RESEARCH ARTICLE

Is COVID-19 Vaccination Associated with Lower Rates of Gestational Diabetes? A Cross-Sectional Study in Karachi, Pakistan

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Abstract

Background
Gestational diabetes mellitus (GDM) is a frequent metabolic disorder in pregnancy linked with increased maternal and neonatal morbidity. The COVID-19 pandemic added further metabolic stressors. While COVID-19 vaccination has been shown to mitigate infection-related complications, its potential role in lowering GDM risk remains underexplored, particularly in low-resource settings.

Methods
A comparative cross-sectional study was conducted at Korangi General Hospital, Karachi (April – May 2022). Two hundred pregnant women (100 vaccinated, 100 unvaccinated) who delivered at the facility were enrolled using purposive sampling. Data on demographics, vaccination details, and obstetric outcomes were obtained via structured questionnaires and verified through hospital records. Gestational diabetes was diagnosed using WHO-endorsed 75-g OGTT criteria (≥140 mg/dL at 2 hours). Statistical analyses employed χ^2 tests, t-tests, and multivariate logistic regression controlling for confounders (age, BMI, hypertension, infection status). Robustness was assessed using propensity-score matching (PSM). ERB approval was obtained (Ref No: SZABIST/PH/2022-042).

Results
GDM prevalence was 6 percent in vaccinated vs 14 percent in unvaccinated participants (p = 0.04). Adjusted analysis showed vaccination reduced GDM odds by 58 percent (aOR 0.42; 95% CI 0.18–0.96; p = 0.04). The association persisted after PSM (aOR 0.44; 95% CI 0.19–0.93; p = 0.04). No significant difference was noted by vaccine type or trimester of vaccination.

Conclusions
COVID-19 vaccination during pregnancy is associated with a significantly lower risk of GDM, possibly via immune-modulation and stress-attenuation pathways. Integrating vaccination within routine antenatal care may confer dual metabolic and infectious-disease protection.

Keywords: COVID-19, Pregnancy, Gestational Diabetes, Vaccination, Maternal Health, Pakistan

Abstracts in اردو، عربی, 中国人, française, русский and español at the end of the article

Layman Summary
Gestational diabetes (GDM) happens when a pregnant woman develops high blood sugar. It can lead to bigger babies and delivery complications. This study compared 200 women in Karachi—half vaccinated against COVID-19 and half unvaccinated—to see if vaccination reduced the chances of GDM. Vaccinated mothers had about half the risk. Scientists think the vaccine may lower inflammation and stress hormones that affect blood sugar. Getting vaccinated protects mothers not only from COVID-19 but may also support a healthier pregnancy.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance first recognized during pregnancy [1]. It affects approximately 10–15 percent of pregnancies globally and has major public-health significance because it increases the risk of preeclampsia, macrosomia, and cesarean delivery [2,3]. Pakistan ranks among countries with the highest burden of maternal metabolic diseases; regional estimates suggest GDM prevalence ranging from 7 to 19 percent [4,5].

The COVID-19 pandemic introduced new challenges for maternal health. Pregnant women infected with SARS-CoV-2 are at increased risk for adverse outcomes such as preeclampsia, preterm birth, and GDM [6-8]. Physiological stress, altered immuno-endocrine responses, and cytokine activation can impair insulin sensitivity and β-cell function [9]. Moreover, lockdowns and reduced activity worsened obesity and glycemic control [10].

Vaccination against COVID-19 has proved safe and effective in pregnancy, with documented reductions in infection, hospitalization, and preterm birth [11-13]. However, its potential metabolic benefits have received limited attention. Emerging evidence suggests that COVID-19 vaccination dampens systemic inflammatory pathways and reduces cortisol-mediated insulin resistance [14-15]. By preventing infection and lowering stress, vaccination may help stabilize maternal glucose metabolism and reduce GDM risk.

Existing studies from high-income countries found neutral effects of vaccination on adverse metabolic outcomes [16-18], but none have evaluated its role in LMIC contexts where baseline GDM risk and vaccine uptake differ. Pakistan presents a unique case due to socioeconomic diversity, variable antenatal care quality, and moderate vaccine coverage.

This study extends previous analyses on the same Karachi cohort that reported lower rates of preterm birth and NICU admission among vaccinated women [19], and reduced maternal anxiety and depression [20]. We now examine whether vaccination is also linked to a lower incidence of GDM, after adjusting for potential confounders and validating results through propensity matching.

MATERIALS AND METHODS

Study Design and Setting

A comparative cross-sectional study was conducted at Korangi General Hospital, a public-sector tertiary care facility in Karachi, Sindh, Pakistan. The study period was April 1 to May 15, 2022.

Ethical Approval

Ethical clearance was granted by the Shaheed Zulfikar Ali Bhutto Institute of Science and Technology Institutional Review Board (ERB Ref No: IERB(10)SZABIST-KHI(LIFE)//191047). Written informed consent was obtained from all participants.

Study Population and Eligibility

Pregnant women aged 18–50 years delivering during the study period were eligible. Exclusion criteria included:
(1) known type 1 or type 2 diabetes, (2) chronic hypertension or renal disease, (3) psychiatric disorders, (4) multiple gestation. After screening, 200 participants (100 vaccinated, 100 unvaccinated) were enrolled.

Sampling Technique

Purposive sampling ensured equal representation of vaccinated and unvaccinated groups. Vaccination status was confirmed via official immunization records and verbal verification.

Variables and Measurements

- Exposure: COVID-19 vaccination status (yes/no), vaccine type (Sinopharm, Sinovac, Pfizer-BioNTech, AstraZeneca), trimester of vaccination.
- Outcome: Gestational diabetes diagnosed by WHO criteria (75 g OGTT, 2-hour plasma glucose ≥ 140 mg/dL).
- Covariates: Age, parity, BMI, gestational hypertension, COVID-19 infection during pregnancy, and socioeconomic status.

Data Collection Procedure

Trained research nurses administered structured questionnaires and extracted clinical data from hospital records. Blood sugar records were verified from antenatal charts. Quality assurance included double data entry and daily cross-checking by the principal investigator.

Sample Size Calculation

Using OpenEpi, a minimum of 91 participants per group was required to detect a 50 percent difference in GDM prevalence (α = 0.05, power = 80%). The sample was rounded to 100 per group to account for dropouts.

Statistical Analysis

Data were analyzed with SPSS v25. Continuous variables were expressed as mean ± SD and compared using t-tests. Categorical variables were analyzed using χ² or Fisher's exact tests. Multivariate logistic regression was performed to estimate adjusted odds ratios (aOR) and 95% CIs. Covariates with $p < 0.10$ in univariate analysis entered the model. Propensity-score matching (1:1 nearest-neighbor) validated results. Significance was set at $p < 0.05$.

RESULTS

Baseline Characteristics

Both groups were comparable in age, parity, and socioeconomic status (Table 1). Unvaccinated women had higher BMI and a greater frequency of COVID-19 infection (p = 0.04).

Table 1. Baseline Characteristics of Participants

Variable	Vaccinated (n = 100)	Unvaccinated (n = 100)	p-value
Mean Age (years)	27.1 ± 4.3	27.8 ± 4.7	0.42
Parity ≥ 2	60 %	57 %	0.69
BMI > 27 kg/m²	29 %	36 %	0.27
COVID-19 Infection	6 %	14 %	0.04 *
Gestational Hypertension	8 %	11 %	0.49

Prevalence of Gestational Diabetes

GDM was diagnosed in 6 vaccinated women and 14 unvaccinated women (p = 0.04). The mean 2-hour plasma glucose was lower in the vaccinated group (128 ± 18 mg/dL vs 137 ± 21 mg/dL; p = 0.01).

Table 2. Obstetric and Neonatal Outcomes

Outcome	Vaccinated %	Unvaccinated %	p-value
Gestational Diabetes	6	14	0.04 *
Preterm Birth	7	15	0.04 *
Preeclampsia	5	8	0.39
NICU Admission	5	12	0.03 *
Mean Birth Weight (g)	3100 ± 460	2920 ± 530	0.02 *

Adjusted Logistic Regression

Vaccination remained an independent predictor of reduced GDM (aOR 0.42; 95% CI 0.18–0.96; p = 0.04). Higher BMI and COVID-19 infection were significant risk factors (Table 3).

Table 3. Multivariate Model for GDM Predictors

Variable	aOR	95% CI	p
Vaccinated (vs Unvaccinated)	0.42	0.18–0.96	0.04 *
BMI > 27 kg/m²	2.31	1.08–4.96	0.03 *
COVID-19 Infection	2.68	1.01–7.13	0.05 *
Age > 30 years	1.21	0.57–2.59	0.61
Gestational Hypertension	1.74	0.69–4.37	0.24

Subgroup Analysis

No significant difference in GDM was observed by vaccine type (Sinopharm 4.8%, Sinovac 6.7%, Pfizer/AstraZeneca 7.1%) or trimester of vaccination (p > 0.6). PSM confirmed robustness (aOR 0.44; 95% CI 0.19–0.93).

DISCUSSION

This study demonstrates a significant inverse association between COVID-19 vaccination and gestational diabetes among pregnant women in Karachi. Vaccinated women had 58 percent lower odds of developing GDM, consistent with a possible anti-inflammatory or stress-mitigating effect.

Our findings extend previous reports showing that vaccination reduces preterm labor and NICU admissions [19] and improves maternal psychological well-being [20]. The biological plausibility lies in vaccination's ability to prevent cytokine surges and reduce cortisol levels, thus improving insulin sensitivity [14,21].

A cohort study from California showed no increase in GDM among vaccinated pregnant women [22], while meta-analysis data from Liu et al. found that vaccination was associated with a reduced risk of COVID-19-related metabolic complications [23]. Our results align with 2023 Korean and UK registry data reporting neutral-to-favorable trends in glycemic outcomes among vaccinated cohorts [24].

However, our findings must be interpreted with caution due to cross-sectional design limitations and potential unmeasured confounders. Nevertheless, the consistency across adjusted and matched models suggests a genuine association.

Strengths and Limitations

Strengths include standardized OGTT measurement, validated vaccination records, and rigorous confounder control. Limitations include single-site sampling, self-reported lifestyle factors, and limited power for subgroup analyses.

Public Health Implications

Integrating vaccination counseling with metabolic risk assessment in antenatal care could improve pregnancy outcomes. The observed metabolic advantage may further strengthen vaccine advocacy among hesitant populations.

CONCLUSION AND RECOMMENDATIONS

COVID-19 vaccination in pregnancy was independently associated with a lower incidence of gestational diabetes. These findings add a novel dimension to the benefits of maternal vaccination. Future prospective multicenter studies should validate this relationship and explore biochemical mediators linking immune modulation to glucose homeostasis.

Recommendations:

1. Integrate GDM screening within vaccine counseling protocols.
2. Prioritize vaccine literacy among obstetricians and midwives.

Conduct biochemical research on cytokine and cortisol markers post-vaccination.

FUTURE RESEARCH IMPLICATIONS

Longitudinal studies using serial glucose and cytokine profiling are needed to establish causality. Exploration of postnatal maternal metabolic recovery and infant glycemic regulation would further illuminate intergenerational benefits.

Authors' Contributions

Conceptualization: RS, TJ
Data Curation: RS, TJ
Formal Analysis: RS, TJ
Investigation: RS, TJ
Methodology: RS, TJ
Project Administration: RS, TJ
Resources: RS, TJ
Software: RS, TJ
Supervision: RS, TJ
Writing – Original Draft Preparation: RS, TJ
Writing – Review & Editing: RS, TJ
RS: Rubia Sami; **TJ:** Tahira Jabeen

What is already known about this topic

- GDM increases adverse pregnancy outcomes in Pakistan.
- COVID-19 infection elevates metabolic stress and GDM risk.
- Vaccination is safe and prevents severe maternal illness.
- No prior LMIC study explored vaccination–GDM association.

What this study adds to the current literature

- Demonstrates 58% lower GDM odds among vaccinated women.
- Highlights plausible immune-metabolic mechanisms.
- Validated through multivariate and propensity-matched models.
- Suggests integrating vaccination within metabolic antenatal care.

SUPPORTING INFORMATION

The questionnaire and the data can be provided by contacting the corresponding author.

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