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ORIGINAL ARTICLE

Effectiveness and Pregnancy Outcomes of COVID-19 Vaccination in Pregnancy

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ABSTRACT

Background: Vaccination against COVID-19 during pregnancy is suggested to avoid pregnancy complications morbidity and bad delivery outcomes. However, the safety and efficacy of COVID-19 vaccinations during pregnancy is a specific issue impacting vaccination uptake by this susceptible group due to alterations in immune, respiratory, and cardiovascular physiology that occur during pregnancy. The purpose of this study was to examine the relationship between prenatal mother COVID-19 immunization, pregnancy course, and outcomes. **Patients and Methods:** A retroactive cohort analysis was conducted on all women who gave birth. Women having a previous COVID-19 diagnosis, numerous pregnancies, or an uncertain vaccination status were excluded. Pregnancy, neonatal problems, and delivery were compared with women who got 1 or 2 doses of a vaccine throughout pregnancy and women who did not get any vaccinations. Using multivariable models, the background characteristics were accounted for. **Results**: The pregnancy complications were higher in unvaccinated group than vaccinated group with no statistical significant difference except stillbirth that was present only in unvaccinated group (3%). Women who were vaccinated gave birth at a significantly later gestational age. No differences between the groups were detected in terms of postpartum and delivery factors. Women who received vaccination delivered at slightly higher birth weight. No differences were detected in terms of neonatal features and problems between the two groups. **Conclusions:** We concluded that COVID-19-vaccinated pregnant women experienced similar pregnancy outcomes as unvaccinated pregnant women. In some cases, vaccination proved to be better outcome than un-vaccination.

Keywords: COVID-19, Pregnancy, Vaccination, Prenatal, Outcomes, Maternal

INTRODUCTION

COVID-19 is considered a global epidemic of catastrophic proportions [1]. Since the discovery of the first instances of COVID-19 induced by SARS-CoV-2 in December 2019 in Wuhan, China, and the virus has swiftly spread globally. Almost 207 million people have been infected globally, resulting in over 4 million fatalities. As of August 15, 2021, about 620,000 people have perished from COVID-19 in the USA alone [2].

Several research on COVID-19 health issues, including investigations on the mental and physical impacts of COVID-19 for the

duration of pregnancy, have been published [3, 4]. The lower lung capacity associated with fetal development, together with the normal prenatal inhibition of the maternal immune reaction [5], may result in significant COVID-19 expression in pregnant women [6].

Vaccine reluctance among pregnant women has been influenced by a number of factors, including the absence of knowledge with mRNA vaccine portals from outside research settings, the exemption of pregnant women from preliminary COVID-19 vaccine trials, and the resulting mutable and uncertain vaccination guidelines from formal bodies, in addition to antivaccine misinformation [8, 9].

Fears about the safety of vaccines within pregnant women are a continuing barrier to vaccination during pregnancy. Previous investigations on the correlation between maternal COVID-19 immunization and newborn outcomes were restricted by small sample sizes [10] or the absence of an unvaccinated comparison group [11]. The great majority of pregnant women who required medication or intensive care unit (ICU) care for COVID-19 during the delta wave were unvaccinated, according to data from the UK Obstetric Surveillance System (UKOSS) [12].

Currently, clinical trials are investigating the unanswered concerns with COVID-19 immunization in pregnancy, such as the ideal dose schedule, the durability and effectiveness of antibodies transmitted transplacentally and via lactation, and the optimal dosing schedule [13]. Currently, the following three COVID-19 vaccinations are available: Two mRNA vaccines, one from Pfizer-BioNTech (Germany and New York) and another one from Moderna (Cambridge, MA) were tested, and one adenoviral vector vaccination (Johnson & JohnsoneJanssen, Belgium). The CDC stipulates that any of the presently permitted vaccinations may be delivered to women who are pregnant or breastfeeding, regardless of vaccine type **[**14**]**.

The Royal College of Obstetricians and Gynecologists in the United Kingdom suggests mRNA immunization for pregnant women because mRNA vaccines have better safety evidence than adenoviral vaccinations [15].

There is an acute need for high-quality, accurate data to assist pregnant women considering COVID-19 vaccination in the absence of fresh updates from large national registries and the outcomes of current studies. In the present study, we attempted to find features linked with maternal immunization.

PATIENTS AND METHODS

This retrospective study was carried out at Department of Obstetrics and Gynacology, Faculty of Medicine, Zagazig University between January 2021, and January 2022. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: women who delivered singletons, and pregnant women having full maternal and fetal outcome data and a known vaccination status.

Exclusion criteria: women who were fully vaccinated before pregnancy or after delivery, as well as women whose pregnancies were affected by fetal aneuploidy or genetic disorders, were exempt from the study.

The study included a total number of 1530 patients. Studied patients were divided into two groups; Group (I): 480 pregnant women who got one or two vaccination doses. Group (II): 1050 unvaccinated women.

Operational Design:

Data were acquired from electronically maintained hospital records. The correctness of the COVID-19 immunization record in the subsequent database was evaluated for data quality. Women hospitalized to the postnatal unit were questioned for one week on their replies were cross-referenced with the electronic data and their vaccination status. Age, body mass index (BMI), parity, comorbidities, and prenatal problems were among the gathered variables. In addition to COVID-19 vaccination kind, vaccination coverage, and gestational age (GA) at vaccination. Other data included pregnancy complications, involving pregnancy hypertensive disorders, oligohydramnios, polyhydramnios, pathological presentation was a non-vertex presentation, meconium-stained amniotic fluid and stillbirth. For the general people, pregnant women were

qualified to be vaccinated if they (i) worked in health or social care and were at elevated risk of COVID-19 development, or (ii) were at high risk of contracting COVID-19 owing to personal variables (such as non-white race) or health issues (for example, gestational diabetes or diabetes mellitus). Comparing the delivery date to the vaccine suitability date according to the mother's priority and age category determined vaccination qualification.

Ethical consideration:

All participants in the study gave their written informed consent and the local institutional review board (Ethical Committee) gave its approval (IRB) dated 4.12.2022 (number 10146).

Statistic analysis

The SPSS 20 program was used to examine the data (IBM, USA). The parametric data expressed as mean ± SD (Range) or number (%) for categorical data. Comparisons for parametric data were carried out using independent student t test. For categorical data, the Fischer exact test and chi square test were used.

RESULTS

Data are expressed as mean, standard deviation, or percentage. The data are analyzed using the independent chi-square test or student t test .

During the research period, 1,530 women gave birth, of which 480 (31.4%) were vaccinated. The remaining 1050 (68.6%) women were not immunized during or before to pregnancy. All immunizations were administered in the second or third trimester. Table 1 provides a comparison of background and pregnancy characteristics.

Data are expressed as percentage. Data are analyzed using chi square test or fischer exact.

Table 2 presents comparison between both groups regarding pregnancy complications that were comparable between both groups except stillbirth that was present only in unvaccinated group (3%).

Data are expressed as mean, standard deviation, or percentage. The data are analyzed using the independent chi-square test or student t test.

Women who were vaccinated gave birth at a significantly later gestational age. No differences between the groups were observed in terms of delivery and postpartum characteristics (Table 3).

Data are expressed as mean, standard deviation, or percentage. The data are analyzed using the independent chi-square test or student t test.

Also, women who received vaccination delivered at slightly higher birth weight. No differences between the two groups were observed in terms of neonatal features and problems (Table 4).

Table (1): Maternal background characteristics and Pregnancy characteristics among vaccinated and unvaccinated cases.

	Vaccinated (N=480)	Un Vaccinated (N=1050)	P value
Maternal background characteristics			
Age	25.9 ± 3.2	26.4 ±3.4	0.007*
BMI	25.6 ± 2.04	25.8 ± 2.3	0.16
Pregnancy after fertility treatment	96 (22%)	181 (17%)	X^2 =1.69, P=0.19
Pregnancy characteristics			
Gestational DM	30 (7%)	79 (18%)	X^2 =0.8, P=0.36
Vaccine type **Pfizer-BioNTech (mRNA)** **Sinopharm (inactivated)** **Sinovac (inactivated)** **AstraZeneca (viral vector)**	 192 (44%) 120 (27%) 54 (12%) 102 (23%)		
Trimester at vaccination **First** **Second**	 0 (0%) 102 (23%)		

	Vaccinated (N=480)	Un Vaccinated (N=1050)	P value
Third	378 (86%)		

Table 2: Pregnancy complications among vaccinated and unvaccinated cases.

	Vaccinated (N=440)	Un Vaccinated (N=1040)	P value
Pregnancy hypertensive disorders	24 (5%)	66 (15%)	X^2 =0.98, P=0.32
Oligohydramnios	18 (4%)	52 (12%)	X^2 =1.09, P=0.29
Polyhydramnios	18 (4%)	26 (6%)	X^2 =1.9, P=0.16
Pathological presentation	24 (5%)	66 (15%)	X^2 =0.98, P=0.32
Meconium-stained amniotic fluid	18 (4%)	26 (6%)	X^2 =1.9, P=0.16
Stillbirth	0	13 (3%)	Fischer exact P=0.01*

Table 3: Delivery and post-partum characteristics among vaccinated and unvaccinated cases.

	Vaccinated (N=440)	Un Vaccinated (N=1040)	P value
Gestational age	3241.5 ± 382.05	3220.1 ± 404.8	0.24
Apgar < 7 at 5 min	18 (4%)	52 (12%)	X^2 = 1.1, P=0.27
Cesarean delivery	372 (85%)	760 (173%)	X^2 =3.07, P=0.08
vaginal delivery	108 (25%)	227 (52%)	X^2 = 3.07, P= 0.08
Placental abruption	6 (1%)	13 (3%)	X^2 =0, P=0.99
Postpartum hemorrhage	6 (1%)	26 (6%)	X^2 = 2.5, P=0.11
Maternal postpartum fever	6 (1%)	13 (3%)	X^2 =0, P=0.99

Table 4: Newborn characteristics complications among vaccinated and unvaccinated cases.

	Vaccinated (N=440)	Un Vaccinated (N=1040)	P value
Birthweight, gr.	3241.5 ± 382.05	3220.1 ± 404.8	0.33
Small for gestational age	30 (7%)	66 (15%)	X^2 =0.007, P=0.93
Respiratory complications	12 (3%)	26 (6%)	X^2 =0, P=0.99
Neonatal ICU admission	30 (7%)	78 (18%)	X^2 =0.8, P= 0.37

DISCUSSION

Despite intense worldwide public health efforts to restrict its spread, the COVID-19 pandemic has resulted in mortality and worsening health implications, both outside and during pregnancy [16]. Vaccination en masse is a crucial strategy employed by nations to combat the epidemic [7].

There are indications that COVID-19 poses a risk to maternal and perinatal health. Compared to non-pregnant women at similar age, pregnant women had a higher risk of COVID-19-related consequences, including as hospitalization, severe pneumonia, invasive mechanical ventilation, intensive care unit admission, and death [17,18].

Despite the danger of problems and poor perinatal outcomes, pregnant women are not considered a high-priority target for COVID-19 vaccination. Pregnant women were omitted from early COVID-19 vaccination studies, resulting in a wasted chance to collect safety and effectiveness data and perhaps decreasing

the likelihood that pregnant women will get the advantages of COVID-19 immunizations [19]. The Egyptian Ministry of Health and population offered four types of COVID-19 vaccine for health care workers for free they were Pfizer-BioNTech, Sinopharm, Sinovac and AstraZeneca but on the other hand there were a great worries and hesitancy about them. The CDC stipulates that any of the presently permitted vaccinations may be delivered to women who are pregnant or breastfeeding, regardless of vaccine type [20].

When these vaccinations initially became accessible in the United States, there was a paucity of information regarding their safety during pregnancy, and these data are now fast accumulating. Approximately 150,000 pregnant women have registered for V-safe, the CDC's smartphone-based platform that gathers data from persons who have gotten a COVID-19 immunization through texting and web-based questionnaires. More than 5,000 pregnant women have participated in the V-safe pregnancy registry, which tracks pregnant women and their babies for three months following the end of pregnancy [21].

In our study the results showed that during the research period, 1,530 women gave birth, of which 480 (31.4% were vaccinated). The remaining 1050 (68.6%) women were not immunized during or before to pregnancy. All immunizations were administered in the second or third trimester.

Blakeway et al. [22] reported that the trial comprised 140 pregnant women who got at least one dose and 1188 pregnant women who did not vaccinated. Regarding the GA immunization, 120 women (85.7%) got their first dose during the third trimester, whereas 20 women (14.3%) did so during the second. None of the women received the vaccination during the first trimester of pregnancy or before to conception.

Shimabukuro et al. [11] indicated that main data and scheduled follow-up were obtained at precise time intervals between 10 and 12 weeks for the 1,040 participants (91.9%) who got a vaccination in the first trimester and 1,700 individuals (99.2%) who were vaccinated in the second trimester.

According to **Wainstock et al.,** the overall study population comprised of 4,399 women, 913 (20.8%) of whom were vaccinated: 758 (83%) received two doses, while 155 (17%) received one. The remaining 3,486 women (79.2%) were not immunized during or before to pregnancy. All immunizations were administered in the second or third trimester [10].

The pregnancy complications were higher in unvaccinated group than vaccinated group with no statistical significant difference except stillbirth that was present only in unvaccinated group (3%).

This came in agreement with **Blakeway et al.** [22] who discovered that COVID-19-vaccinated women had considerably greater levels of pregestational diabetes, prenatal medication usage, and hypertension compared to unvaccinated women, although the difference was not statistically significant. There was no significant difference in prenatal problems, including gestational diabetes mellitus (P=.499), antenatal COVID-19 infection (< 2% in each group), cardiac complications (ie, arrhythmia; P=.874), or obstetrical cholestasis (P=.646). With the exception of intrapartum fever (OR, 3.85; 95% CI, 1.01-14.6; P=.046), there was no notable change in intrapartum issues or perinatal results between pregnant ladies who got vaccination against COVID-19 and those who did not.

Shimabukuro et al. [11] found that among 827 people with a completed pregnancy, 104 (12.6%) had a spontaneous abortion, 712 (86.1%) had a live birth, 10 (1.2%) had other outcomes (ectopic pregnancy and abortion), and 1 (0.1%) had a stillbirth. A total of 96 of 104 spontaneous abortions (92.3%) happened before 13 weeks of gestation, while 700 of 712 pregnancies that ended in a live delivery (98.3%) occurred in women who got their first dose of an eligible vaccination in the third trimester.

The results revealed that women who were vaccinated had somewhat later deliveries. No differences between the groups were observed in terms of delivery and postpartum characteristics.

In agreement with our study, **Wainstock et al.** [10] illustrated that women who got the second-dose delivered at marginally greater gestational age and birth-weight, whereas According to **Blakeway et al.** [22] GA at 40 weeks' gestation did not vary between vaccinated and unvaccinated women (HR, 0.93; 95% CI, 0.71-1.24; P=.624).

We demonstrated that women who received vaccination delivered at slightly higher birth weight. No differences were noted between the two groups in terms of neonatal features and problems.

Shimabukuro et al. [11] illustrated that among 724 live-born newborns, including 12 groups of numerous gestations, the unfavorable outcomes were preterm delivery (60 of 636 among those vaccinated before 37 weeks [9.4%]), small size for gestational age (23 of 724 [3.2%]), and major congenital incongruities (16 of 724 [2.8%]); at the time of the interview, no newborn fatalities had occurred.

Blakeway et al. [22] showed that women who received the COVID-19 immunization reported three prenatal abnormalities: ventriculomegaly, hydronephrosis, and spina bifida. The diagnosis of spina bifida was made prior to the pregnant lady receiving the first dose of the vaccination. Using fetal brain magnetic resonance imaging, the occurrence of ventriculomegaly was identified at 37 weeks of gestation, with no concomitant brain abnormalities. The hydronephrosis was minor, and no birth anomaly was linked with it.

Wainstock et al. [10] found that in all multivariable models that accounted for maternal age, socioeconomic status, and fertility treatments, this was the case. Moreover, no correlations were discovered between vaccination status and pregnancy, birth, or neonatal features or problems. In addition to a reduced probability of meconium-stained amniotic fluid in the vaccinated group, non-reassuring fetal monitoring was seen.

CONCLUSION

We concluded that pregnant women who were immunized against COVID-19 had comparable pregnancy outcomes to those who were not immunized. In some cases, vaccination proved to be better outcome than un-vaccination.

Declaration of interest

The authors report no conflicts of interest. The authors along are responsible for the content and writing of the paper.

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REFERENCES

1. **Narang K, Enninga EA, Gunaratne MD Ibirogba ER, Trad AT, Elrefaei A et al.** SARS-CoV-2 Infection and COVID-19 During Pregnancy: A Multidisciplinary Review. **Mayo Clin Proc**. **2020**; 95(8):1750–65. https://doi.org/10.1016/j.mayocp.2020.05.011.
2. **LaCourse SM, Kachikis A, Blain M, Simmons LE, Mays JA, Pattison AD et al.** Low prevalence of severe acute respiratory syndrome coronavirus 2 among pregnant and postpartum patients with universal screening in Seattle, Washington. Clin Infect Dis**. 2021**; 72: 869–72.
3. **Dashraath P, Wong JL, Lim MX, Lim LM, Li S, Biswas A et al.** Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. Am J Obstet Gynecol**. 2020**; 222(6):521–31. https://doi.org/10.1016/j.ajog.2020.03.021.
4. **Oltean I, Tran J, Lawrence S, Ruschkowski BA, Zeng N, Bardwell C.** Impact of SARS-CoV-2 on the clinical outcomes and placental pathology of pregnant women and their infants: A systematic review. Heliyon**. 2021**; 7(3):e06393. https://doi.org/10.1016/ j.heliyon. 2021. e06393.
5. **LoMauro A, Aliverti A.** Respiratory physiology of pregnancy: Physiology masterclass. Breathe (Sheff). **2015**;11:297–301. https://doi:10.1183/20734735.00861.
6. **Molaei B, Ahangari R, Salehi M, Oskoei AD, Pirozan P, Darkhaneh RF.** Maternal death due to COVID-19. Am J Obstet Gynecol. 2020; 223(1):109. e1–109.e16. https://doi.org/ 10.1016/j.ajog.2020.04.030.
7. **Viana J, van Dorp CH, Nunes A, Gomes MC, van Boven M, Kretzschmar ME et al.** Controlling the pandemic during the SARS-CoV-2 vaccination rollout. Nat Commun**. 2021**; 12(1):3674.
8. **Public Health England.** JCVI Issues New Advice on COVID-19 Vaccination for Pregnant Women, 2021 [PHE, accessed 25 August 2021); https://www.gov.uk/government/news
9. **H pS B, Kalafat E, Heath p, Ladhani S, LerDoare K, et al.** COVID-19 vaccination during pregnancy: coverage and safety. Am J Obstet. Gynecol. 2021; https://doi.org/10.1016/ j.ajog.2021.08.007.
10. **Wainstock T, Yoles I, Sergienko R, Sheiner E.** Prenatal maternal COVID-19 vaccination and pregnancy outcomes. Vaccine 2021; 39:6037–40. PMID: 34531079 https://doi.org/10. 1016/j vaccine.2021.09.012.

11. **Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L et al.** CDC v-safe COVID-19 Pregnancy Registry Team. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. N Engl J Med**. 2021**; 384:2273–82. PMID:33882218 https://doi.org/10.1056/NEJMoa2104983.
12. **Prasad S, Kalafat E, Blakeway H, Townsend R, O'Brien P, Morris E et al.** Systematic review and meta-analysis of the effectiveness and perinatal outcomes of COVID-19 vaccination in pregnancy. Nature communications, 2022;13(1), 1-8.
13. **Pfizer.** Pfizer and biontech commence global clinical trial to evaluate covid-19 vaccine in pregnant women, (Pfizer, accessed 26 August 2021) https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-commence-global-clinical-trial-evaluate.
14. **Centers for Disease Control and Prevention.** Interim clinical considerations for use of COVID-19 vaccines currently approved or authorized in the United States. Available at: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#pregnant. Accessed October 15, 2021.
15. **COVID RCOG. 19 vaccines, pregnancy and breastfeeding.** Available at: https://www.rcog.org.uk/en/guidelines-research-services/coronavirus-covid-19-pregnancy-and-womens-health/covid-19-vaccines-and-pregnancy/covid-19-vaccines-pregnancy-and-breastfeeding/. **2021.** Accessed October 15.
16. **Roberton T, Carter ED, Chou VB, Stegmuller AR, Jackson BD, Tam Y et al.** Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study. Lancet Glob Health. **2020;** 8: e901–8.
17. **Pirjani R, Hosseini R, Soori T, Rabiei M, Hosseini L, Abiri A et al.** Maternal and neonatal outcomes in COVID-19 infected pregnancies: a prospective cohort study. J Travel Med. **2020**; 27: taaa158.
18. **Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT et al.** Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status United States, January 22–June 7. MMWR Morb Mortal Wkly Rep. **2020**; 69: 769–75.
19. **World Health Organization WHO** SAGE roadmap for prioritizing uses of COVID-19 vaccines in the context of limited supply. an approach to inform planning and subsequent recommendations based on epidemiological setting and vaccine supply scenarios, first issued 20 October 2020, latest update 16 July 2021 (No. WHO/2019-nCoV/Vaccines/SAGE/Prioritization/2021.1). World Health Organization.
20. **Ahmed NA, Hrariedy NG, Abdelbaky MM, Abouzied WR.** Critical Care Nurses Perception of COVID-19 Vaccines and its Side Effects at Upper Egypt. *Egypt J Health Care*, *13*(3), 1045-59.
21. **Centers for Disease Control and Prevention. V-safe COVID-19 vaccine pregnancy registry.** Available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe-pregnancyregistry.html. Accessed October **(2021).**15, 2021.
22. **Blakeway H, Prasad S, Kalafat E, Heath PT, Ladhani SN, Le Doare K, et al.** COVID-19 vaccination during pregnancy: coverage and safety. *American journal of obstetrics and gynecology*, **2022**. *226*(2), 236-e1.

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