EFFECTS OF SARS-COV-2 INFECTION ON PREGNANT WOMEN AND THEIR BABIES: ASSESSING THE IMPACT OF COVID-19 VACCINES AVAILABILITY

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Introduction

Pregnant women face a higher risk of severe COVID-19 compared to non-pregnant women of the same age, due to physiological changes during pregnancy [1, 2]. The living systematic review and meta-analysis by Allotey et al. (2022) [3], which includes 435 studies worldwide conducted before the end of April 2021, reported that pregnant women with COVID-19 have a higher likelihood of being admitted to an intensive care unit, death, preterm birth, caesarean section, and admission of their newborns to neonatal units compared to pregnant women without the infection. Furthermore, in the development of the COVID-19 vaccines, pregnant women were not included in clinical trials [4], leading to a lack of knowledge at the time of the conditional approval of whether the vaccines were efficient and safe during pregnancy. Initially, vaccination guidelines worldwide for pregnant women were discordant, spanning from contraindicated to permitted or recommended [5]. Worldwide observational studies have subsequently pointed out the safety and efficacy of vaccines, particularly during the second and third trimesters of pregnancy [4-9].

Objectives

Given the potential adverse consequences of SARS-CoV-2 on pregnancy and its outcome, the research question of this project is to investigate whether the availability of vaccines has reduced the impact of COVID-19 on pregnancy outcomes. Specifically, the aim of the first research objective (RO1) is to evaluate the effect of COVID-19 within three months before conception on preterm birth, intrauterine growth restriction and pathological course of pregnancy. The second research objective aims to examine the effects of COVID-19 during pregnancy on preterm birth.

Methods

The data source is the Healthcare Utilization Database of Lombardy, which contains information for almost 10 million individuals. The cohort is constructed from the certificates of delivery assistance (CeDAP), consisting of 183,157 pregnancies that occurred in Lombardy from May 2020 to June 2023, with a minimum gestational age of 22 weeks, mothers aged between 18 and 45 years and with the domicile in Lombardy during the year of delivery.

To assess the impact of vaccines, two periods are considered: the pre-widespread vaccination era (Era 0) and the post-widespread vaccination era (Era 1). The cutoff to distinguish between the two eras is set at July 31, 2021, and sensitivity analyses are conducted by moving the cutoff date to April 30, 2021, and October 31, 2021.

Classification into Era 0 or Era 1 for exposed pregnancies is based on when the infection occurred, while unexposed pregnancies reaching 20 weeks in Era 0 are classified there; otherwise, they are classified in Era 1. Considering RO1, exposure is represented as a time-fixed binary variable, and logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals for each outcome. In RO2, Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals of the outcome, considering exposure as a time-varying binary variable and two scenarios. In the second scenario, three different models are considered to explicitly account for the trimester of exposure.

Results
Regarding RO1, adjusted odds ratios (aOR) show no associations in both eras for preterm birth (Era 0: aOR = 0.93 [0.71-1.19], Era 1: aOR = 0.98 [0.86-1.12]) and pathological course of pregnancy (Era 0: aOR = 1.02 [0.89-1.17], Era 1: aOR = 1.00 [0.92-1.08]. A negative association is observed in Era 0 (aOR = 0.64 [0.46-0.87]) but not in Era 1 (aOR = 0.99 [0.85-1.14] for intrauterine growth restriction. Assessing RO2, the first scenario results show a positive association between exposure and preterm birth in Era 0 (aHR = 1.30 [1.14-1.48]), while no association was found in Era 1 (aHR = 0.95 [0.89-1.01]). In the second scenario, a positive association was found in Era 0 considering exposure in the first trimester (aHR =1.76 [1.46-2.11]), but not in Era 1 (aHR = 1.09 [0.99-1.18]). No association was found in Era 0 considering exposure in the second trimester (aHR = 1.07 [0.85-1.35]) and third trimester (aHR = 0.92 [0.69-1.23]), while a negative association was found in Era 1 for both trimesters (aHR = 0.84 [0.75-0.94] and aHR = 0.74 [0.64-0.85]). The sensitivity analyses show consistent results.

Conclusions
Our data show that COVID-19 before pregnancy does not increase the risk of preterm delivery and pathological course of pregnancy in both eras. The negative association observed in Era 0, but not in Era 1, when considering intrauterine growth restriction as outcome might be attributed to lifestyle changes during lockdowns. A lack of information in literature about this topic does not allow comparison to other studies. COVID-19 during pregnancy seems to have increased the risk of preterm birth in Era 0, aligning with literature, but not in Era 1, hypothesizing a mitigating effect of the vaccines. The risk seems to be higher for infections in the first trimester, but further analyses are needed to confirm these results and to explain the negative association for exposure in the second and third trimester in Era 1, which might be attributed to some unknows factor that act as confounders.

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