Clinical severity of SARS-CoV-2 infection among vaccinated and unvaccinated pregnancies during the Omicron wave

The Omicron variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is highly contagious and has significant alterations to its spike protein structure, providing it with significant ability to evade immune response elicited by coronavirus disease 2019 (COVID-19) vaccines. This variant caused a record number of new cases worldwide and supplanted the Delta variant as the dominant strain in most countries, including the UK and Turkey. Recent reports suggest that Omicron-related COVID-19 is milder compared with Delta-related COVID-19 and that the overall mortality rate for vaccinated individuals may be close to that of seasonal flu. However, these reports are based on data derived mostly from countries with a high vaccination rate, and there are no data on the outcome of Omicron variant infection in vaccinated and unvaccinated pregnant women.

Gray literature articles have contained significant coverage of reduced effectiveness of existing COVID-19 vaccines against Omicron infection and the better prognosis of Omicron cases. These factors may affect negatively the vaccination rates of pregnant women whose uptake of vaccination is already relatively low. Therefore, for evidence-based counseling, it is important to document the effect of vaccination on the disease severity specific to this variant.

To this end, we conducted a retrospective cohort study including real-time reverse transcriptase polymerase chain reaction (RT-PCR)-positive SARS-CoV-2 cases during pregnancy. Three tertiary care facilities participated in the study (Sancaktepe Training and Research Hospital, Istanbul, Turkey; Koc University Hospital, Istanbul, Turkey; and St George’s University Hospital, London, UK), and cases identified between 27 December 2021 and 1 February 2022 were included. By mid-December 2021, more than half of new cases were related to the Omicron variant in both countries, which gained complete dominance over the Delta variant by the second half of January 2022. 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 (Comirnaty, messenger RNA (mRNA) and CoronaVac, inactivated) 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. 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. 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 ≥ 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.

During the inclusion period, there were 135 pregnant women with PCR-confirmed SARS-CoV-2 infection, of whom 83 were vaccinated and 52 were not. Among the vaccinated, 70 (84.3%) pregnant women had two doses of vaccine and 13 (15.7%) had three or more doses. Among vaccinated women, 78 (94.0%) had the mRNA vaccine and a minority received the inactivated vaccine (n = 2) or a combination of mRNA and inactivated vaccines (n = 3).

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/m², P = 0.284), rate of obesity (16.9% vs 21.2%, P = 0.606) or pregnancy trimester at diagnosis (P = 0.254) (Table 1). Few vaccinated women had significant medical comorbidities, including asthma (7.2%), pregestational diabetes...
(2.4%), hypothyroidism (7.2%), malignancy (1.2%) and immunosuppression (1.2%). There was a statistically non-significant trend for fewer unvaccinated compared with vaccinated pregnant women to have comorbidities (Table 1).

All cases of SARS-CoV-2 were either asymptomatic or mild in the vaccinated pregnancies; in contrast, five (9.6%) unvaccinated women presented with moderate or severe SARS-CoV-2. The need for oxygen support was significantly lower in the vaccinated compared with unvaccinated group (0.0 vs 9.6%, P = 0.015). Two unvaccinated cases were managed with nasal oxygen support, two with CPAP and one required intubation. The rate of intensive care unit admission was 3.8% in the unvaccinated group compared with 0% in the vaccinated group. There were no maternal deaths in either group.

Fully vaccinated pregnant women infected with SARS-CoV-2 during the Omicron wave had milder illness and were less likely to require oxygen supplementation and intensive care compared with their unvaccinated counterparts. Our findings emphasize the importance of full SARS-CoV-2 vaccination to protect pregnant women during the Omicron wave despite its apparently lower effectiveness against PCR-confirmed infection with the Omicron variant. Our findings are limited by the sample size, potential selection bias conditioned on RT-PCR testing and inclusion based on the time period rather than viral genotyping. It is possible that the distribution of variants differed between vaccinated and unvaccinated women. However, both Delta and Omicron variants have significant immune evasion capabilities and it is impossible to ascribe the observed effect to a single variant. It is important to emphasize that our findings relate to infection during the Omicron wave (starting after the time when Omicron accounted for the majority of cases) rather than infection with a specific variant.

Table 1 Baseline characteristics and clinical severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in vaccinated and unvaccinated pregnant women during the SARS-CoV-2 Omicron wave

| Variable                        | Vaccinated (n = 83) | Unvaccinated (n = 52) | P       |
|---------------------------------|--------------------|-----------------------|---------|
| Age (years)                     | 31.0 (28.0–34.0)   | 31.0 (26.0–35.0)      | 0.730   |
| BMI (kg/m²)                     | 26.7 (24.9–29.0)   | 27.3 (25.0–29.5)      | 0.284   |
| BMI > 30 kg/m²                  | 14 (16.9)          | 11 (21.2)             | 0.606   |
| Parous                          | 55 (66.3)          | 41 (78.8)             | 0.116   |
| Smoker                          | 1 (1.2)            | 2 (3.8)               | 0.311   |
| GA at diagnosis                 |                    |                       |         |
| First trimester                 | 11 (13.3)          | 4 (7.7)               | 0.254   |
| Second trimester                | 20 (24.1)          | 8 (15.4)              |         |
| Third trimester                 | 52 (62.7)          | 40 (76.9)             |         |
| Vaccine doses                   |                    |                       |         |
| Regular (n = 2)                 | 70 (84.3)          | NA                    | NA      |
| Boosted (n ≥ 3)                 | 13 (15.7)          | NA                    | NA      |
| Vaccine type                    |                    |                       |         |
| mRNA                            | 78 (94.0)          | NA                    | NA      |
| Inactivated                     | 2 (2.4)            | NA                    | NA      |
| Mixture                         | 3 (3.6)            | NA                    | NA      |
| Comorbidity                     |                    |                       |         |
| CH                              | 0 (0.0)            | 0 (0.0)               | NA      |
| Hypothyroidity                  | 6 (7.2)            | 4 (7.7)               | 0.920   |
| Asthma                          | 6 (7.2)            | 2 (3.8)               | 0.417   |
| Prepregnancy diabetes           | 2 (2.4)            | 0 (0.0)               | 0.692   |
| Malignancy                      | 1 (1.2)            | 0 (0.0)               | 0.999   |
| Immunosuppression               | 1 (1.2)            | 0 (0.0)               | 0.999   |
| Clinical severity at diagnosis  |                    |                       | 0.015   |
| Asymptomatic or mild            | 83 (100)           | 47 (90.4)             |         |
| Moderate or serious             | 0 (0.0)            | 5 (9.6)               |         |
| Oxygen support                  |                    |                       |         |
| Any                             | 0 (0.0)            | 5 (9.6)               | 0.015   |
| Nasal                           | 0 (0.0)            | 2 (3.8)               | 0.285   |
| Non-invasive mechanical         | 0 (0.0)            | 2 (3.8)               | 0.285   |
| Invasive mechanical             | 0 (0.0)            | 1 (1.9)               | 0.812   |
| ECMO                            | 0 (0.0)            | 0 (0.0)               | NA      |
| Maternal ICU admission          | 0 (0.0)            | 2 (3.8)               | 0.285   |
| Maternal death                  | 0 (0.0)            | 0 (0.0)               | NA      |

Data are given as median (interquartile range) or n (%). BMI, body mass index; CH, chronic hypertension; ECMO, extracorporeal membrane oxygenation; GA, gestational age; ICU, intensive care unit; mRNA, messenger RNA; NA, not applicable.
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