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

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The Omicron variant of SARS-CoV-2 is highly contagious and has significant alterations to its spike protein structure, providing it with significant evasion of immunity elicited by COVID-19 vaccines[1]. 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[2]. Recent reports suggest Omicron-related COVID-19 illness is milder compared with Delta, and that the overall mortality rate for vaccinated individuals may be close to that of seasonal flu[3]. However, the data are mostly derived from countries with high vaccination rate, and there are no data on the outcome of Omicron variant infection in vaccinated and unvaccinated pregnant women.

Gray literature articles carried significant coverage of reduced effectiveness of existing COVID-19 vaccines against Omicron infection and the better prognosis of Omicron cases[4]. These factors may negatively affect the vaccination rates of pregnant women who already have relatively low vaccination rates[5,6]. Therefore, it is important to document the effect of vaccination on the disease severity specific to this variant for evidence-based counseling.

This was a retrospective cohort study including RT-PCR positive SARS-CoV-2 cases during pregnancy. Three tertiary care facilities participated in the study (Sancaktepe Training and Research Hospital, Istanbul; Koc University Hospital, Istanbul, Turkey; St. George's University Hospital, London, UK), and cases identified between December 27, 2021 and 01 February 2022 were included. By mid-December, more than half of new cases were related Omicron in both countries, which gained complete dominance over Delta by the second half of January[7,8]. 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 (a single dose) were excluded from the analysis. Vaccines on the World Health Organization Emergency Use List (Comirnaty, mRNA and Coronavac, inactivated) that were received within the last 6 months before diagnosis were eligible for inclusion. RT-PCR tests were 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 vaccinations/doses and comorbidities) were annotated. Maternal age, body mass index and gestational age at infection were treated as potential confounders[9]. 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[10]. In brief, mild cases had symptoms of COVID-19 without lower respiratory tract involvement (dyspnea, 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 breather mask, non-invasive mechanical ventilation with continuous positive airway pressure (CPAP), mechanical ventilation with intubation or extracorporeal membrane oxygenation (ECMO).

Baseline characteristics and outcomes 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-proven 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 an mRNA vaccine and a minority received inactivated vaccines (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/m^2, P=0.284), rate of obesity (16.9% vs. 21.1%, P=0.606) or 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 (vs vaccinated) pregnant women to have significant comorbidities (Table 1).

All cases of SARS-CoV-2 were either asymptomatic or mild in the vaccinated pregnancies as opposed to five (9.6%) unvaccinated women presenting with moderate or severe. The need for oxygen support was significantly lower in the vaccinated compared to 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 cohort compared with 0% in the vaccinated group. There were no maternal deaths.

Fully vaccinated pregnant women infected with SARS-CoV-2 during the Omicron wave had milder illness and were less likely to require oxygen supplementation or intensive care compared to their unvaccinated counterparts. Our findings emphasize the importance of full SARS-CoV-2 vaccination for protecting pregnant women during the Omicron wave despite its apparently lower effectiveness against PCR-proven infection[11]. Our findings are limited by the sample size, potential selection bias conditioned on RT-PCR testing and inclusion based on 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 any one variant. Regardless, 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.

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Table 1. Baseline characteristics and clinical severity of SARS-CoV-2 infections during the SARS-CoV-2 Omicron wave

Variable	**Vaccinated (n=83)**	**Unvaccinated (n=52)**	***P value***
Maternal age in years, median (IQR)	31.0 (28.0 – 34.0)	31.0 (26.0 – 35.0)	.730
Maternal BMI in kg/m^2, median (IQR)	26.7 (24.9 – 29.0)	27.3 (25.0 – 29.5)	.284
Maternal obesity (BMI > 30 kg/m^2), n (%)	14 (16.9)	11 (21.1)	.606
Multiparous, n (%)	55 (66.3)	41 (78.8)	.116
Smoker, n (%)	1 (1.2)	2 (3.8)	.311
Gestational age at diagnosis			.254
— First trimester, n (%)	11 (13.2)	4 (7.7)	
— Second trimester, n (%)	20 (24.1)	8 (15.4)	
— Third trimester, n (%)	52 (62.7)	40 (76.9)	
Number of vaccine doses, n (%)			
— Regular	70 (84.3)	–	NA
— Boosted	13 (15.7)	–	NA
Vaccine type, n (%)			
— mRNA	78 (94.0)	–	NA
— Inactivated	2 (2.4)	–	NA
— Mixture	3 (3.6)	–	NA
Comorbidities, n (%)			
— Chronic hypertension	0 (0.0)	0 (0.0)	NA
— Hypothyroidism	6 (7.2)	4 (7.7)	.920
— Asthma	6 (7.2)	2 (3.8)	.417
— Pre-pregnancy diabetes	2 (2.4)	0 (0.0)	.692
— Malignancy	1 (1.2)	0 (0.0)	.999
— Immunosuppression	1 (1.2)	0 (0.0)	.999
Clinical severity at diagnosis, n (%)			.015
— Asymptomatic or mild	83 (100.0)	47 (90.4)	
— Moderate or serious	0 (0.0)	5 (9.6)	
Oxygen support requirement, n (%)			
— Any	0 (0.0)	5 (9.6)	.015
— Nasal	0 (0.0)	2 (3.8)	.285
— Non-invasive mechanical	0 (0.0)	2 (3.8)	.285
— Invasive mechanical	0 (0.0)	1 (1.9)	.812
— ECMO	0 (0.0)	0 (0.0)	NA
Maternal ICU admission, n (%)	0 (0.0)	2 (3.8)	.285
Maternal death, n (%)	0 (0.0)	0 (0.0)	NA

BMI: body mass index, ECMO: extracorporeal membrane oxygenation, IQR: interquartile range; NA: not applicable; ICU: intensive care unit