Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

[u] *Centre régional de pharmacovigilance, service hospitalo-universitaire de pharmacotoxicologie, Hospices civils de Lyon, CHU de Lyon, 69424 Lyon, France*
* Corresponding author. Regional Pharmacogivilance Centre, Clinical Pharmacology Department, Amiens-Picardie University Hospital, 80054 Amiens, France.
E-mail address: gras.valerie@chu-amiens.fr (V. Gras-Champel)

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COVID-19 vaccines and pregnancy: What do we know?

Keywords COVID-19; COVID-19 vaccine; Pregnancy; Adverse drug reaction

Abbreviations

ANSM	*Agence nationale de sécurité du médicament et des produits de santé* (French Drug Agency)
CDC	Centres for Disease Control and Prevention
COVACPREG	COvid VACcine PREGnancy
COVID-19	coronavirus disease 2019
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2

Since the start of the coronavirus disease 2019 (COVID-19) pandemic, concerns have been raised about how to manage and prevent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in pregnant women [1]. COVID-19 during pregnancy is associated with substantial risk of morbidity and mortality in mothers and in their infants [2,3], with for example preeclampsia, intensive care unit admission, infections, as well as preterm birth and low birth weight. These complications are more likely in women with pre-existing co-morbidities, such as overweight, diabetes, hypertension or cardiac and chronic respiratory diseases [4]. Moreover, detection of viral RNA in the placenta or in foetal membranes shows that vertical transmission of SARS-CoV-2 from mother to foetus is rare but possible [5]. Vaccination is therefore needed in this vulnerable population, and characterising vaccine adverse reactions in pregnancy is a major concern.

Animal studies conducted with the Pfizer, Moderna and Janssen vaccines have not found any teratogenic or fetotoxic effects for any of these vaccines [6,7]. Experimental studies on the AstraZeneca vaccine assessing the risk of malformation are still ongoing.

Some companies having developed COVID-19 vaccines may plan to include pregnant women in clinical trials in the future, but all current studies have excluded pregnant participants. Thus, very little information is currently available on safety and efficacy in pregnancy. During Pfizer and Moderna clinical trial, 12 and 6 pregnant women were respectively inadvertently enrolled in the vaccine groups. These vaccine-exposed pregnancies are ongoing without complications.

A recent Centres for Disease Control and Prevention (CDC) publication [8] reported that over 30,000 women have been exposed to mRNA vaccines in the United States, representing a roughly equal number of Pfizer and Moderna vaccines. Injection-site pain was reported more frequently among pregnant women than among non-pregnant women, whereas headaches, myalgia, chills and fever were reported less frequently. Pregnant women did not report having serious reactions more frequently than non-pregnant women, except for nausea and vomiting, which were reported slightly more frequently only after dose two. A total of 827 pregnancy outcomes were collected among the 5,230 pregnant women included in the v-safe prospective registry [8]. These pregnancies resulted in a live birth in 712 cases (86.1%), in spontaneous abortion in 104 cases (12.6%), in stillbirth in one case (0.1%) and in other outcomes (induced abortion and ectopic pregnancy) in 10 cases (1.2%). Among 724 live-born infants, including 12 sets of multiple gestation, 9.4% were born preterm (60 of 636 among those vaccinated before 37 weeks), 3.2% had a small size for gestational age and 2.2% major congenital anomalies; no neonatal deaths were reported at the time of interview. These incidences of spontaneous miscarriage, pregnancy complications, prematurity and birth defects were comparable to those expected in the general population.

Preliminary American data [9] demonstrated transmission of maternal antibodies to the foetus via the placenta, although it is too early to conclude that this will protect future newborns.

The mode of action of non-live vaccines makes a risk of malformation unlikely. Data on other non-live vaccines, such as that for influenza, are reassuring [10]. Based on what is known about how mRNA vaccines act locally (at the site of injection) and are rapidly degraded and removed by the lymphatic system, the likelihood of the vaccine reaching and crossing the placenta is believed to be low.

In view of this data, vaccination can be considered for pregnant women from the 2nd trimester (period carrying a lower risk of teratogenic effects and pregnancy termination), particularly in the presence of important risk factors (obesity, diabetes, etc.) for severe COVID-19 or if there is a high risk of contamination (medical profession, school environment, etc.). Moreover, on the recommendations of the French *Conseil d'orientation de la stratégie vaccinale* (Vaccine Strategy Steering Committee), the Directorate-General of Health extended priority access to COVID vaccination in France on 3 April 2021 to pregnant women with or without comorbidities from the 2nd trimester. The mRNA vaccines (Pfizer and Moderna) seem preferable for this population given the lack of animal data to date for the AstraZeneca vaccine and a higher frequency of post-vaccination influenza-like illnesses. Finally, for women wanting to fall pregnant, it may be preferable to suggest that they postpone the pregnancy until the end of the vaccination schedule, if this is not already the case.

There is still very little data on COVID-19 vaccination during pregnancy. It is essential that we improve our knowledge of these vaccines and of their adverse drug reactions in this sensitive population of pregnant women, which is why the French pharmacovigilance centres and the *Agence nationale de sécurité du médicament et des produits de santé* (ANSM), the French Drug Agency, have set up a ''COVACPREG'' (COvid VACcine PREGnancy) cohort in May 2021. The aim of this study is to monitor potential adverse drug reactions of vaccination in pregnant women in real time. Primary online enrolment will be carried out at the time of vaccination at the main vaccination sites, with the pregnant woman's consent. Information will be collected on her medical history, history of COVID-19, her pregnancy (dates of conception and expected deliver) and other possible medicinal or non-medicinal exposures since the start of pregnancy. One month after each injection of the vaccine, information will be collected on any vaccination-related adverse reactions (fever, hypertension, etc.). Finally, in the 2 months following the expected delivery date, information will be collected on the outcome of the pregnancy (delivery, spontaneous abortion, etc.), the new-born infant (term, weight, malformations, neonatal clinical signs) and maternal clinical signs (pre-eclampsia, gestational hypertension, gestational diabetes, etc.). We have planned to include nearly 5,000 vaccinated pregnant women in this study. Final results are expected by the end of 2022 but reported adverse drug reactions will be continuously analysed (alert system) and an interim analysis will be carried out in the middle of the study.

Disclosure of interest

The authors declare that they have no competing interest.

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Judith Cottin[a], Justine Benevent[b], Sophie Khettar[a], Isabelle Lacroix[b,*]

[a] *University Hospital Department of Pharmacotoxicology, Public Health Unit, Hospices Civils de Lyon, 69002 Lyon, France*

[b] *Medical and Clinical Pharmacology Department, Toulouse University Hospital, University of Toulouse, Inserm CERPOP (Centre for Population Health Research and Epidemiology), 37, allées Jules Guesde, 31000 Toulouse, France*

* Corresponding author.

E-mail address: isabelle.lacroix@univ-tlse3.fr (I. Lacroix)

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Pneumopathie médicamenteuse ou liée à la COVID-19 : un train peut en cacher un autre !

Amiodarone or COVID induced-pneumopathy: One train can hide another one!

Mots clés Réflexe iatrogène ; Pneumopathie médicamenteuse ; Amiodarone

Keywords Iatrogenic reflex; Drug-induced pneumopathy; Amiodarone

Abréviations

COVID-19 *coronavirus disease* 2019
DFG débit de filtration glomérulaire
OMS Organisation mondiale de la santé
RT-PCR *reverse transcription-polymerase chain reaction*