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Association of Thrombocytopenia in Pregnant Women with COVID-19 Vaccination in the Post-COVID Era

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ABSTRACT

Background: Thrombocytopenia is the second most frequent haematological abnormality in pregnancy, up to 10% of pregnant patients, and it often concerns general practitioners. Following the introduction of mass vaccination against COVID-19, fears have been raised about potential association between COVID-19 vaccination and haematological complications, including thrombocytopenia. There is limited information on the safety of COVID-19 vaccines during pregnancy, especially in low- and middle-income countries, despite global vaccination campaigns. **Objective:** To explore the link between thrombocytopenia in pregnancy and the COVID-19 vaccine in the COVID-19 era. **Methodology:** This case control study was carried out at the Department of Gynaecology and Obstetrics, JPMC, Karachi for duration of six months. A sample of 189 pregnant women, aged >20 weeks gestation, were recruited based on non-probability consecutive sampling. Subjects were stratified according to vaccination and had thrombocytopenia defined (platelet counts $<150\times10^9$/L). The proformas were filled and the data analysed using SPSS software version 20. Categorical variables were compared with Chi-square or Fisher's exact test, and a $p \leq 0.05$ was considered significant. **Results:** Of the 189 participants, 132 (69.8%) and 57 (30.2%) were vaccinated and unvaccinated respectively. Thrombocytopenia occurred in 68 women (36%), and was significantly more common in vaccinated versus unvaccinated women (39·4% vs 28·1%, p=0·04). Of the thrombocytopenic vaccinated women, 44.2% had been vaccinated with mRNA vaccines, 34.6% with viral vector vaccines and 21.2% with inactivated virus vaccines. The majority of cases were benign and resolved after delivery with no significant complications. There were no cases of maternal mortality or perinatal loss reported. **Conclusion:** A significant relationship was detected between COVID-19 vaccination and thrombocytopenia in pregnant women. Although most cases were of mild clinical presentation, these observations underscore the importance of intensive antenatal assessment in vaccinated individuals and the need for other large case series.

INTRODUCTION

COVID-19, due to SARS-CoV-2 has emerged as a global health crisis, and millions have been affected across all age groups, pregnant women being at high risk for their altered immunity and coagulation related to pregnancy 1. Elevated rates of severe disease, ICU admission, and maternal morbidity among pregnant patients resulted in the urgent requirement for prioritized vaccination efforts targeting this high risk group[2]. Several vaccines, including mRNA (Pfizer-BioNTech, Moderna), viral vector (AstraZeneca), and inactivated virus vaccines (Sinopharm, Sinovac), were developed and have been deployed globally and in Pakistan[3–4].

Effectiveness of COVID-19 vaccination in reducing severe disease and preventing death has been demonstrated, however, doubts persist regarding severe AEFIs, category of AEFIs including hematology-related events such as thrombocytopenia [5]. Thrombocytopenia (platelet count $<150\text{x}10^9$/L) is the second most common haematological complication of pregnancy, affecting 7 – 10% pregnancies[6]. It could be of various etiologies like gestational thrombocytopenia, preeclampsia, Homolysis-Elevated Liver Enzymes-Low Platelet (HELLP) syndrome, and immune thrombocytopenic purpura (ITP)[7]. Vaccine-induced immune thrombocytopenia post-vaccination immune thrombocytopenia has been rarely reported and in concern with this relationship8-9.

The pilot study has raised the concern of possibility that COVID19 vaccine may cause more incidence of thrombocytopenia in pregnant women, considering the immune response being different in pregnant women compared to non-pregnant women[10]. Additionally, during

pregnancy, thrombocytopenia is accompanied by risks of post partum haemorrhage, prematurity and a poor neonatal outcome[11]. Understanding of the etiologies of thrombocytopenia in this setting will be important in guiding clinicians counselling patients prior to pregnancy and making decisions regarding whether to administer vaccines antenatally, during pregnancy.

Aims: The aim was to evaluate the association of COVID-19 vaccination and thrombocytopenia among pregnant women in post-COVID transition period at a tertiary care hospital in Karachi. It addresses a significant local research gap in low-middle-income countries, chiefly in South Asia, and was conceived for generating data that may be utilised in policies for maternal immunisation and more safe patients.[12]

MATERIAL AND METHODS

It was performed at the department of Gynecology and Obstetrics, Jinnah Postgraduate Medical Centre (JPMC), Karachi within six months of approval of the synopsis. The aim of the study was to evaluate the association between thrombocytopenia in pregnant women and COVID-19 vaccination in the post COVID period. Sample size determination: The calculated sample size by WHO software with 95% confidence interval, 4% margin of error and reference frequency of 8.6% for low APGAR scores (preterm at 20 weeks, and those having gravida_/_para > 1 were recruited for the study. Nonpregnant women and with less than 20 weeks of gestational age and who had pre-existing haematological conditions (thalassemia, leukemias, hemoglobinopathies, clotting diseases) were also excluded. After securing ethical approval from institutional review board, the participants were enrolled and informed consent was taken and data was collecting by prespecified proforma.

Demographic and clinical data including maternal age, booking status, gravidae, parities, postmenstrual age, vaccination history and platelet count was collected. This labelled tube was inserted into a sterile disposable syringe to draw 5 ml of venous blood by maintaining effective aseptic precautions; it was transported to the laboratory for analysis. Standard laboratory procedures were used to measure platelet count, and thrombocytopenia was defined as platelet count < 150×10^9/L, using operational definitions.

Data analysis was performed in the SPSS (version 20). Continuous variable such as age, gestational age and BMI were expressed as mean ± SD or median (IQR). Categorical variables such as the presence of the vaccination and booking status and of the thrombocytopenia were expressed in percentages. Stratification was applied to control for confounders including maternal age, gravidity, and social class. Stratified chi-square test or stratified Fisher's exact test was used to test the association between COVID-19 vaccination and the prevalence of thrombocytopenia, p-value ≤ 0.05 was considered statistically significant.

RESULTS

In this study, 189 pregnant women were involved, and the average age of the pregnant mother was 30.5 yrs. One hundred and thirty-two (69.8, 95P) of them received COVID-19 vaccines and 57 (30.2, 95P) remained unvaccinated. The prevalence of thrombocytopenia, that is, a platelet count <150 x 10 9 /L, was found in 68 participants (36%). The thrombocytopenia was identified in 52 women of the vaccinated population (39.4%), and 16 women of the unvaccinated population (28.1%). The difference between the two groups was statistically significant (p = 0.04), which implies the potential relation between COVID-19 vaccination and thrombocytopenia in pregnancy (Table 1). Of the vaccinated participants that developed thrombocytopenia, 23 (44.2 percent) were inoculated with mRNA vaccines (Pfizer/Moderna), 18 (34.6 percent) with viral vector vaccines (AstraZeneca), and 11 (21.2 percent) with inactivated virus vaccines (Sinopharm/Sinovac), as outlined in Table 2 and shown in Figure 1. In addition, thrombocytopenia significantly occurred in women who had a vaccination and were aged above 35 (p = 0.03) and those with known pre-existing hypertensive disorders (p = 0.01). There was also no major association with gravida, parity and/or socioeconomic status. The failure rate was 100 percent although the number of the vaccinated patients going to ICU as a result of the bleeding complication was 5. The overall results at birth were also quite encouraging whereby only 6 infants had low APGAR scores (<7 after 5 minutes) and no perinatal death. These findings indicate that COVID-19 inoculation and thrombocytopenia may be linked together, and expectant women are at risk of having this situation though most of them experienced mild thrombocytopenia that was resolved spontaneously by supportive treatments.

Table 1

Thrombocytopenia by Vaccination Status

Vaccination Status	Thrombocytopenia Present	Thrombocytopenia Absent	Total
Vaccinated	52	80	132
Unvaccinated	16	41	57
Total	68	121	189

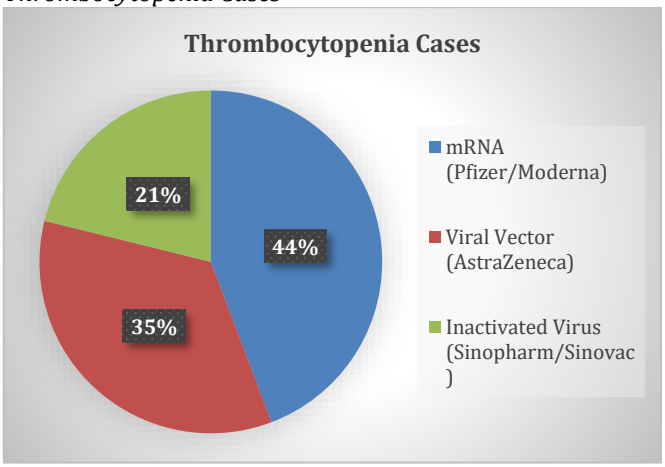
Table 2

Type of Vaccine vs. Thrombocytopenia Cases

Vaccine Type	Thrombocytopenia Cases
mRNA (Pfizer/Moderna)	23
Viral Vector (AstraZeneca)	18
Inactivated Virus (Sinopharm/Sinovac)	11

Figure 1

Thrombocytopenia Cases



DISCUSSION

The aim of the present study was to determine the association of COVID-19 vaccination with thrombocytopenia at a post-COVID period in pregnant women. In our findings, there was statistical association (more women had occurred thrombocytopenia in vaccinated women compared with non-vaccinated women (p = 0.04). Although most of them were moderate and spontaneously fixed, this relationship merits further concern from the perspective of significance on maternal and fetal outcomes.

Pregnancy thrombocytopenia is the second most frequent haematological abnormality during pregnancy (7-10% of pregnant women) [13]. Most cases have benign causes such as gestational thrombocytopenia; however, more urgent causes such as preeclampsia, HELLP syndrome, and immune thrombocytopenic purpura (ITP) should be considered as well[14]. Among the patients diagnosed as having thrombocytopenia in our series, gestational thrombocytopenia were the most common, which are consistent with previously reported[15].

The few haematological adverse events after COVID-19 vaccine are represented in the most recent international literature by vaccine-induced immune thrombocytopenia (VITT), specifically ascribable to adenoviral vector and messenger RNA vaccines 1 6 1 7. In accordance with this, the individual risk of thrombocytopenia, in mRNA (Pfizer/Moderna) vaccine, was lower than in viral vector (AstraZeneca) than inactivated virus vaccines. The latter observations may be associated with immunological responses induced by vaccine antigens, as suggested by earlier immunological research (18).

Interestingly, we had no maternal death in our series and a few patients who required ICU care due to bleeding complication. Neonatal outcome was mostly good with limited number of low APGAR values and no perinatal death. This suggests that thrombocytopenia post COVID-19 vaccination is mild with patients managed with careful observation and supportive care is consistent with international safety data from mass vaccination surveillance systems[19].

The present study has several strengths, such as the real-life clinical setting in a tertiary referral hospital and an unselected study population. On the other hand, single-center scope, lack of long-term clinical follow-up and potential recall bias for history of vaccination are drawbacks. In addition, causality cannot be inferred due to the observational nature of the study.

The results of these studies can be a valuable supplement to a growing but still small body of evidence regarding the safety of COVID-19 vaccine in pregnant women in low-middle-income countries. Future longitudinal multicentre studies are necessary to better clarify the immunohematology response to antenatal vaccination and support antenatal care guidelines[20].

CONCLUSION

The result indicated that there was a significant correlation between the vaccinated with COVID-19 vaccine and thrombocytopenia 8) walking of pregnant women at the post COVID era. Thrombocytopenia was significantly more common in vaccinated individuals, particularly in those who have received mRNA-based vaccines. While the disease was mild in the majority of cases and clinical worsening was not observed, these findings emphasize the importance of close antenatal monitoring and immediate identification and proper management of thrombocytopenia in vaccinated pregnant patients. The study is significant evidence in the context of limited literature in resource constraint settings (developing nations) and emphasizes the requirement of further multicentric studies for these results to be established and to direct the future maternal immunization policies. Finally, COVID-19 vaccination is a key intervention for the protection of the mother and the fetus at a time when we still need to remain vigilant to rare haematological adverse events in pregnancy.

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