

## A Hospital-Based Study to Assess the Symptomatology and Course of COVID-19 Infection among Vaccinated and Unvaccinated Pregnant Women

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Received: 25-11-2022 / Revised: 18-12-2022 / Accepted: 20-01-2023

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Conflict of interest: Nil

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### Abstract

**Aim:** The aim of the present study was to assess the symptomatology and course of COVID-19 infection among vaccinated and unvaccinated pregnant women in Bihar region.

**Methods:** The present study was conducted at Nalanda Medical College and Hospital, Patna, Bihar, India for the period of one year. During the inclusion period, there were 150 pregnant women with PCR-confirmed SARS-CoV-2 infection, of whom 100 were vaccinated and 50 were not.

**Results:** No significant differences were observed between the vaccinated and unvaccinated pregnant women in age (median, 31.0 vs 31.0 years,  $P=0.730$ ), body mass index (median, 26.7 vs 27.3 kg/m<sup>2</sup>,  $P=0.284$ ), rate of obesity (16.9% vs 21.2%,  $P=0.606$ ) or pregnancy trimester at diagnosis ( $P=0.254$ ). Few vaccinated women had significant medical comorbidities, including asthma (7%), pregestational diabetes (2%), hypothyroidism (7%), malignancy (1%) and immunosuppression (1%). There was a statistically non-significant trend for fewer unvaccinated compared with vaccinated pregnant women to have comorbidities.

**Conclusion:** In this retrospective cohort study of pregnant women, vaccination compared with no vaccination was associated with a significantly lower risk of SARS-CoV-2 infection. Interpretation of study findings is limited by the observational design.

**Keywords:** COVID-19, Vaccinated, Unvaccinated, Pregnant Women.

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### Introduction

Comprehensive whole-population data on COVID-19 vaccine uptake in pregnancy and SARS-CoV-2 infection rates and COVID-19 outcomes are lacking. [1] Such data are required to help guide decision making by women, clinicians and policymakers on measures to prevent and

control COVID-19 in pregnancy, in particular, vaccination.

Pregnant women do not seem to be more susceptible to SARS-CoV-2 infection than non-pregnant women, but they are at higher risk of severe COVID-19 disease. [2-4] Compared to non-pregnant women of

same reproductive age. Pregnant women with SARS-CoV-2 infection are more likely to be admitted to critical care, receive invasive ventilation and extracorporeal membrane oxygenation and die.<sup>2,3</sup> COVID-19 in pregnancy is associated with increased risk of the pregnancy specific complications pre-eclampsia, preterm birth and stillbirth. [2,5-7]

Despite widespread recognition of potential vulnerability to COVID-19, pregnant women were excluded from pre-marketing clinical trials studying COVID-19 vaccines. [8,9] As a result, evidence to inform decision making on vaccination was largely absent when vaccination programs started and recommendations on vaccination in pregnancy have varied over time as well as by country. [10] Post-marketing surveillance data suggest that COVID-19 vaccine effectiveness is broadly similar to that in non-pregnant individuals. [11,12] Data on the safety of vaccines in pregnancy comes from preclinical studies of COVID-19 vaccines in animals [13], findings from women who had unanticipated pregnancies while participating in clinical trials [14] and accumulating pharmacovigilance data [15], all of which are reassuring regarding COVID-19 vaccine safety in pregnancy.

The aim of the present study was to assess the symptomatology and course of COVID-19 infection among vaccinated and unvaccinated pregnant women in Bihar region.

### Materials and Methods

The present study was conducted at Nalanda Medical College and Hospital, Patna, Bihar, India for the period of one year. During the inclusion period, there were 150 pregnant women with PCR-confirmed SARS-CoV-2 infection, of whom 100 were vaccinated and 50 were not.

Inclusion criteria were PCR-confirmed SARS-CoV-2 infection during the

specified period and pregnancy at the time of diagnosis. Fully vaccinated (two doses), booster vaccinated (more than two doses) and unvaccinated women were included, but those who were partially vaccinated (single dose) were excluded from the analysis. Women who received vaccines on the World Health Organization Emergency Use List within 6 months before diagnosis were eligible for inclusion. RT-PCR testing was performed in pregnant women with symptoms, those who had contact with infected individuals or as part of screening at admission for unrelated reasons.

Baseline characteristics (e.g. maternal age, body mass index, smoking status, gestational age at diagnosis, number of vaccine doses and comorbidities) were recorded. Maternal age, body mass index and gestational age at infection were treated as potential confounders. [16] The main outcome measures were disease severity at the time of diagnosis and the need for oxygen supplementation. Disease severity was categorized according to the National Institutes of Health classification. [17] In brief, mild cases had symptoms of COVID-19 without lower respiratory tract involvement (no dyspnea or abnormal lung imaging). Moderate cases had lower respiratory tract

involvement without significant hypoxemia (oxygen saturation on room air  $\geq 94\%$ ). Severe cases showed signs of hypoxemia, as evidenced by oxygen saturation ( $< 94\%$ ) or imaging showing lung infiltrates  $> 50\%$ . Cases without any symptoms were classified as asymptomatic. Levels of oxygen support were classified as oxygen support via nasal cannula or non-rebreather mask, non-invasive mechanical ventilation with continuous positive airway pressure (CPAP), mechanical ventilation with intubation or extracorporeal membrane oxygenation.

Baseline characteristics and outcome were compared using chi-square test or Mann–

Whitney U-test, as appropriate. All analyses were performed using R for Statistical Computing Software and P-

values <0.05 were considered statistically significant.

### Results

Variable	Vaccinated (n=100)	Unvaccinated (n=50)	P
Age (years)	31.0 (28.0–34.0)	31.0 (26.0–35.0)	0.730
BMI (kg/m <sup>2</sup> )	26.7 (24.9–29.0)	27.3 (25.0–29.5)	0.284
BMI >30 kg/m <sup>2</sup>	16 (16)	10 (20)	0.606
Parous	65 (65)	40 (80)	0.116
Smoker	1 (1)	2 (4)	0.311
GA at diagnosis			0.254
First trimester	12 (12)	4 (8)	
Second trimester	24 (24)	8 (16)	
Third trimester	60 (60)	40 (80)	
<b>Vaccine doses</b>			
Regular (n=2)	85 (85)	NA	NA
Boosted (n≥3)	15 (15)	NA	NA
<b>Vaccine type</b>			
mRNA	95 (95)	NA	NA
Inactivated	2 (2)	NA	NA
Mixture	3 (3)	NA	NA
<b>Comorbidity</b>			
CH	0	NA	NA
Hypothyroidism	7 (7)	4 (8)	0.920
Asthma	7 (7)	2 (4)	0.417
Prepregnancy diabetes	2 (2)	0	0.692
Malignancy	1 (1)	0	0.999
Immunosuppression	1 (1)	0	0.999
Clinical severity at diagnosis			0.015
Asymptomatic or mild	100 (100)	45 (90)	
Moderate or serious	0	5 (10)	0.015
<b>Oxygen support</b>			
Any	0	5 (10)	0.015
Nasal	0	2 (4)	0.285
Non-invasive mechanical	0	2 (4)	0.285
Invasive mechanical	0	1 (2)	0.812
ECMO	0	0	NA
Maternal ICU admission	0	2 (4)	0.285
Maternal death	0	0	NA

No significant differences were observed between the vaccinated and unvaccinated pregnant women in age (median, 31.0 vs 31.0 years, P=0.730), body mass index (median, 26.7 vs 27.3 kg/m<sup>2</sup>, P=0.284), rate of obesity (16.9% vs 21.2%, P=0.606) or pregnancy trimester at diagnosis (P=0.254). Few vaccinated women had significant medical comorbidities,

including asthma (7%), pregestational diabetes (2%), hypothyroidism (7%), malignancy (1%) and immunosuppression (1%). There was a statistically non-significant trend for fewer unvaccinated compared with vaccinated pregnant women to have comorbidities.

## Discussion

During pregnancy, alterations in hormonal levels and immune system function may increase women's vulnerability to viral infections. [18] Although SARS-CoV-2 infection in pregnant women is mostly asymptomatic or mild, [19] it may result in severe complications, including admission to the intensive care unit and mechanical ventilation, [20] particularly during the third trimester. [21] Symptomatic SARS-CoV-2 infections in women also have been linked to a greater likelihood of preterm delivery [22] and fetal intrapartum distress. [23]

The benefit from the vaccine may be somewhat attenuated among this population compared with the general public because pregnant women were generally advised to take extra precautions during the pandemic and to maintain particular adherence to social distancing guidelines, regardless of vaccination status. Immunologic response may also be different among pregnant women compared with the general population. Increased herd immunity protects both vaccinated and non-vaccinated pregnant women and could attenuate the observed treatment effect over time, as previously reported with cholera vaccines. [24] Moreover, during the same period there was increased media attention in Israel to SARS-CoV-2 complications, specifically among pregnant women (including reports of pregnant women hospitalized for severe SARS-CoV-2 complications, as well as the stillbirth of a fetus infected by SARS-CoV-2), which not only led to a rapid increase in vaccination among this population but also may have increased adherence to social distancing recommendations among unvaccinated pregnant women. [25]

The strengths of this analysis include the use of a very large Cohort with detailed demographic and clinical information on vaccination status, SARS-CoV-2 infection, and other comorbidities.

The matching process and the lack of association with vaccination during the first 10 days after the first dose suggest that the results are minimally affected by bias.

This study has several limitations. First, given the observational design, there is the potential for important unmeasured residual confounding. Given the small absolute risk differences, residual bias may account for significant findings. Second, the reported nominal level of P values from the time varying model may be underestimated because the placement of knots was data driven, derived from examination of residuals from an initial model that assumed a constant HR. Third, the findings are susceptible to bias if women who were unvaccinated were more prone to present for testing than those who were vaccinated because of concerns about their ongoing vulnerability. Fourth, the study design did not provide adequate power to statistically assess differences in adverse events.

## Conclusion

In this retrospective cohort study of pregnant women, vaccination compared with no vaccination was associated with a significantly lower risk of SARS-CoV-2 infection. Interpretation of study findings is limited by the observational design.

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