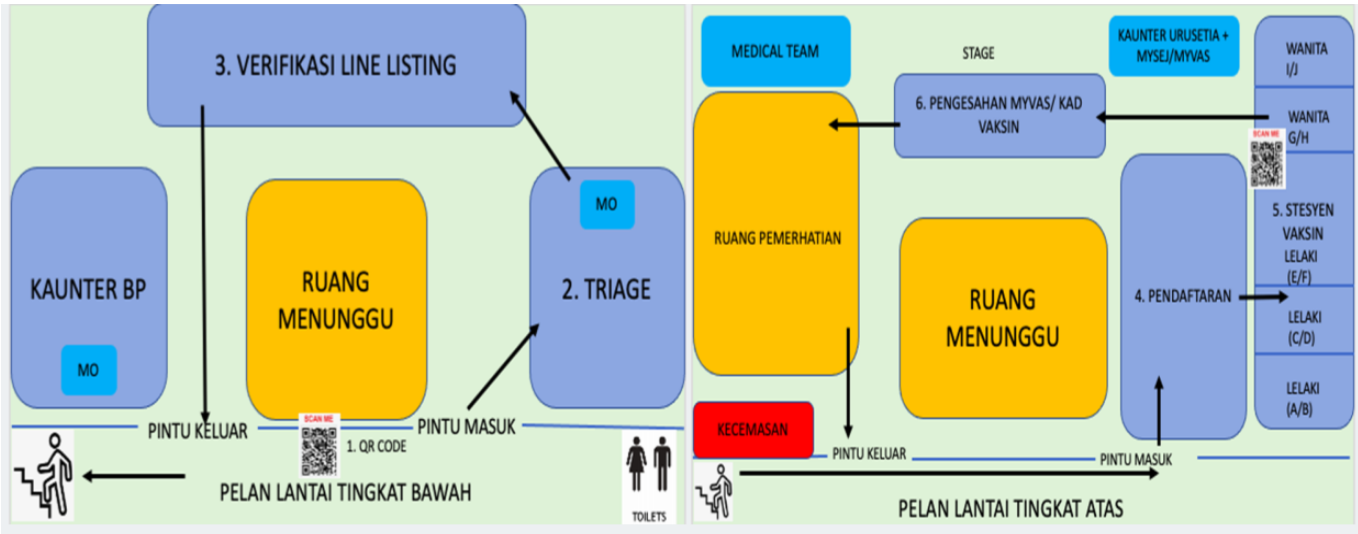



**Figure 1:** Example of Floor Plan (Image from Dr. Norzaihan's slide presentation https://www.slideshare.net/ICRInstituteForClini/webinar-roll-out-vaccine-share-slide-05052021)

The **Figure 2** depicts the flowchart we made for the mass vaccination. There are seven stations altogether. First station would be the triage counter, followed by the verification station of line listing (list of vaccine recipients for the day). If necessary, the vaccine recipients will go to the blood pressure (BP) counter. We selected those with hypertension and history of allergy to go to BP check-up counter. Next, they will go to the registration and get their vaccine administered. Once they have been verified through MyVAS system, a vaccine card will be given. They would be observed for a duration of 15 to 30 minutes, before they were allowed to leave the vaccine centre.

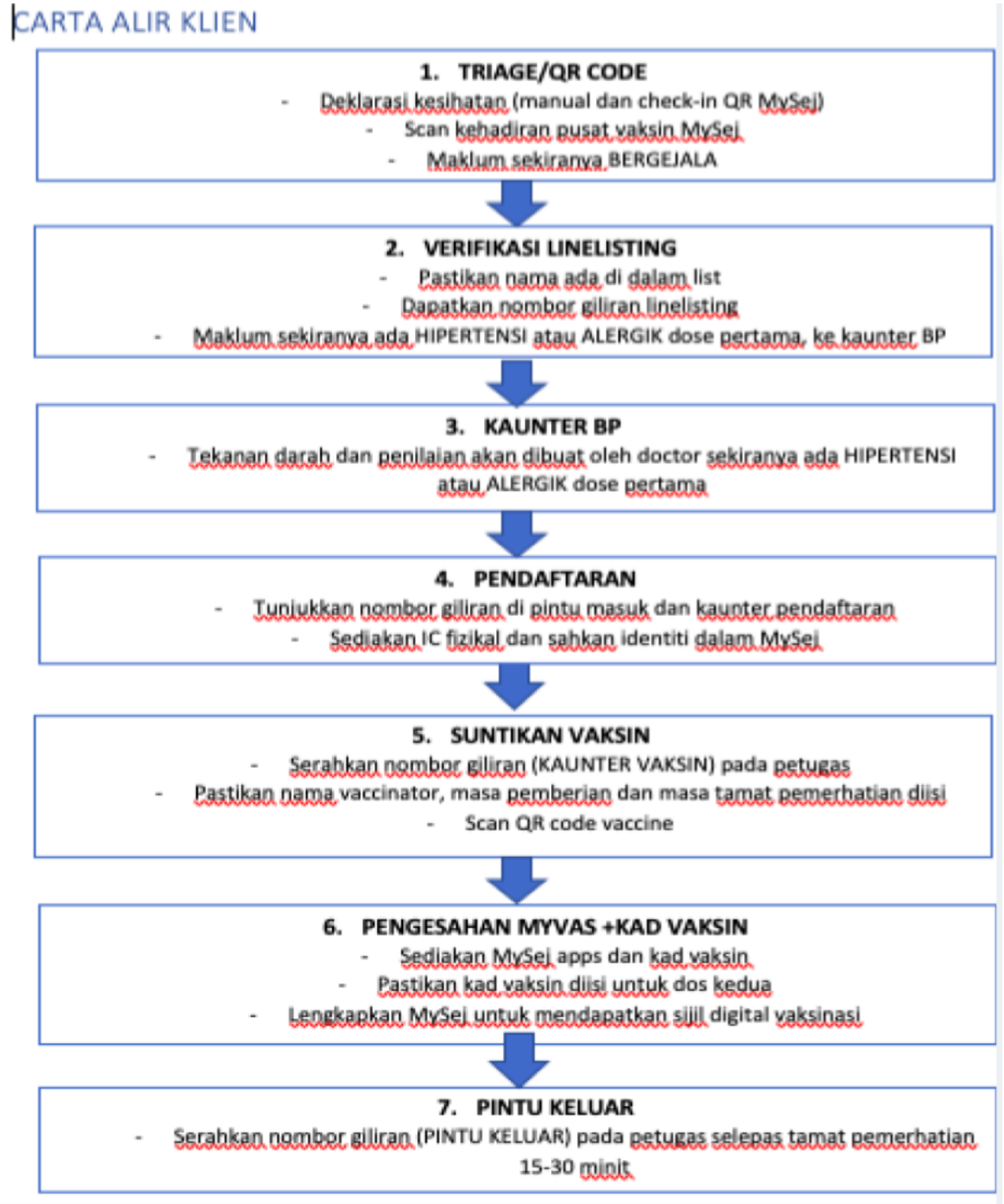



**Figure 2:** Flowchart for Mass Vaccination (Image from Dr. Norzaihan's slide presentation https://www.slideshare.net/ICRInstituteForClini/webinar-roll-out-vaccine-share-slide-05052021)

## Collaboration

For collaboration with other agencies, the Person in Charge needs to ensure their staff (vaccine recipients) in the line listing can comply to the designated vaccination appointment date and time. The police will escort the vaccine from PSV to PPV to ensure the safety and security of the vaccines.

## Technology

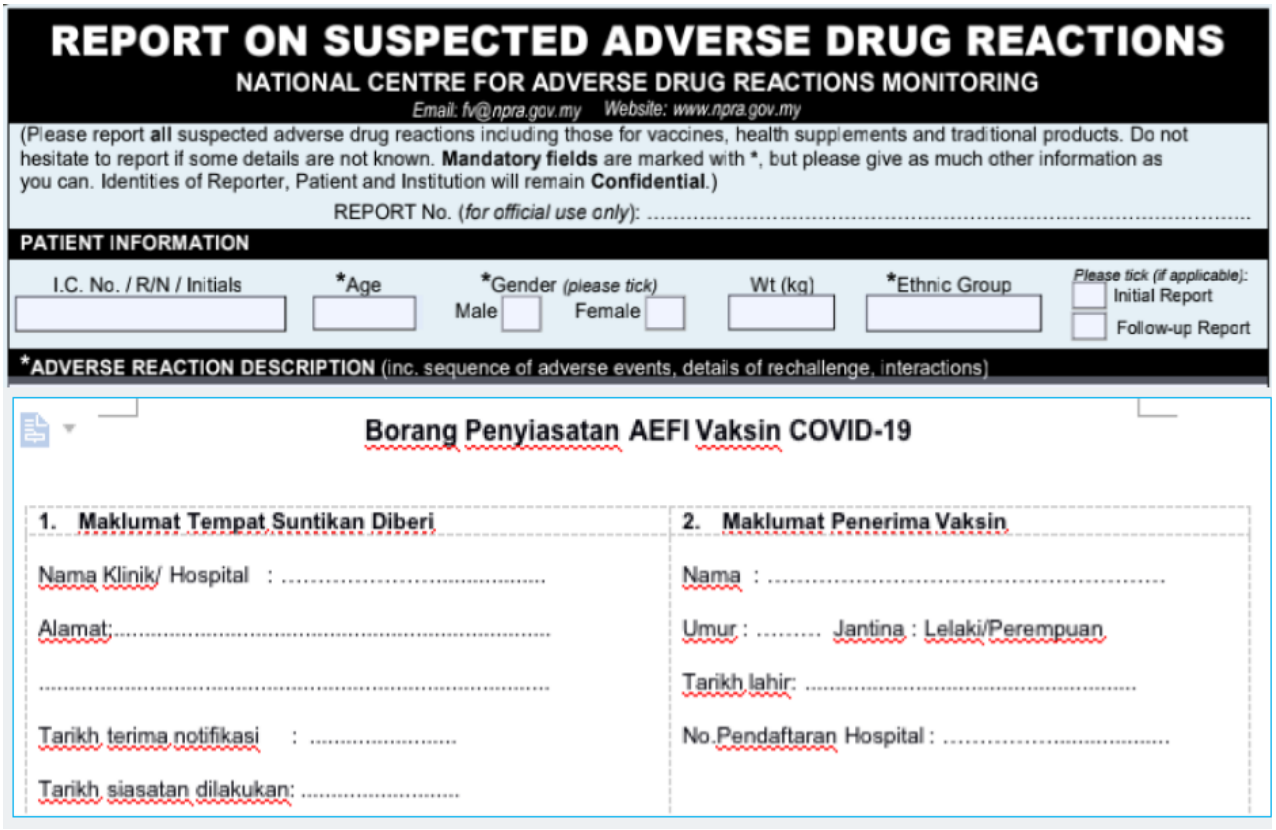
As mentioned earlier, for vaccine recipients' briefing, we use pre-recorded video with slides. We also provided a dedicated MyVAS helpdesk for those who may have problems with MySejahtera application. It is important to have an adequate number of laptops, and stable internet connection. In our case, we used a mobile broadband.

## Line Listing

For the line listing, the Person in Charge needs to understand the selection criteria of priority group as they need to sort out who needs to be injected first. In our experience, the arrangement of priority group has been done well. The list started with the healthcare workers, followed by the group of at-risk front liners and those working in high-risk institutions like prison and nursing homes. For a backup list of vaccine recipients, they are also selected from the priority groups.

## Management of Immediate Side Effects

We prepared materials like printed algorithms for the management of anaphylaxis as well as the Adverse Event Following Immunization (AEFI) and Adverse Drug Reactions (ADR) forms to facilitate the staff in charge of the observation station, if there is a case of immediate side effects.



**REPORT ON SUSPECTED ADVERSE DRUG REACTIONS**

NATIONAL CENTRE FOR ADVERSE DRUG REACTIONS MONITORING

*Email: fv@npra.gov.my Website: www.npra.gov.my*

(Please report **all** suspected adverse drug reactions including those for vaccines, health supplements and traditional products. Do not hesitate to report if some details are not known. **Mandatory fields** are marked with *, but please give as much other information as you can. Identities of Reporter, Patient and Institution will remain **Confidential**.)

REPORT No. (*for official use only*): .....

**PATIENT INFORMATION**

I.C. No. / R/N / Initials | *Age | *Gender *(please tick)* Male ☐ Female ☐ | Wt (kg) | *Ethnic Group | *Please tick (if applicable)*: ☐ Initial Report ☐ Follow-up Report

***ADVERSE REACTION DESCRIPTION** (inc. sequence of adverse events, details of rechallenge, interactions)*

**Borang Penyiasatan AEFI Vaksin COVID-19**

| 1. Maklumat Tempat Suntikan Diberi | 2. Maklumat Penerima Vaksin |
|---|---|
| Nama Klinik/ Hospital : ..... | Nama : ..... |
| Alamat:..... | Umur : ..... Jantina : Lelaki/Perempuan |
| ..... | Tarikh lahir: ..... |
| Tarikh terima notifikasi : ..... | No.Pendaftaran Hospital : ..... |
| Tarikh siasatan dilakukan: ..... | |

**Figure 3:** Adverse Drug Reactions (ADR) Forms (Image from Dr. Norzaihan's slide presentation)

## Returns: Doses of COVID-19 vaccine used should tally with MyVAS

For the returns, we have to make sure that the COVID-19 vaccine doses given tally with the total number of vaccine recipient registered in MyVAS. So, every day, our staff will prepare the vaccination returns (documentation) to ensure the number of "vaccine out" are the same as the total number of vaccine given. We have provided colour-coded tagging (**Figure 4**), where the vaccine recipient has to return this tagging paper to the staff for us to count the number of vaccines, which should be equal to the number of signed consent forms and the vaccination given. So, this will ensure we get the correct data for every vaccination session conducted daily.

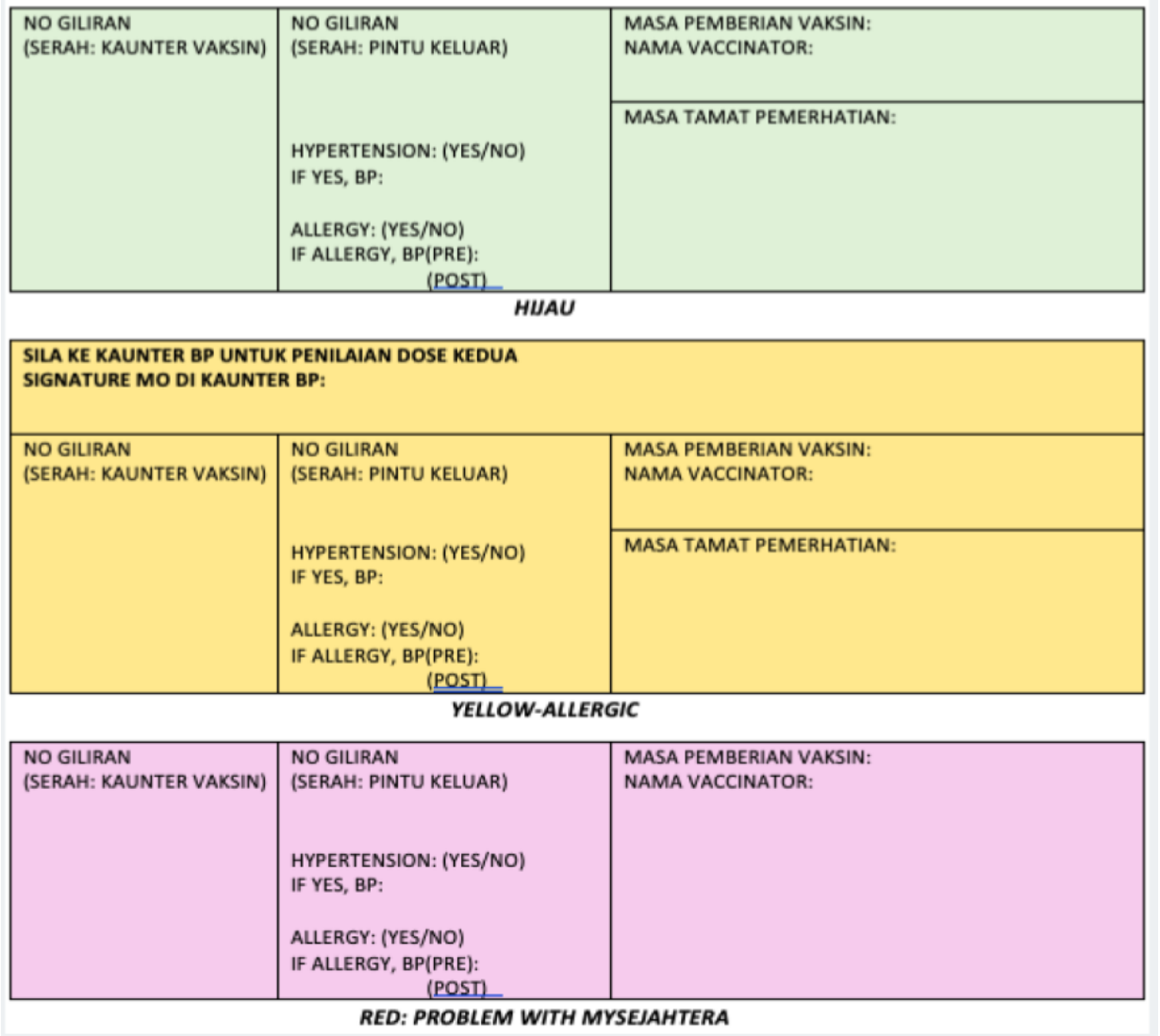



**Figure 4:** Sample of Returns provided in colour-coded tagging. An initiative to ensure doses of vaccines tally with MyVAS system (Image from Dr. Norzaihan's slide presentation).

# Outcome from the 1st Cohort

The first COVID-19 vaccination cohort started from 28th of February 2021 to 25th of March 2021. We have completed both first and second doses for the first cohort. We managed to achieve zero wastage KPI.

A total of 2035 vaccine recipients received their second dose. 71 of the vaccine recipients or 3.37% did not turn up for their second dose. Out of this, 6 vaccine recipients found out they were pregnant after the first dose, and they will reschedule for the second vaccine dose after 14 weeks of pregnancy. 32 of them had symptoms like URTI (upper respiratory tract

infection). So they cannot go to the vaccination centre for their second dose, and thus we need to reschedule for them. Four of them had to get their vaccine shot in health clinic setting, and not in mass vaccination centre because they have some form of medical problems like uncontrolled asthma.

One vaccine recipient had moderate allergic reaction that occurred within 72 hours after the first Pfizer vaccine dose whereby she is not eligible for the second dose because she is allergic to Pfizer vaccine. One of them actually refused to receive the second dose because she had immediate side effect. About 15 minutes after her first jab, she had moderate dizziness. Another 27 of them who did not turn up for their second dose and they gave explanation like they were outstation, got admitted in hospital, and had other active medical problems. For those who are eligible to receive the second dose, we will reschedule their appointment.

Out of 2035 vaccine recipients, 322 of them had some form of comorbidities. The comorbidities reported were mainly diabetic, hypertension, asthma, heart disease, and others. All 322 of them were successfully vaccinated. None of them had allergic reaction or anaphylaxis. I also asked the other vaccination centres. They told me, so far, no anaphylaxis case. Hopefully there will not be any case of anaphylaxis in Phase II and Phase III. Only one person complained of dizziness, and she was sent to the yellow zone in the emergency department for short observation, a few hours. Two clients experienced immediate side effects like vomiting and dizziness within 30 minutes post vaccination.

None of the vaccine recipients infected with COVID-19 after the first dose, but three of the health care workers were infected with COVID-19 after the second dose of vaccine. Those who have had history of anaphylaxis, but not to the COVID-19 vaccine component like PEG or polysorbate have successfully vaccinated in hospital setting.

## Challenges and How To Overcome

Despite all the planning and trainings that we have done, we still have some challenges, and we would also like to share how we overcome these challenges. First, some clients did not follow the staggered appointments given, and we found it difficult to follow the new norm SOP like physical distancing.

How to overcome this? The person in charge provided by the respective agency needs to remind their staff to come according to the staggered appointment. However, some agencies

did not provide the name of a person in charge. Hence, our staff have to do the task. They had to call each client to remind them and to confirm their attendance. So, it is important to have a Person in Charge of each agency to help us. If not, this will burden our staff.

Interestingly, some clients claimed that they have been forced to enrol in the vaccination programme. They tried to skip the vaccination station. We have to be vigilant in controlling each station to avoid anyone from skipping any station. We use a line listing number which it will be collected at the vaccine station. This is to identify those who have actually been injected or not. At the end of the day, we will collect all these data, we total up the papers. The number of tagging papers must be the same as the number of consent form and the data entered in MyVAS system.

Another challenge is that, sometimes we do not have enough vaccine recipients for one vial of Pfizer-BioNTech COVID-19 vaccine. They either refuse or dropout at the last minute. So, we have to prepare backups every day, and we have to tell them to stand by when needed, as we will call.

There are also challenges in data collection, such as mistake in data entry during registration in the vaccination centre. For example, wrong name, wrong IC or batch number. So, the vaccinators should be trained by the MyVAS team and if possible, the same staff should do the same tasks/rotation in the first few days so that they can be familiarized with the procedures. For verification purpose, vaccine recipients should bring along their identity card (IC).

There is no case of true anaphylaxis, but there were cases of immune stress related response (ISRR) which sometimes may have similar presentation to allergy reactions. For instance, they have symptoms of dizziness, palpitations or near syncope. We have to train our staff on how to differentiate between anaphylaxis or ISRR.

Another challenge is the dilemma faced by patients with comorbid. Who should we check their blood pressure? It is not feasible to check the blood pressure reading of all the vaccine recipients as it is very time-consuming, and we have limited manpower. So, we prioritized those who have known hypertension and history of allergy. This group of patients would be asked to go to the blood pressure station to check their blood pressure.

One of the technical problems faced during phase one was the data management. Sometimes, the status in MyVAS is incomplete, or it was showing the ‘status is in progress’. So, we need to call the vaccine recipient. However, some of them do not answer the call, some of them

gave the wrong phone number, and some of them did not actually go to the verification station, which led to incomplete data in MyVAS. In other words, they did not follow the vaccine recipient flow and hence, this caused the Person in Charge to take longer time to correct the data. Sometimes, it can take up to hours and days to solve the problem as we have to find out the reason for each vaccine recipient who had the 'status arrived' or 'status progress' in MyVAS. We have to determine whether did the client miss any station on the day of vaccination or was it due to poor internet connection? For this issue, we have to have dedicated staff to show the direction to ensure each client will go to the correct designated station, and nobody will not miss any station.

## The Way Forward

We thought of using a card reader for the first vaccine dose registration. This will minimize most technical errors (mistake in data entry) in MyVAS. Unfortunately, for now, according to our IT officer, it is not feasible as our IT team did not have access to MyVAS coding.

## Summary

In summary, planning is very important to ensure the vaccine cold chain is maintained and the client in line listing will turn up for vaccination. We need adequate manpower and a well-organized vaccination schedule. For mass vaccination, we require an efficient and a dedicated team, so that the program will run smoothly, new norm SOP is adhered to at all times, good record keeping that would allow us to send the correct data.

I would like to take this opportunity to thank all our staff for their commitments in the first phase of the vaccination program. Thank you.

# Reference

Link to Dr Norzaihan's slide:
https://www.slideshare.net/ICRInstituteForClini/webinar-roll-out-vaccine-share-slide-05052021

Video Link: https://youtu.be/lfyJY2zEI-M

Podcast Link:
https://anchor.fm/clinupcovid/episodes/Real-issues-for-COVID19-Vaccine-Immunization--Pregnancy-e109e6n

# “COVID-19 Vaccination In Pregnancy And Breastfeeding” by Dr. Muniswaran Ganeshan

Thank you so much, Datuk Thomas for the very kind introduction. A very good evening, ladies and gentlemen. First and foremost, I would like to thank the Malaysian Society of Infection Control and Infectious Diseases (MyICID), and the Institute for Clinical Research (ICR) for this very kind invitation and for considering this very important topic. I've been given the task to speak on COVID-19 vaccination in pregnancy, but I will also include breastfeeding in my talk. This will be a 20-minute talk.

Firstly, I would like to dedicate this talk to the 1,574 patients who have died due to COVID-19, the 420,000 over confirmed patients throughout the nation, and the tireless frontliners who continued to battle this pandemic, my heart and thoughts, and I dedicate this talk to all of them.

I do not have any disclaimers in this presentation. This is purely intended for health professionals. Thoughts and Committee opinions are purely based on the national guidelines on COVID-19 in pregnancy.

Ladies and gentlemen, in the last 13 months, you have seen the COVID-19 pandemic, but I must, for once say that it is not just a pandemic, there are various other pandemics. One which is far more important than the COVID-19 pandemic, I think, is the misinformation, infodemic. Sadly, there has been a lot of misinformation with regard to pregnancy and breastfeeding. Sadly, the vulnerable group; those who breastfeed, those who are pregnant, have not been included in clinical trials.

These are some of the headlines that I would like to share which came out somewhere during late February 2021, the pregnant, breastfeeding mothers were advised against vaccination, where some experts claimed that vaccinations are not safe in pregnancy. We have had headlines saying that pregnancy should take a backseat and some important articles and some committee members have actually been misquoted in the past. So, I would like to put an end to this ‘mis-infodemic’. The next 20 minutes I would like to justify on why is it important to include pregnant mothers and breastfeeding mothers with regard to vaccination in pregnancy.

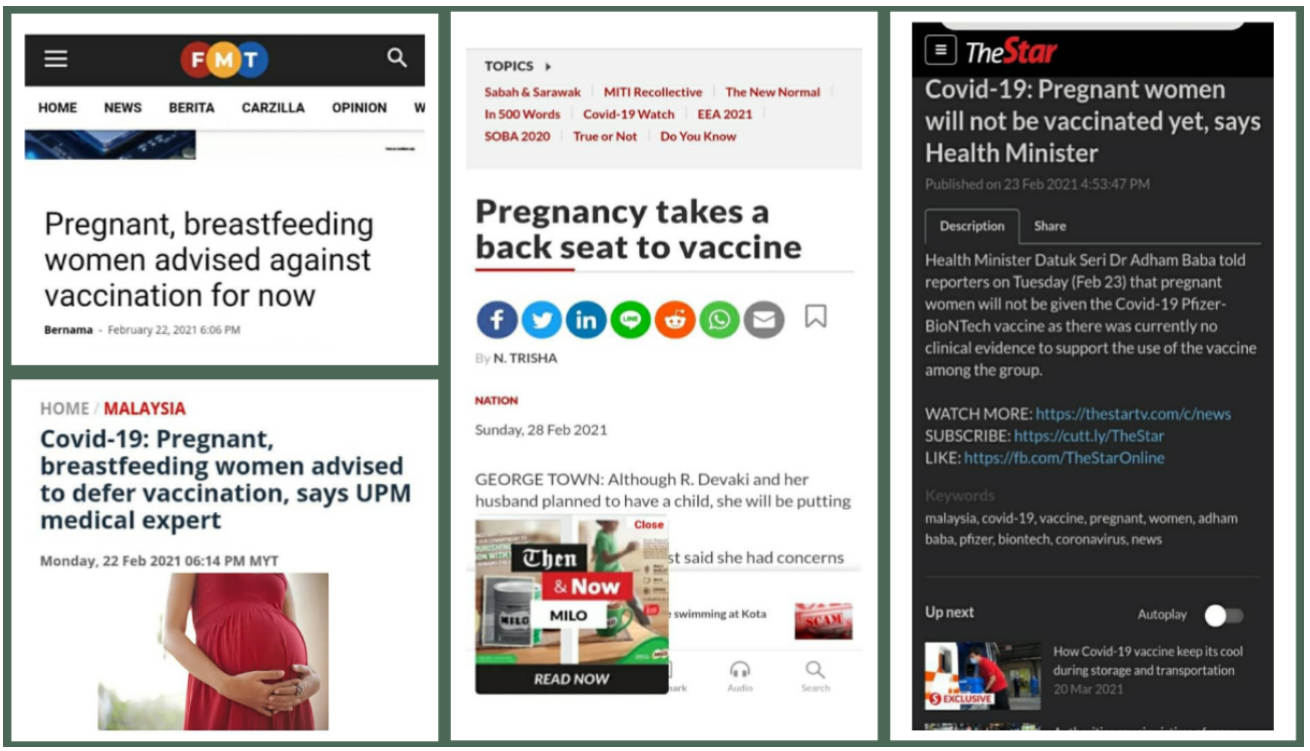



**Figure 5:** 'Mis-infodemic' (misinformation) with regard to COVID-19 vaccination in pregnancy and breastfeeding (Image from Dr. Muniswaran's slide presentation)

# Overview

I'd like to divide my talk into three important parts. Let's talk about the implications of COVID-19 in pregnancy, then we shall justify why we need to vaccinate and protect pregnant and breastfeeding mothers. And finally, this era, it's all about counselling. It's all about a shared decision-making that seems to be even more important now than ever before.

# Implications of COVID-19 in Pregnancy (Pregnancy and Infections)

What are the implications of COVID-19 in pregnancy? Based on our experience in regard to infections in pregnancy, it is a common thought that, pregnant mothers are more susceptible to viral infections, especially in the second and third trimester. And this is extremely relevant after our experiences in managing influenza patients, varicella patients and even malaria patients. Pregnant mothers are all known to be more susceptible, especially in the second and third trimester. So, when we first encountered COVID-19, way back somewhere in March and April 2020, this was our notion.

## Earlier Studies…

Unfortunately, ladies and gentlemen, I think we were swayed towards the wrong side. Initial studies and papers from Wuhan showed that pregnant mothers were actually not at risk when 92% of them had mild diseases, and only a small minority of them had severe diseases. Following papers from Wuhan also showed that majority of them were asymptomatic, and only a small minority of 1.9% of them had severe infection. So, ladies and gentlemen, in the earliest days of COVID-19, we were falsely misinformed about the implications of COVID-19 in pregnancy.

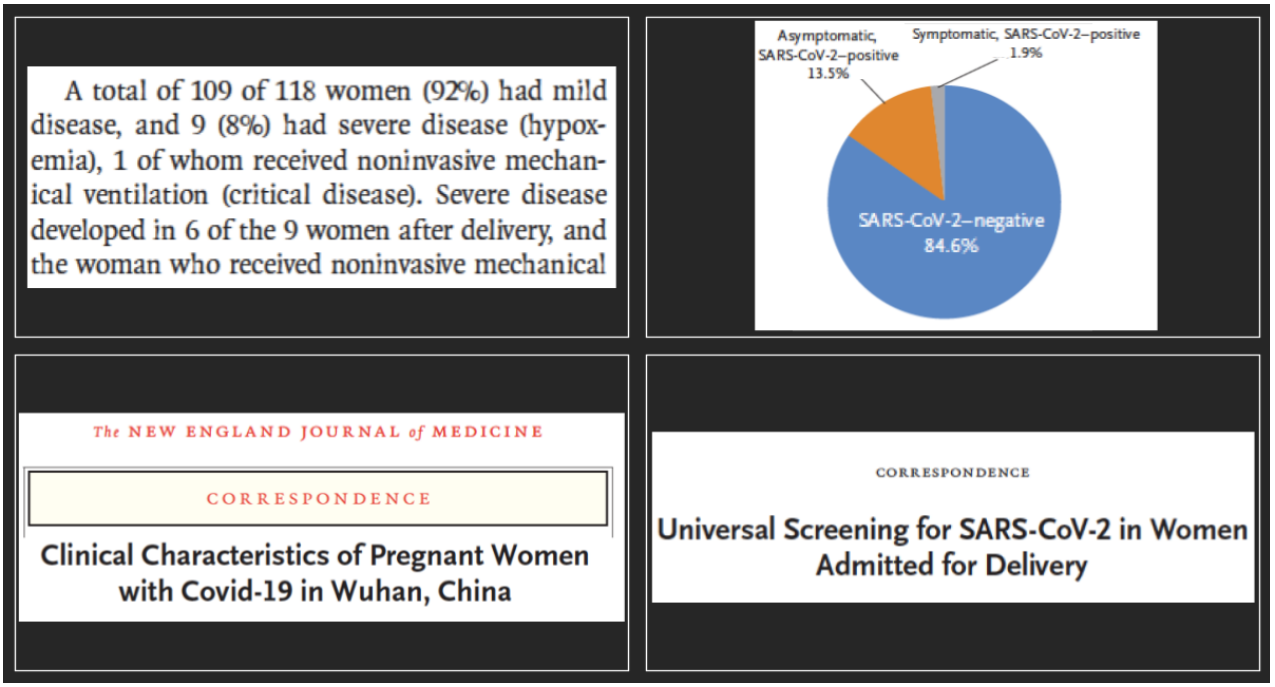



**Figure 6:** Misinformation about the implications of COVID-19 in pregnancy from earlier publications. (Image from Dr. Muniswaran's slide presentation)

## Current evidence from a few large studies and meta-analysis

Let me bring your attention to one large meta-analysis, "Clinical Manifestations, risk factors and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis" by J Allotey et al. (**Figure 7**). Now, this is the living systematic review and meta-analysis published in the BMJ. The last update was three weeks ago. This is the largest systematic review up to date. It has included 64,676 pregnant women, 569,000 in the reproductive age group. It has included 82 studies and 92 studies related to outcomes.

Based on this meta-analysis, if you are pregnant, the maternal outcomes are poorer. The maternal mortalities increased 2.85%, if the mother has got COVID-19 infection. The ICU admissions are increased. The preterm births before 37 weeks are increased. The caesarean section rates are increased. Similarly, COVID-19 infection is associated with poorer fetal outcomes, namely the increased incidence of still births, increased neonatal deaths, increased admissions to ICU, increased incidence of abnormal Apgar scores at five minutes, and the increased incidence of fetal distresses. Ladies and gentlemen, COVID-19 has significant implications in pregnancy.

**Table 1 | Outcomes in pregnant and recently pregnant women with coronavirus disease 2019 (covid-19)**

| Outcomes | No of studies | Women (No with event/No in group (%)) | | Odds ratio (95% CI) | $I^2$ (%) |
|---|---|---|---|---|---|
| | | Pregnant women with covid-19 | Comparison group | | |
| **Comparison group: non-pregnant women of reproductive age with covid-19** | | | | | |
| All cause mortality | 8 | 103/34 047 (0.3) | 3388/567 075 (0.6) | 0.96 (0.79 to 1.18) | 0 |
| ICU admission | 7 | 616/34 035 (1.8) | 9568/567 073 (1.7) | 2.13 (1.54 to 2.95) | 71.2 |
| Invasive ventilation | 6 | 270/34 001 (0.8) | 3280/567 043 (0.6) | 2.59 (2.28 to 2.94) | 0 |
| ECMO | 2 | 17/30 446 (0.1) | 120/431 490 (0.0) | 2.02 (1.22 to 3.34) | 0 |
| Oxygen through nasal cannula | 2 | 8/48 (16.7) | 49/106 (46.2) | 0.21 (0.04 to 1.13) | 65.7 |
| ARDS | 1 | 0/17 (0) | 0/26 (0) | 1.51 (0.03 to 79.93) | NE |
| Major organ failure | 1 | 0/17 (0) | 0/26 (0) | 1.51 (0.03 to 79.93) | NE |
| **Comparison group: pregnant women without covid-19** | | | | | |
| Maternal outcomes: | | | | | |
| All cause mortality | 8* | 8/1195 (0.7) | 8/3625 (0.2) | 2.85 (1.08 to 7.52) | 0 |
| ICU admission | 7* | 64/1508 (4.2) | 4/3482 (0.1) | 18.58 (7.53 to 45.82) | 0 |
| Preterm birth <37 weeks | 18 | 147/1184 (12.4) | 572/7365 (7.8) | 1.47 (1.14 to 1.91) | 18.6 |
| Caesarean section | 21*† | 669/1854 (36.1) | 4221/11842 (35.6) | 1.12 (0.91 to 1.38) | 57.6 |
| Perinatal outcomes: | | | | | |
| Stillbirth | 9* | 9/1039 (0.9) | 26/4755 (0.5) | 2.84 (1.25 to 6.45) | 0 |
| Neonatal death | 8* | 4/970 (0.4) | 5/3316 (0.2) | 2.77 (0.92 to 8.37) | 0 |
| Admission to neonatal unit | 10* | 329/1285 (25.6) | 519/4588 (11.3) | 4.89 (1.87 to 12.81) | 96.2 |
| Abnormal Apgar score at 5 minutes | 6 | 13/662 (2.0) | 46/2823 (1.6) | 1.38 (0.71 to 2.70) | 0 |
| Fetal distress | 2 | 11/77 (14.3) | 13/263 (4.9) | 2.37 (0.77 to 7.31) | 0 |

**Figure 7:** Outcomes from the Meta-Analysis (Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis BMJ 2020; 370 :m3320 doi:10.1136/bmj.m3320)

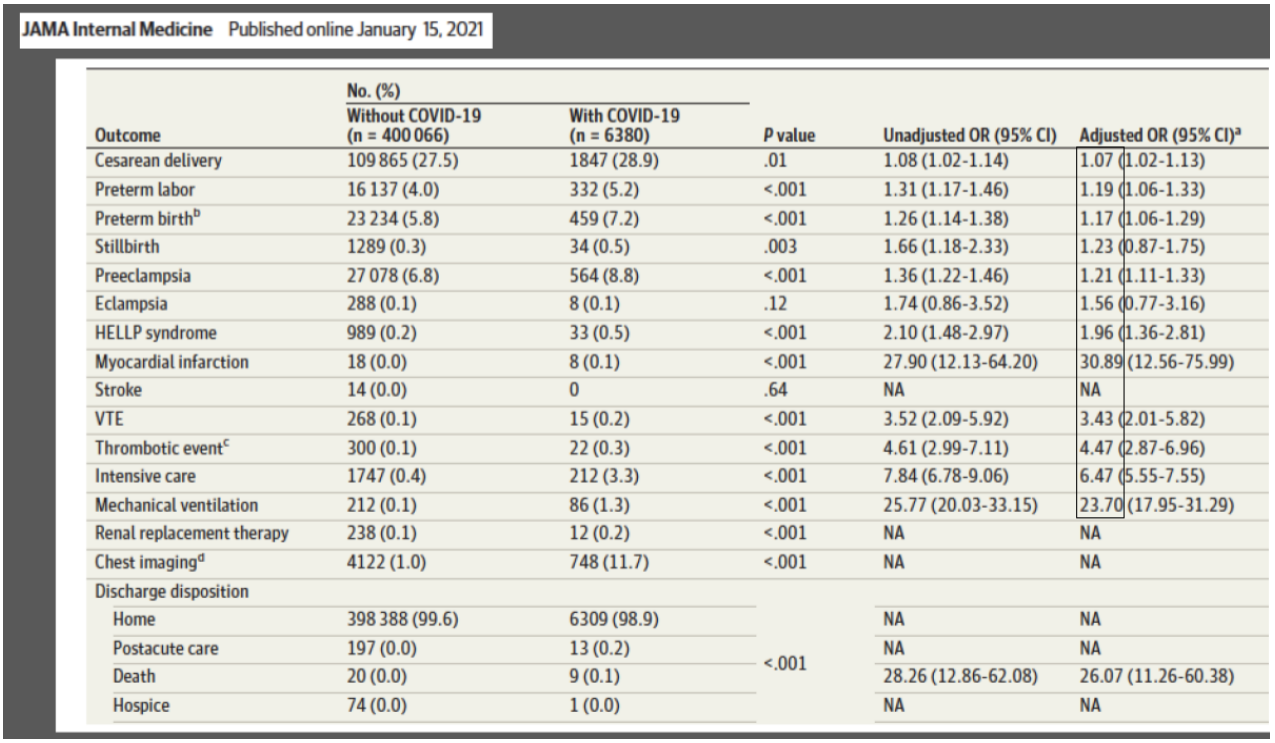
A similar paper, "Risk factors for illness severity among pregnant women with confirmed SARS-CoV-2 infection – Surveillance for Emerging Threats to Mothers and Babies Network, 20 state, local, and territorial health departments, March 29, 2020 - January 8, 2021" by Galang RR et al. published a few weeks ago, from the US cohort which looked into threats to mothers and babies in 20 states, local and territorial health departments from March 2020 to January 2021. The findings were similar. If a mother was to have COVID-19 in pregnancy, the mortalities increased, the need for ICU admissions were increased, and the risk factors were the same. The common risk factors were elderly, from low socioeconomic group and obese.

Let's take a look at another systematic review "SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes" by Khalil A. et al., also recently published about the implications of COVID-19 in pregnancy (**Figure 8**). This paper once again had similar outcomes to report. If you have COVID-19 in pregnancy, the fetal distresses are higher, preterm deliveries are higher namely to aid maternal respiration. Spontaneous preterm birth is also high, and as is the number of caesarean sections is high.

| | | | | |
|---|---|---|---|---|
| ***Maternal complications*** | | | | |
| Bacteria or viral co-infection¶ | 1 | 5/60 | 8.3% (3.5–18.5%) | – |
| Maternal intensive care unit admission | 13 | 159/1591 | 7.0% (4.4–10.9%) | 81.7% |
| Oxygen support (nasal or non-invasive ventilation) | 10 | 295/1623 | 18.2% (9.8–31.1%) | 95.5% |
| Intubation and mechanical ventilation | 11 | 92/1680 | 3.4% (1.5–7.7%) | 90.2% |
| Maternal ECMO | 12 | 13/1896 | 0.7% (0.4–1.2%) | 0.0% |
| Maternal death | 15 | 43/2468 | 0.9% (0.4–2.3%) | 73.4% |
| ***Obstetric outcomes*** | | | | |
| Delivered cases | 10 | 746/1650 | 52.4% (37.9–66.5%) | 96.1% |
| Delivery due to COVID-19 related reasons | 8 | 95/497 | 19.0% (8.9–36.0%) | 89.4% |
| Delivery due to fetal distress | 6 | 15/238 | 5.3% (2.3–11.8%) | 40.2% |
| Preterm birth (any) | 10 | 183/746 | 21.8% (14.6–31.3%) | 82.3% |
| Spontaneous preterm birth | 7 | 22/440 | 5.0% (3.3–7.5%) | 0.0% |
| Medically indicated preterm birth | 6 | 92/430 | 18.4% (8.3–35.8%) | 87.4% |
| Preterm birth $< 34^{+0}$ weeks | 4 | 13/147 | 3.3% (0.2–31.9%) | 87.0% |
| Caesarean delivery | 10 | 390/746 | 48.3 (34.1–62.7%) | 91.5% |
| ***Perinatal outcomes*** | | | | |
| Perinatal death | | | | |
| Stillbirth†† | 8 | 12/1362 | 0.9% (0.5–1.5%) | 0.0% |
| Neonatal death | 8 | 4/688 | 0.6% (0.2–1.5%) | 0.0% |
| SARS-CoV-2 PCR positivity after delivery | 9 | 19/751 | 1.4% (0.4–4.7%) | 59.8% |

**Figure 8:** Results from paper by Khalil A et al. **(**Khalil A, Kalafat E, Benlioglu C, O'Brien P, Morris E, Draycott T, et al. SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. EClinicalMedicine. 2020;25. 100446. doi: 10.1016/j.eclinm.2020.100446)

Since the BMJ report was published, a similar study (**Figure 9**) published in the JAMA Internal Medicine in January this year, also showed similar evidence that the COVID-19 is associated with significant medical implications, namely caesarean delivery, preterm birth, ICU admissions and the need for ventilation.



JAMA Internal Medicine Published online January 15, 2021

| Outcome | No. (%) Without COVID-19 (n = 400 066) | With COVID-19 (n = 6380) | *P* value | Unadjusted OR (95% CI) | Adjusted OR (95% CI)[a] |
|---|---|---|---|---|---|
| Cesarean delivery | 109 865 (27.5) | 1847 (28.9) | .01 | 1.08 (1.02-1.14) | 1.07 (1.02-1.13) |
| Preterm labor | 16 137 (4.0) | 332 (5.2) | <.001 | 1.31 (1.17-1.46) | 1.19 (1.06-1.33) |
| Preterm birth[b] | 23 234 (5.8) | 459 (7.2) | <.001 | 1.26 (1.14-1.38) | 1.17 (1.06-1.29) |
| Stillbirth | 1289 (0.3) | 34 (0.5) | .003 | 1.66 (1.18-2.33) | 1.23 (0.87-1.75) |
| Preeclampsia | 27 078 (6.8) | 564 (8.8) | <.001 | 1.36 (1.22-1.46) | 1.21 (1.11-1.33) |
| Eclampsia | 288 (0.1) | 8 (0.1) | .12 | 1.74 (0.86-3.52) | 1.56 (0.77-3.16) |
| HELLP syndrome | 989 (0.2) | 33 (0.5) | <.001 | 2.10 (1.48-2.97) | 1.96 (1.36-2.81) |
| Myocardial infarction | 18 (0.0) | 8 (0.1) | <.001 | 27.90 (12.13-64.20) | 30.89 (12.56-75.99) |
| Stroke | 14 (0.0) | 0 | .64 | NA | NA |
| VTE | 268 (0.1) | 15 (0.2) | <.001 | 3.52 (2.09-5.92) | 3.43 (2.01-5.82) |
| Thrombotic event[c] | 300 (0.1) | 22 (0.3) | <.001 | 4.61 (2.99-7.11) | 4.47 (2.87-6.96) |
| Intensive care | 1747 (0.4) | 212 (3.3) | <.001 | 7.84 (6.78-9.06) | 6.47 (5.55-7.55) |
| Mechanical ventilation | 212 (0.1) | 86 (1.3) | <.001 | 25.77 (20.03-33.15) | 23.70 (17.95-31.29) |
| Renal replacement therapy | 238 (0.1) | 12 (0.2) | <.001 | NA | NA |
| Chest imaging[d] | 4122 (1.0) | 748 (11.7) | <.001 | NA | NA |
| Discharge disposition | | | | | |
| Home | 398 388 (99.6) | 6309 (98.9) | <.001 | NA | NA |
| Postacute care | 197 (0.0) | 13 (0.2) | | NA | NA |
| Death | 20 (0.0) | 9 (0.1) | | 28.26 (12.86-62.08) | 26.07 (11.26-60.38) |
| Hospice | 74 (0.0) | 1 (0.0) | | NA | NA |

**Figure 9:** Study published in JAMA Internal Medicine on January 15, 2021(Image from Dr. Muniswaran's slide presentation)

## All about the COVID-19 (Sars-CoV-2) Strains

What about implications of the first and second strain? What about the newest strains?

**Figure 10** showed results which were published two weeks ago, based on the UK Obstetric surveillance system. It is now more clear that younger women are having a higher rate of infections based on the new strain and more of them are symptomatic. So, the newest strains are affecting younger cohort as compared to the initial strains.

Once again, when is the time when most pregnant mothers are vulnerable? It is usually towards the second and the third trimester. This is correlating with what we have already known and is associated with the physiological changes in practice.

So, ladies and gentlemen, the conclusion from the recently published UK obstetric surveillance system was if you think this is a disease which is purely related to men, it is not true. This is because most pregnant mothers are asymptomatic, they will actually present to the obstetric ward when you actually screen them during admissions and during labour. So, it is not a disease related to men itself. It is the disease which equally affects men and women. Most pregnant mothers will be asymptomatic. But if the mother has got COVID-19 in

pregnancy, the incidence of death is 1%, while the preterm birth is 18%. This is way higher and significant as compared to the background rates.

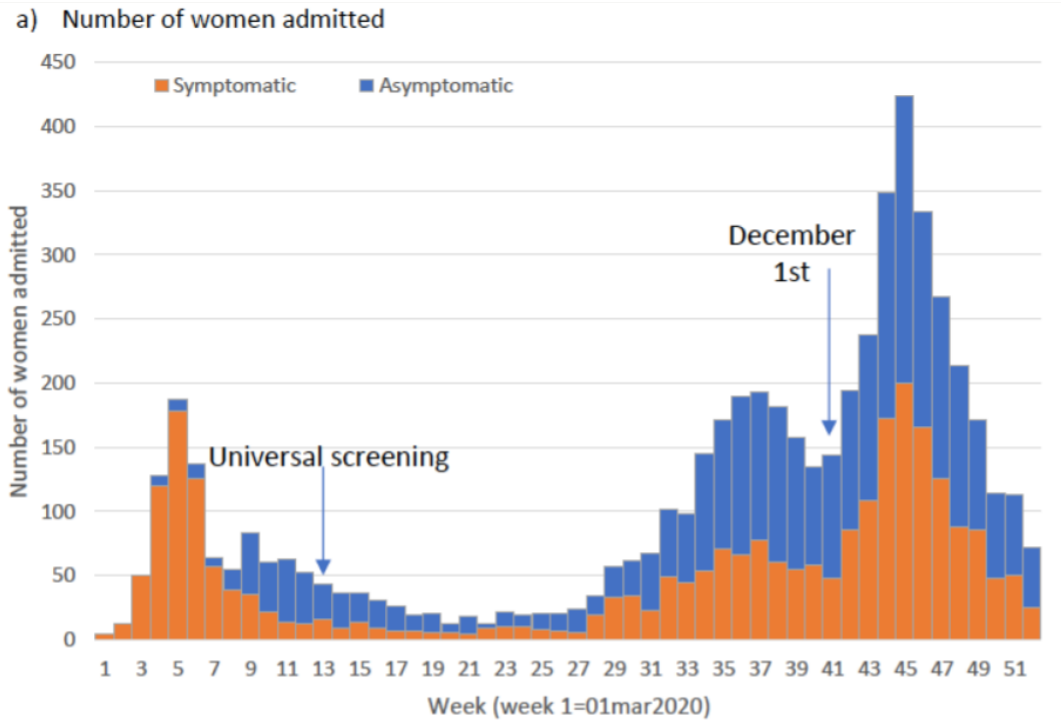



**Figure 10:** Admissions of pregnant women with confirmed SARS-CoV-2 to UK hospitals and symptomatology (n=5490) [UKOSS]

What is sad? There have been numerous trials and studies about COVID-19 in pregnancy, but the evidence in pregnancy is extremely rare, because pregnant mothers and those who breastfeed have been excluded from clinical trials. What is important is that these newer strains seem to be affecting women, more common and younger women are having these newest strains. They are being more symptomatic as compared to the initial strains.

To summarize my talk on implications of COVID-19 in pregnancy, ladies and gentlemen, these few facts are essential. (1) Most mothers will be asymptomatic. (2) The need for ICU admissions are increased. (3) If you are pregnant, and you have COVID-19, the need for ventilation is increased. (4) The maternal mortality is increased by 2.8 folds. (5) It does not just affect the mother, the incidence of preterm delivery to aid maternal ventilation is increased. (6) The caesarean section rate is increased, and similarly, stillbirths and neonatal deaths are increased.

So, ladies and gentlemen, pregnant mothers are vulnerable. It is our priority and responsibility to protect pregnant mothers and also to reduce the maternal and fetal implications of COVID-19.

# Importance of Vaccinating Pregnant and Breastfeeding Mothers

This brings to the second portion of my talk, the importance of vaccinating pregnant and breastfeeding mothers. Interestingly, pregnant mothers are now prioritized in the Phase II, and they are a group of attention. So, if you include high risk patients in the Phase II namely aged, those immunocompromised patients such as though who have HIV infections, patients with medical illnesses, pregnant mothers with these risk factors are recommended to be vaccinated in the Phase II.

So, why is this essential? I have already justified that pregnant mothers are vulnerable. Based on systematic review and meta-analysis, there are significant maternal and fetal implications. Based on our experience of vaccination, the live-attenuated vaccines are contraindicated in pregnancy, but the mRNA vaccine does not seem to cause any infection and is not contraindicated in pregnancy. For the live-attenuated vaccine, the COVI-VAC vaccine from India is not recommended, but the mRNA vaccine is not a contraindication. It is recommended, but it is a personal choice. It is the decision of the patient to choose willingly if she needs the vaccine, or she wants to take it.

The whole idea of vaccination is to reduce maternal and fetal implications in the second and third trimester. The CDC recommends three COVID-19 vaccines in pregnancy, the Moderna vaccine, the Pfizer vaccine and the J&J vaccine. But, if you are pregnant or if you are breastfeeding in Malaysia, based on our COVID-19 vaccination guidelines, you will only get one vaccine, which is the Comirnaty vaccine. Why is that so? This is because the Pfizer vaccine has got the best safety profile and evidence which has been reported in pregnancy. Despite Malaysia having access to numerous types of vaccines, if you are pregnant, you will only get one type of vaccine, the Comirnaty vaccine.

What is the recommended window for vaccination? The recommended window is between 14 and 33 weeks. Why the magic number of 14? We wanted to vaccinate pregnant mothers after the period of organogenesis. Although there are no concerns about vaccination in pregnancy, the first trimester is the period of organogenesis where we would usually like to limit unknown exposure. That is why we recommended vaccination after 14 weeks. Now, why the

upper limit of 33 weeks? Ladies and gentlemen, if you want to vaccinate pregnant mothers, you want to vaccinate them before the late second trimester, before the third trimester when the implications are significant. Hence, our upper limit is of 33 weeks and this is based on our recommendations.

If you vaccinate the mother, there is no evidence that it protects the baby as compared to the Tdap (Tetanus, Diphtheria, Pertussis) vaccination which has got some neonatal protection and the influenza vaccination as well has got some neonatal protections. Based on currently literature, vaccinating the mother does not protect the baby at this moment of time. When you give the mother COVID-19 vaccines, she can also take Anti-D vaccine and other vaccines, but the recommended interval is at least 14 days.

## Who are the high-risk pregnant mothers?

Who are the high-risk pregnant mothers? The list is in **Figure 11**, but it is not extensive. These are the recommended patients who should be included in Phase II. Those who are elderly, those who are obese, those who have got underlying significant medical conditions, those who are immunocompromised, those who are on immunosuppressive therapies, and those who have had splenectomy. These are the patients who are recommended to have the COVID-19 vaccination in pregnancy.

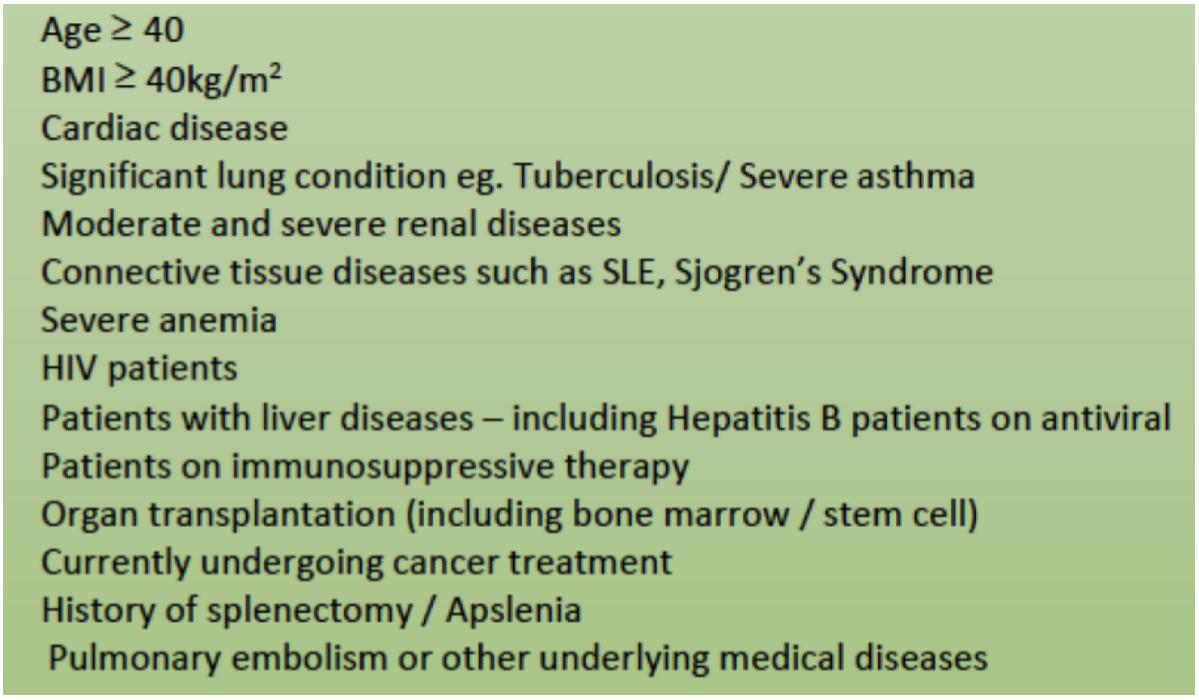



**Figure 11:** Who are considered high risk in pregnancy?

What are the other Obstetrics societies current recommendation? I think one of the first college to recommend the vaccination was the American College, who came out strongly at the end of last year, recommending the vaccination in pregnancy. That was followed by the CDC, the Royal College of Obstetricians and Gynaecologists, and the International Federation of Gynaecology and Obstetrics. The last society, who now recommends vaccination is the Joint Committee on Vaccination and Immunization (JCVI), United Kingdom, who just came out with a statement three weeks ago, advising that pregnant women should be offered the COVID-19 vaccine, at the same time as the rest of the population.

If you look into countries that have actually included vaccinating pregnant mothers, I am proud to say that among all these countries, Malaysia is also a frontier. Israel, Belgium, Canada, Ireland, Germany, United Kingdom, United States, Scotland, Croatia and Malaysia are among the first countries who recommend vaccination among pregnant mothers. It is compulsory in Israel and Belgium. In Malaysia, it is based on voluntary basis. I'm extremely proud that we are actually one of the frontier countries who are protecting our pregnant women.

One of the biggest safety data in regard to vaccination in pregnancy is the v-safe data registry (**Figure 12**), which is based on those who have been vaccinated in the USA. Up to March and end of March, there were already about 63,000 over pregnant mothers who have been vaccinated in the US. Now, we have a little bit of data about those who have been vaccinated in pregnancy.

Based on this v-safe data registry, the average age of vaccination for mothers were 33 weeks. The average gestational age was 13 weeks. 51% of them were vaccinated in the first trimester, although our recommendation is to vaccinate after the first trimester. Majority of them got the Pfizer vaccine. A significant number of them had the Moderna vaccine, and this is based on 154 patients who were evaluated in the v-safe file registry.

| Characteristic | |
|---|---|
| Maternal age in years, median (range) | 33 (16–51) |
| Gestational age in weeks at time of vaccination when reported, median (range) | 13 (2–38) |
| **Trimester of pregnancy at time of vaccination** | **n (%)** |
| First (0-13 weeks) | 60/118 (51) |
| Second (14-27 weeks) | 36/118 (31) |
| Third (28+ weeks) | 22/118 (19) |
| **Vaccine** | |
| Pfizer-BioNTech | 97 (63) |
| Moderna | 56 (36) |
| Unreported | 1 (0.6) |

CDC + FDA
VAERS

**Figure 12:** Characteristics of COVID-19 vaccine pregnancy reports to VAERS through February 16, 2021 (N=154)

Based on this registry, what are the implications of having vaccination in pregnancy? (**Figure 13**) The first report published somewhere around the middle of February showed that the incidence of miscarriage was slightly increased, but the incidence of stillbirth was similar to the normal population. It did not cause an increase in eclampsia, GDM, preeclampsia, and intrauterine growth restriction (IUGR). Vaccination did not cause fetal anomalies, preterm births, neonatal deaths, and small for gestational age.

| Outcomes | Background rates* | V-safe pregnancy registry overall |
|---|---|---|
| **Pregnancy outcome** | | |
| Miscarriage (<20 weeks) | 26% | 15%† |
| Stillbirth (≥ 20 weeks) | 0.6% | 1% |
| **Pregnancy complications** | | |
| Gestational diabetes | 7-14% | 10% |
| Preeclampsia or gestational hypertension§ | 10-15% | 15% |
| Eclampsia | 0.27% | 0% |
| Intrauterine growth restriction | 3-7% | 1% |
| **Neonatal** | | |
| Preterm birth | 10.1% | 10% |
| Congenital anomalies‡ | 3% | 4% |
| Small for gestational age^ | 3-7% | 4% |
| Neonatal death | 0.38% | 0% |

**Figure 13:** V-safe pregnancy registry outcomes of interest in COVID-19 vaccinated pregnant women as of February 18, 2021

Interestingly, this paper (**Figure 14**) "Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons" by Shimabukuro TT et al. was just published a few weeks ago in the New England Journal of Medicine, also extrapolated data from the v-safe pregnancy. There were some concerns about a slight increased risk of miscarriage if you take it in the first trimester. However, there was no increased risk of stillbirths and preterm deliveries.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

**Table 4. Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.**

| Participant-Reported Outcome | Published Incidence* | V-safe Pregnancy Registry† |
|---|---|---|
| | % | *no./total no. (%)* |
| Pregnancy loss among participants with a completed pregnancy | | |
| Spontaneous abortion: <20 wk[15-17] | 10–26 | 104/827 (12.6)‡ |
| Stillbirth: ≥ 20 wk[18-20] | <1 | 1/725 (0.1)§ |
| Neonatal outcome among live-born infants | | |
| Preterm birth: <37 wk[21,22] | 8–15 | 60/636 (9.4)¶ |
| Small size for gestational age[23,24]‖ | 3.5 | 23/724 (3.2) |
| Congenital anomalies[25]** | 3 | 16/724 (2.2) |
| Neonatal death[26]†† | <1 | 0/724 |

**Figure 14:** Paper extrapolating data from the v-safe pregnancy (Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, Marquez PL et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. N Engl J Med. 2021 Apr 21. doi: 10.1056/NEJMoa2104983)

Ladies and gentlemen, I would like to bring your attention towards this paper "COVID-19 vaccine response in pregnant and lactating women: a cohort study" by Gray KJ et al., just published in The Green Journal (Obstetrics & Gynecology: COVID-19). This just came out in the early April. This was a study looking into a cohort of pregnant and lactating mothers. Based on this paper, if you were to vaccinate the pregnant women, there has been a robust humoral immunity in the pregnant and lactating mothers with immunogenicity and reactivity which has been observed as compared to the non-pregnant women. Interestingly, the vaccine-induced response was far greater in the vaccination cohort, as compared to those who

have had natural infection. We do know that the IgG is transferred via placenta and breast milk. The amount of IgG transferred was higher for those who have been vaccinated. It did not cause infection in the fetus. It was not significant enough to cause protection. It is interesting that the amount of transferred was far greater in the vaccination cohort as compared to those who have had natural infections. It is important that we continue to watch this space.

So, ladies and gentlemen, one of the first study that showed the ability of the IgG to be transferred was this paper from Israel which showed that if you vaccinated pregnant women or those who had COVID-19 infection, they have got significant IgG which has been found in the placenta, and via the breast milk **(Figure 15**). But this does not render protection, or neither does this infect the fetus. So, this is quite interesting.

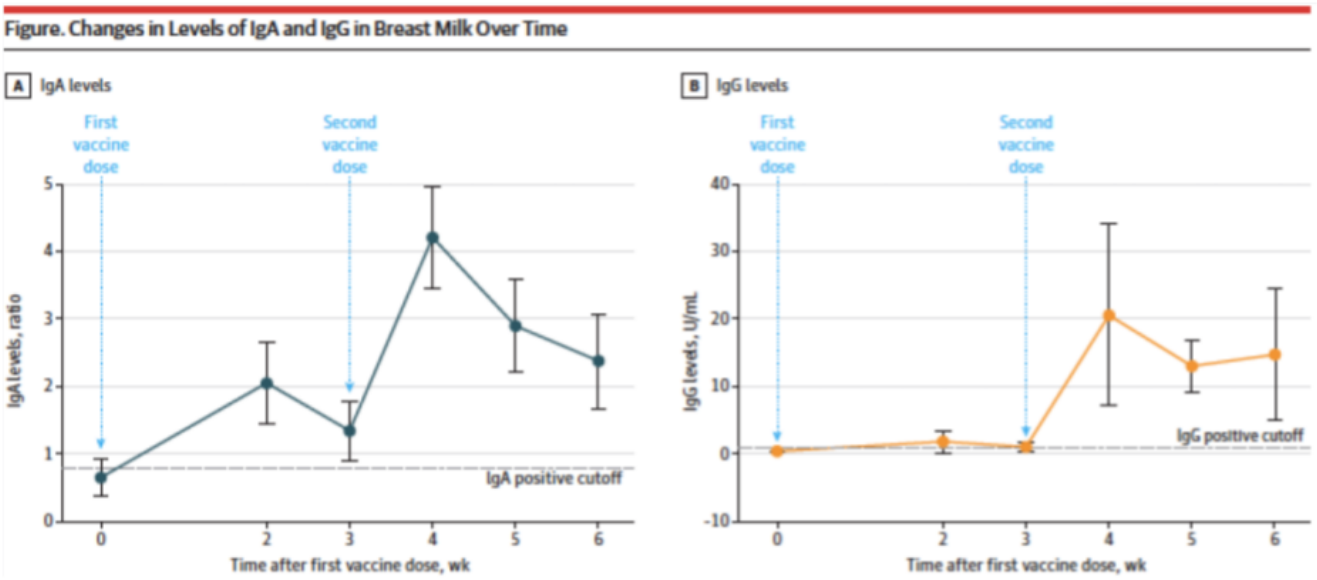



**Figure 15:** Characterization of SARS-CoV-2 RNA, Antibodies and Neutralizing Capacity in Milk Produced by Women with COVID-19

# Counselling and Shared Decision Making

## Pregnant women and breastfeeding mothers

Coming to the third part of my talk, it is all about counselling, and shared decision-making. I think my key takeaway point from this third part is you should not deny a pregnant woman or a mother who is breastfeeding the COVID-19 protection via vaccination, but you should have

a neutral counselling, and it should be a shared decision-making made between the obstetrician, the physician, and the patient.

In the first immunization cohort, if you're a frontliner, you are extremely vulnerable. Your risk of having the infection is extremely high. It is important that you are protected. The benefit outweighs the risk of vaccination. If you are high risk, if you are elderly, if you have a high BMI or if you have got an underlying medical condition, your risk of having severe COVID-19 infection is increased and the benefit outweighs the risk. If you are a pregnant mother currently staying in the Klang Valley, the risk of having the COVID-19 infection is extremely high, the benefit outweighs the risk. On the other hand, if you are a low-risk mother living in a population where there's low risk of transmission, this is the only time you have to sit down, talk about the benefit and risk of vaccination. I believe in Malaysia, we just implemented a movement control order. I think the risk of you having an infection in the community is high. If you are high risk and pregnant, you should always discuss the benefits of vaccination.

## Fertility treatment group

What about fertility? It is clear that a vaccination does not cause infertility. If you are already on infertility treatment, it is not right to stop your treatment midway. The recommendation is to continue treatment, but it is okay to be vaccinated in pregnancy. If you are thinking of embarking on an infertility treatment, if you think you are high risk, if you think you are elderly, if you are obese or if you have got medical problems, it is important to be vaccinated first, and you will be incorporated in the Phase II high risk group. Then later embark on an infertility treatment. On the other hand, if you are absolutely low risk, if you are healthy or if you are young, you might not have the vaccine as soon as August. Hence, it is perhaps not wise to delay your fertility treatment until you have the vaccine. So, it is a discussion that you should make with your infertility expert. It is reasonable not to delay your fertility treatment if you are low risk. However, it is important to get vaccinated first before your fertility treatment, if you are high risk. We should counsel all our patients in the prepregnancy stage.

Now interestingly, the British Fertility Society came out with a very strong statement. They said that a vaccine does not affect fertility. What is the interval between vaccine and fertility treatment? There is no magic interval. If you have completed the second vaccine, you can actually have your fertility treatment soon after the second vaccine, but it is not recommended having your fertility treatment in between vaccinations.

How about egg and sperm donation and vaccines? Just like your ability to donate blood, the recommended magic number is a seven-day interval. This is based on The Human Fertility and Embryo Association. You can donate your egg, or your sperm seven days after having the vaccine, but there's no need to delay fertility treatment after the second vaccine.

What if we have had recurrent miscarriages? Contrary to the evidence from The New England Journal of Medicine, the British Fertility Association did say that if you have recurrent miscarriages, it is not a contraindication for vaccination.

So, the recommendation to be vaccinated is between 14 and 33 weeks.

What if we had a patient who had the vaccine and later found out that she was pregnant? What are the options of counselling? We have got three options. (**Figure 16**)

Option number one, you ideally do not want to vaccinate her in the first trimester, namely because of the concerns of the increase in risk of miscarriage. So, if the woman had the Pfizer vaccine, it is okay to delay her second vaccination after 14 weeks, because now we know that if you vaccinate her within 12 weeks, the IgG response is better, and she is still protected. So, after the first vaccine jab, delay the second vaccine dose at her 14 weeks of pregnancy, as long as the interval is within 12 weeks.

Option number two, if the pregnant woman finds that this is not acceptable. It is actually okay just to have one vaccine. If we have the Pfizer vaccine, we do know that the protection can be as high as 87%.

Option number three, the pregnant lady finds both options one and two to be not acceptable. It is okay to have the second dose as routine scheduled because based on the v-safe study, all the 51% of the 154 patients who had the vaccine, there were no increased incidence of fetal anomalies. There was no increased incidence of stillbirths, although there was a slight increased risk of miscarriage. So, these are your options on counselling of pregnant mothers who had the vaccine in between pregnancies.


**Figure 16:** Options of counselling for pregnant others who found out that they are pregnant after vaccination

# List of FAQ

Here are some other commonly asked question:

a) *I got COVID-19 vaccine. Can I take the Tdap (Tetanus, Diphtheria, Pertussis) vaccine?*

   Yes.

b) *I've got the COVID-19 vaccine. Do I need the influenza vaccine?*

   Yes.

c) *I have allergies. Can I be vaccinated?*

   It is not a contraindication. It is best to discuss with your physician.

d) *Does vaccination cause fetal anomaly?*

   No.

e) *Can I take the anti-tetanus jab if I had the COVID-19 vaccine?*

   First and foremost, you do not really need the anti-tetanus injection in pregnancy, it is no longer a recommendation. But it is okay to take the anti-tetanus injection after having the COVID-19 vaccine.

f) *Do you need a detailed scan of the vaccine?*

   No.

g) *Do I need to routinely check the urine pregnancy test before vaccination?*

There is no need for a routine check. But, if you get pregnant after a vaccination, we have three options which are mentioned earlier.

# Take Home Message

Healthcare professionals and high-risk pregnant mothers are vulnerable. Most of them will be asymptomatic. The maternal and fetal implications of COVID-19 are extremely significant, namely ICU admissions, mortality, preterm deliveries and caesarean sections. Do not deny a pregnant lady or breastfeeding mother a proven preventive method. Vaccinations save lives. Vaccine has been proven to significantly reduce hospitalizations and deaths. I think it is a shared decision made between the physician and the patient. The patient then has the right to choose. I personally feel denying a safe intervention is a violation of human rights. Do not deny pregnant mothers the potential benefits of the vaccine.

**Figure 17** shows the references based on the updated guidelines on COVID-19 vaccination in Obstetrics and Gynaecology (version 1) published on 23rd of March 2021 **(Link:** slideshare.net/ICRInstituteForClini/clinical-guidelines-on-covid19-vaccination-in-malaysia-2nd-edition).

I would like to bring your attention to this infographic (**Figure 17**) , which you can use in your own daily practice to counsel patients. I would like to end with a quote, “women do not die because of illnesses that we cannot treat. They unfortunately die because the society still has not decided that their lives are worth saving.” It is important that we continue to save lives. It is important that we continue to protect the vulnerable. We should be protecting the high risk pregnant and breastfeeding mothers. With that, thank you so much for your kind attention.

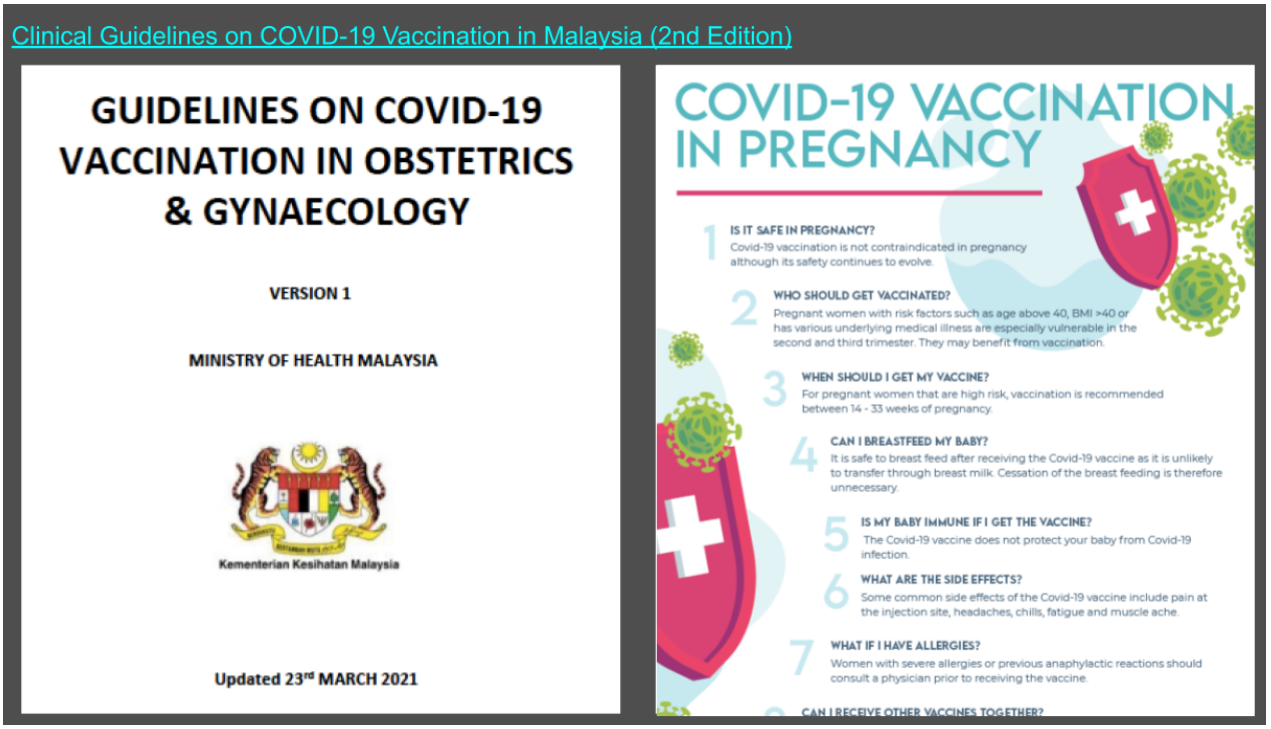



**Figure 17:** Clinical Guidelines on COVID-19 Vaccination in Malaysia (Image from Dr. Muniswaran's slide presentation)

# Reference

Link to Dr Muniswaran's slide: https://www.slideshare.net/ICRInstituteForClini/covid19-vaccination-in-pregnancy-breastfeeding

Video Link: https://youtu.be/lfyJY2zEI-M

Podcast Link: https://anchor.fm/clinupcovid/episodes/Real-issues-for-COVID19-Vaccine-Immunization--Pregnancy-e109e6n

# Updates on vaccination in pregnancy and breastfeeding

*N.B.: This is an additional update added after the webinar session. The information last updated on 12th June 2021.*

- **Safety of mRNA vaccination in pregnancy – NEJM 21st April 2021**

Based on the recent New England Journal of Medicine (NEJM) publication using the V-safe after vaccination health checker, the study concluded that mRNA vaccines were safe to be used during pregnancy without any significant safety signals and this is coherent with the MOH guidelines recommending the Pfizer vaccine among pregnant and breastfeeding mothers in Malaysia. The side effects were uncommon, mild, transient and treatable.

- **Efficacy of vaccines in pregnancy**

Studies show that the efficacy of the mRNA vaccine is similar in pregnancy as compared to non-pregnant mothers. Although the vaccine induced immune response fared better as compared to those with natural COVID-19 infection, the risk of infection to the fetus is insignificant, although the protective benefits remains to be evaluated.

- **Timing of vaccine between 14-33 weeks of pregnancy**

In keeping with the principles as to avoid the vaccine during the essential period of organogenesis in the first trimester and also as to ensure that mothers are vaccinated and offered protection before the vulnerable late second and third trimester, it is also our priority to ensure that mothers are not denied the vaccine during pregnancy. So, the current recommendations is to administer the first dose of the vaccine during this period while the second dose can be administered beyond 33 weeks based on the schedule.

- **Use of Oxford/AstraZeneca among pregnant and breastfeeding mothers**

Although there are no reported concerns with regard to the use of Oxford/AstraZeneca vaccine in pregnancy and breastfeeding, there is less experience with this vector based

vaccine as compared to the mRNA vaccine. Thus, Pfizer or the mRNA-based vaccine remains the preferred option based on the availability of safety data.

If pregnant mothers are keen to take Oxford/AstraZeneca vaccines in pregnancy, it is not entirely contraindicated as it is not a live vaccine, and it is best to discuss with their doctors as to weigh the benefits and risk before making an informed decision.

For those who have completed their first dose of the Oxford/AstraZeneca vaccine and were later confirmed to be pregnant, the recommendation is to take the second dose of the same vaccine after 14 weeks as the vaccine-induced immune thrombotic thrombocytopenia (VITT) risk associated with the vector based vaccine is the highest following the first dose while there is limited evidence with regard to the benefits and implications of mixing different types of vaccines as for now.

However, the Oxford/AstraZeneca is not contraindicated among breastfeeding mothers and the WHO Strategic Advisory Group of Experts on Immunization (SAGE) interim guidelines on Oxford/AstraZeneca does not recommend discontinuation of breastfeeding following vaccination.

- **WHO interim guidelines on Sinovac in pregnancy – 24th May 2021**

The WHO interim recommendations for the use of Coronavac, developed by Sinovac recommends the use of Sinovac in pregnancy and breastfeeding mothers has the benefits outweighs the potential risk from the vaccine despite the lack of safety data related to the use of Sinovac in pregnancy. As a principle, live vaccines are contraindicated in pregnancy while Sinovac, being an inactivated vaccine, is potentially not contraindicated in pregnancy.

However, in view of the vast and best safety evidence is still related to the Pfizer mRNA vaccine where 123,165 women being vaccinated in UK as of 7th June 2021 while 5100 being enrolled in the study, MOH currently recommends the Pfizer vaccine as the preferred option although the studies and data continues to evolve with regard to safety in pregnant and breastfeeding mothers.

For mothers who have taken the Sinovac vaccine and were later confirmed to be pregnant, is it recommended taking the second dose beyond 14 weeks of pregnancy as the vaccine is not contraindicated in pregnancy while the benefits, safety and efficacy of mixing vaccines in pregnancy is yet to be established.

- **CDC updates on co-administration of other vaccines**

The initial recommendations was to have a 14-day interval between the COVID-19 vaccine with other concurrent vaccinations.

However, the experience following the COVID-19 vaccinations now demonstrates that the immunogenicity and adverse profiles are similar and tolerable. The updated CDC recommendations now suggest co-administration of other vaccines together with COVID-19 vaccines either simultaneously or at any time before or after the vaccine is reasonably safe without the need for a specific delay or interval.

- **Pregnancy and fertility following vaccination**

Current literature remains consistent that all types of COVID-19 vaccinations does not affect fertility or future reproductive health, and those who have completed their vaccination schedule can safely embark on a pregnancy without a need for a specific interval or delay. However, contraception is recommended in between the first and second dose of vaccinations.

- **Mixing vaccines and change of dosing intervals**

The implications of mixing different types of vaccines and intervals is currently still being evaluated in clinical trials and until better evidence, especially with regard to safety among pregnant mothers; it is best to use a similar type of vaccine for now. The COM-COV trial is one of the many trials evaluating the efficacy of mixing vaccines.

- **Combined hormonal contraception and Oxford/AstraZeneca**

Based on the Faculty of Sexual Reproductive Healthcare (FSRH) of the Royal College of Obstetricians and Gynaecologists (RCOG), despite the rare association related to the risk of thrombosis and thrombocytopenia with the use of Oxford/AstraZeneca vaccine, the current recommendations is not to stop the combined oral contraceptive hormones before or immediately after the vaccine. Temporary discontinuation of hormonal contraception does not render protection against the rare incidence of thrombosis, while not optimizing effective or alternative contraceptive measures increases the risk of unplanned pregnancies. If patients are concerned of their risk and medications, it is best to consult with their doctors first without discontinuing medications and contraceptive practices.

# Q&A SESSION

1. **Hi Dr, just a general question. If the patient has received the 1st dose of vaccination, prior to the 2nd dose, if the patient falls sick (common cold), can he proceed with the 2nd dose?**

   *Dr. Norzaihan binti Hassan*

   As we know, COVID-19 infection clinically can present with fever, cough, and runny nose like a common cold as well. So, I would advise this patient to go to a local clinic first. Because like in our state (ie. Kelantan), we have a guideline that said if a patient has clinical COVID-19 symptoms, we have to proceed with a swab and COVID-19 PCR testing first. If the test is negative and once the symptoms have subsided, then he or she can proceed with the second dose.

   *Dr. Muniswaran Ganeshan*

   I think this is similar to pregnancy as well. It is important to assess. The protocols for pregnant and non-pregnant mothers are the same.

2. **Is there any gap for anti-tetanus injection for patients post COVID-19 vaccination?**

   *Dr. Muniswaran Ganeshan*

   I believe these are the pregnancy cohorts. It was covered in my lecture. Having the COVID-19 vaccination per se is not a contraindication for other vaccinations in pregnancy. So, it is okay to give the anti-tetanus injection, although currently we are moving away from routine anti-tetanus injection in pregnancy. So the vaccines which are recommended in pregnancies now, apart from COVID-19 vaccine for high risk mothers are the influenza vaccine and the Tdap vaccine, which protects the baby from pertussis infection. It is recommended, but the interval for Good Clinical Practice is 14 days from the COVID-19 vaccine.

   *Dr. Norzaihan binti Hassan*

   Yes, it is also similar in other patients, non-pregnant patients, the interval between 2 vaccines is about 2 weeks post COVID-19 vaccine.

3. **The guideline stated that the 1st dose of Cominarty vaccine should be given between 14 and 33 weeks, but can the 2nd dose be given after 33 weeks of pregnancy?**

   *Dr. Muniswaran Ganeshan*

   This is a very relevant question, it is a common clinical question which has been asked since February. Ladies and gentlemen, although the guideline stated 33 weeks as the upper limit, our rationale was these patients ideally should complete their second dose by 33 weeks because the risk of having severe infection is highest in the late 2nd trimester

and the 3rd trimester. But if by some unknown reasons, she has not been able to complete vaccination by 33 weeks but has had her first dose, then it is okay and logical that she completes her second dose. It is not a contraindication, but the recommendation ideally is that she should try to complete the vaccination before the 3rd trimester because that gives the best maternal and fetal benefits.

4. **Dr Norzaihan, for those who get pregnant after the 1st dose, what is the policy in your setting in delaying the 2nd dose? What is the maximum number of days after dose 1?**

   *Dr. Norzaihan binti Hassan*

   What we practice actually we follow the guideline. If the patient gets pregnant after the 1st dose, we wait for 14 weeks of gestation before giving the 2nd dose.

   *Dr. Muniswaran Ganeshan*

   I would like to add on to this. Thank you Dr Elya Zetti for asking this question. I think you need to reassess the whole situation. What is her risk? Is she high risk or low risk? What is the risk of having COVID-19 infection? What is her perception of having the COVID-19 vaccination in the first trimester?

   From the v-safe data, there was a slight increased risk of miscarriage. So, I would give her all this information, and then I will give her the 3 options. Option 1, just take 1 (dose). Option 2, delay up to 14 weeks. In the UK, they are now giving the 2nd dose of vaccine after a 12-week interval, and they showed that if you give it after 12 weeks, there was a raised in immunity (IgG levels are higher after 6 weeks).

   Therefore, this is also a reasonable recommendation. I think it is a shared decision-making. We should give the patient all the information, and based on our current guidelines, you and the patient must make an informed decision. So, that would be my advice to you. The maximum interval should be within 12 weeks. That is what we know. Ideally, it should be after 14 weeks of pregnancy. These are the 2 magic numbers. Those are good clinical practice points, but these are not absolute contraindications.

5. **If a patient receives the 1st dose of Pfizer vaccine at 9 weeks, but the patient did not know she was pregnant at the time, should we arrange for a detailed scan?**

   *Dr. Muniswaran Ganeshan*

   So, what we know from the v-safe data is that vaccination does not cause fetal anomaly. So if you had the vaccine alone, it is not an indication for a detailed scan. It is okay to treat her as per usual and that is what the current guidelines recommend as well.

6. **How long to monitor pregnant recipients after the vaccination? Which of the current COVID-19 vaccines may confer passive immunity to the children (if breastfeeding)?**

   *Dr. Muniswaran Ganeshan*

   For the first question, it is the same for pregnant and non-pregnant mothers. The recommendations of monitoring after a vaccine remains the same as presented by Dr. Norzaihan.

   As for the evidence of passive immunity to the children, giving the COVID-19 vaccine injection in pregnant lady does not offer passive immunity to the baby. IgG has been found in breast milk, but it is not sufficient to cause immunity to the baby.

   Therefore, COVID-19 vaccination does not cause immunity to the baby. The only idea of vaccination is to protect the mother.

7. **Hi Dr, I just want to ask if we can administer intramuscular (IM) drugs such as zuclopenthixol/flupenthixol and COVID-19 vaccine on the same day? Since both medicines are administered through IM.**

   *Dr. Norzaihan binti Hassan*

   I would advise it should be individualized. Let's say this is the first time you are injecting this (zuclopenthixol/flupenthixol) medication, you will probably have problems in terms of side effects. Is it due to this drug or the vaccine? So, I would prefer to give a gap in between, if it is the first time you are injecting this drug.

   If this is the case whereby you have been given follow-up and there are no side effects with these IM medications, I think there are no contraindications to give the COVID-19 vaccination on the same day.

   This is not in the guidelines.

8. **For breastfeeding mothers (still exclusive breastfeeding) below 6 months, which brand of vaccine will be given?**

   *Dr. Muniswaran Ganeshan*

   The best scientific evidence for pregnancy and breastfeeding women are still the Pfizer vaccine.

   The Malaysian Guideline only recommends one type of vaccine for this cohort of patients, which is the Pfizer vaccine. The CDC, on the other hand, recommends the Moderna, BioNtech, and the J&J vaccine.

   If you're breastfeeding in Malaysia, you will probably only get the Pfizer vaccine.

9. **After receiving the second dose of vaccine, how long is the period before someone can try to conceive?**

   *Dr. Muniswaran Ganeshan*

   There is no magic number as long as you have completed the 2nd dose of vaccine. If you are not high risk, you can try to conceive on the same day itself. It is not an absolute contraindication.

10. **How long should a lady at reproductive age wait to conceive after getting the vaccine?**

    *Dr. Muniswaran Ganeshan*

    I think it depends on the patient's risk factors. If she is high risk, above 40 years of age, obese, have medical disorders in pregnancy, the recommendation is to get vaccinated first. She will be in Phase II, and then she can embark on pregnancy.

    On the other hand, if she is young, healthy, fit, and has no risk factors, it is perhaps not reasonable to delay any fertility treatment until she has got her vaccine. So, for the 2nd group it is okay to try.

    For the high risk, it is recommended to get vaccinated first. There is no magic interval.

11. **For pregnant mothers not fulfilling high risk criteria but live in the Klang Valley area, should she be included in Phase II vaccination roll out?**

    *Dr. Muniswaran Ganeshan*

    Yes. We do have a national protocol that is comprehensive which covers equally throughout the nation and I must highlight it is not limited to the Klang Valley alone. If you are high risk, if you are pregnant, if you fulfil the criteria, irrespective of where you stay or live, you eventually would have been assessed and would have discussions about the benefits of the vaccine.

12. **How about pregnant or breastfeeding mothers taking AstraZeneca? Is it recommended?**

    *Dr. Muniswaran Ganeshan*

    I am afraid both the Malaysian and CDC guidelines do not recommend AstraZeneca COVID-19 vaccine.

    What are the implications in pregnancy? The general consensus is the incidence of thrombosis following the AstraZeneca vaccination is extremely rare. Pregnancy per se is

not an absolute contraindication. Fortunately, if you're in Malaysia, you will likely not get the AstraZeneca vaccine if you are pregnant or breastfeeding. You will only get the Pfizer vaccine.

**13. If the patient missed her 2nd dose for more than 12 weeks, do we repeat the vaccine course?**

*Dr. Norzaihan binti Hassan*

In the guidelines, we do not repeat the 1st and 2nd dose. We would just proceed with the 2nd dose.

**14. A patient with positive PCR results was given the 1st dose of Pfizer once his or her PCR result of negative was achieved. COVID-19 mutant variant was later detected. Any suggestions on when to administer the 2nd dose?**

*Dr. Muniswaran Ganeshan*

Based on current recommendations, irrespective of the type of mutant, the current (Pfizer) vaccination does render significant benefits with regard to deaths and hospitalization irrespective of the type of variant. I think despite it being a mutant variant, I believe there are no changes in the current vaccination protocol.

*Dr. Norzaihan binti Hassan*

Current studies have shown that Cominarty is effective to neutralize the coronavirus strains and those variants in Brazil and in the United Kingdom. But for Coronavac, it needs further trial.

**15. Is there a need to do long term follow-up for pregnant mothers and their children? For example, after delivery?**

*Dr. Muniswaran Ganeshan*

I think what they are trying to do throughout the world is to evaluate and follow up on pregnant mothers who have been vaccinated, and I think we in Malaysia are also embarking on similar strategies. There are many things which remain unanswered about COVID-19 and often, there are more questions than answers. But believe me, science is evolving as fast as the virus. I think our main aim is to try to put off the fire, try to protect as many pregnant mothers as possible because we do know that vaccines are extremely beneficial.

Is there a need to follow up these mothers and children? Ideally, yes. Do we have to? Yes. I believe that will be after they have completed Phase III and I believe that is something that we have to wait and watch. That is my personal take.

# Closing Remarks

*Dr. Muniswaran Ganeshan*

As a take home message, I would like to conclude that it is important for us as responsible clinicians, taking care of pregnant and breastfeeding mothers, to have directed counselling: to assess the risk, to provide personalized care or individualized care, and to provide pregnant mothers the information before making a shared decision on what is best for her.

*Dr. Norzaihan binti Hassan*

I would like to appeal all the healthcare workers to counsel appropriately and to increase the take-up of COVID-19 vaccination among all Malaysians, so that we would obtain the herd immunity and resume our normal life. All the best for the Phase II and Phase III implementation of COVID-19 Immunization Programme.

*Dr. Noel Thomas Ross*

We hope that the people who are in the line listing for COVID-19 vaccination would appear according to their vaccination schedule because vaccines very precious and should not be wasted. There are many people out there who are waiting to be vaccinated. Looking at our current third wave of COVID-19 infection, the number of cases are so high. So, do attend your vaccination session and get vaccinated.

# The Panellists

# Moderator

**Datuk Dr. Noel Thomas Ross** is the Head of Acute Medicine and a Consultant Physician working in Kuala Lumpur Hospital. He currently an appointed member in the Malaysian Adverse Drug Reactions Advisory Committee, National Pharmaceutical Regulatory Agency, Ministry of Health, Malaysia.

# Speakers

**Dr. Norzaihan binti Hassan** is a Family Medicine Consultant and heads the Klinik Kesihatan Bandar at Kota Bharu. She is also a Honarary lecturer in Universiti Sains Malaysia (USM).

She has contributed to the Management of Type 1 Diabetes Mellitus in children and adolescents Clinical Practice Guideline (CPG) and a member of the review committee for the Management of Diabetes in pregnancy CPG.

**Dr. Muniswaran Ganeshan** is a Consultant Obstetrician and Gynaecologist with a subspeciality in Maternal Fetal Medicine. He is the Unit Head at the Maternal Fetal Medicine Unit at the Women and Children's Hospital, Tuanku Azizah Hospital Kuala Lumpur. He is also a visiting consultant to the National Heart Institute (IJN).

He is a member of the Royal College of Obstetricians & Gynaecology, and was awarded the gold medal for the Masters in Obstetrics & Gynaecology from University Malaya in 2011. Having completed his subspecialty training in the United Kingdom, he initiated and successfully runs the Obstetric Medicine clinic; oversees the management of patients with complex medical diseases in pregnancy.

He has contributed to numerous national guidelines and is a member of the Confidential Enquiries of Maternal Deaths in Malaysia. He is actively involved in training of doctors and midwives in Malaysia and is a principle trainer for the Intensive Course in Obstetric Emergencies and has authored the “Handbook in Obstetric Emergencies”. His passion is

to establish Obstetric Medicine services in Malaysia and to improve the quality of care for women with medical complications in pregnancy.

Click the link below to view the panellists' information and details of the webinar:

https://clinupcovid.mailerpage.com/resources/a9d9v0-vaccination-in-pregnancy-lessons

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Healthcare professionals and high-risk pregnant mothers are vulnerable during COVID-19 pandemic. Most of them will be asymptomatic. The maternal and fetal implications of COVID-19 are significant. Vaccine has been proven to significantly reduce hospitalizations, complications and deaths. **Dr. Muniswaran Ganeshan**, a Maternal Fetal Medicine Consultant, **Dr. Norzaihan binti Hassan**, a Family Medicine Consultant and **Datuk Dr. Noel Thomas Ross**, the Head of Acute Medicine and Consultant Physician shared some insights in the phase 1 mass COVID-19 vaccination and current evidence, safety and COVID-19 vaccine concerns among pregnant and breastfeeding mothers.

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