RESEARCH ARTICLE

Determinants of Covid vaccine uptake and perinatal outcome in pregnant women at a tertiary care center

Sofia Butt,[1] Pooja Setlani,[2] Mehwish Iftikhar,[3] Mahwish Samuel,[4] Saba Rafiq Mughal,[5] Kashif Shafique,[6] Nazli Hossain[7]

Abstract

Objective: To determine the factors for hesitancy and uptake of coronavirus disease-2019 vaccine, and to compare perinatal outcomes in vaccinated and nonvaccinated pregnant women.

Method: The cross-sectional study was conducted from November 2021 to February 2022 at the Ruth Pfau Civil Hospital, Karachi, and the Holy Family Hospital, Karachi, and comprised pregnant women admitted in delivery suite for operative or vaginal delivery. Data was collected using a self-designed questionnaire which also explored knowledge about vaccine, contextual factors and reasons for and against vaccination. Perinatal outcomes included stillbirth, preterm delivery, low birth weight and Appearance-Pulse-Grimace-Activity-Respiration score. Also, 3cc blood was collected from the umbilical cord at the time of delivery, and enzyme-linked immunosorbent assay technique was used for antibodies titre. Data was analysed using SPSS 24.

Results: Of the 186 women, 114(61.3%) with mean age 27.9±4.1 years were vaccinated, and 72(38.7%) with mean age 27.5±5.2 years were not vaccinated. Physician's advise 104 (91.2%), vaccine safety and its effect on foetus 52(72.2%) were main determinants for vaccine uptake and refusal, repectively. Family and peer pressure was also responsible in 19(26.4%) cases for vaccine refusal. Body mass index, parity, level of education, socioeconomic status, history of coronavirus disease-2019 infection, booking status and presence of gestational diabetes mellitus were significantly different between the vaccinated and unvaccinated groups ($p<0.05$). Antibody titers and Appearance-Pulse-Grimace-Activity-Respiration score at 1 minute were significantly higher in the group of vaccinated women ($p<0.05$).

Conclusion: Vaccine uptake was found to be low. Safety concern against vaccine, and doctor's advice were the main determinants for hesitancy and uptake. Antibody titers in newborns were higher in the group of vaccinated women.

Key Words: COVID-19 infection, Pregnancy, Vaccine, Antibody titers.

(JPMA 73: 1212; 2023) **DOI: 10.47391/JPMA.6593**

Submission completion date: 14-04-2022— **Acceptance date:** 30-01-2023

Introduction

Coronovairus disease-2019 (COVID-19) infection during pregnancy has been identified with increased morbidity and mortality in women. There are increased risks for operative delivery, postpartum haemorrhage, preterm delivery and chances of intensive care unit (ICU) admission for both mother and newborn.[1] Apart from measures like social distancing, face mask, regular washing of hands with soap and water, vaccination has played an important role in the control of the disease. Vaccination during pregnancy has always been a matter of concern both for the women and for treating physicians. The COVID-19 pandemic brought the matter to the forefront in recent times. From public point of view, safety concerns for the foetus are always there. Vaccines against COVID-19 infection utilised the principle of greater public benefit. In the initial stages, pregnant women were not included in the vaccination drive, and they were not included in vaccine trials.

The guidelines from various governing bodies in the initial days of the pandemic also advised against vaccination since no details on maternal and foetal safety were available. For example, the Joint Commission on Vaccination and immunisation (JCVI, United Kingdom, advised vaccination of pregnant women only in April 2021.[2] Similarly, local guidelines (https://nhsrc.gov.pk)[3]

for vaccination against COVID-19 infection introduced vaccination for pregnant women much later than for the masses at large. This resulted in confusion among

[1-3,7]Department of Obstetrics and Gynaecology, Dr. Ruth K.M Pfau, Civil Hospital and Dow Medical College, Karachi, Pakistan, [4]Holy Family Hospital, Karachi, Pakistan, [5,6]School of Public Health, Dow University of Health Sciences, Karachi, Pakistan.

Correspondence: Nazli Hossain. Email: nazli.hossain@duhs.edu.pk

pregnant women as well as among health professionals whether or not to opt for vaccination in such cases. This phenomena of inconsistent messages from different health organisations were seen globally.[4] Data subsequently started accumulating, showing that vaccination does decrease the rate of infection among pregnant women.[5] Literature shows that humoral immunity induced by vaccination among pregnant women is better than the immunity induced by acquiring natural infection.[6] COVID-19 vaccination has also been carried out in women planning to conceive. In a registry-based survey, it was found that the risk of spontaneous miscarriage was the same among women who got themselves vaccinated during preconception period and the risk among society at large.[7]

However, reservations regarding COVID-19 vaccination were common in healthcare providers and pregnant women globally.[8] Other factors identified for low COVID-19 vaccination acceptance among pregnant women included mistrust, religiosity, easy availability, and lack of knowledge about severe infection and safety concerns[9].

The current study was planned to identify determinants of vaccine uptake and hesitancy among pregnant women, and to compare perinatal outcomes and antibody titers in newborns between vaccinated and non-vaccinated women.

Subjects and Methods

The cross-sectional study was conducted at the Ruth Pfau Civil Hospital, Karachi, and the Holy Family Hospital, Karachi, from November 2021 to February 2022. During this period only women who had symptoms of COVID-19 infection were screened for active infection.

After approval from the institutional ethics review boards of both the hospitals, the sample size was calculated using OpenEpi calculator[10] with 3% margin of error at 95% confidence level and proportion of 98.3% positivity in line with literature.[11] The actual sample was inflated by >100% to have better sudy power.

The sample was raised from among pregnant women admitted in the delivery suite for operative or vaginal delivery. Also included were women who gave history of confirmed COVID-19 infection in the preceding 6 months. Pregnant women with anamolus babies or with diagnosed intrauterine demise, and those having active or suspected COVID-19 infection during admission or hospitalisation were excluded.

After taking informed verbal consent, a detailed history was taken from the subjects in the labour suite regarding vaccination, type and date of vaccination or history of infection while being pregnant. The vaccination status of women were confirmed from the government's official website.(https://nims.nadra.gov.pk/nims/certificate)[12] The gestational age was calculated from the recall of last menstrual period, or first available ultrasound. All the women had face-to-face interview either at the time of admission in the delivery suite or after delivery in the postnatal ward. Data was collected using a self-designed questionnaire which also explored knowledge about vaccine, contextual factors and reasons for and against vaccination. The perinatal outcomes included stillbirth, preterm delivery, low birthweight (LBW) and neonatal admission to intensive care unit (ICU), and Appearance-Pulse-Grimace-Activity-Respiration (APGAR) score.[13] Stillbirth was defined as foetal death ≥28 weeks of gestation. Preterm birth was defined as birth <37 completed weeks of gestation. Also, 3cc blood was collected from the umbilical cord at the time of delivery, and enzyme-linked immunosorbent assay (ELIZA) technique (Cobas 6000) was used for antibodies titre. All the tests were run at the Central Laboratory of Dr Ruth Pfau Civil Hospital. The samples collected at the Holy Family Hospital were stored and transferred within 24 hours of collection to the Central Laboratory.

Data was analysed using SPSS 24. Frequencies and percentages were used to express categorical variables, while mean and standard deviation were used for quantitative variables. Data normality was checked using Shapiro-Wilk test. Mean differences of quantitative variables were checked using Independent t test or Mann-Whitney test, as appropriate. Association between vaccination status and qualitative variables were assessed using Chi-square or Fisher exact test, as appropriate. Antibody titers were categorised into 2 groups on the basis of median values (Low = ≤236U/mL; High = >236U/mL). Binary logistics regression analysis was carried out and odds ratios (OR) with 95% confidence interval (CI) were calculated for high antibody titers to assess the association with other independent factors. $P<0.05$ was considered statistically significant.

Results

Of the 1,438 obstetric admissions during the period, 186(13%) women were included. Of them, 114(61.3%) with mean age 27.9±4.1 years were vaccinated, and 72(38.7%) with mean age 27.5±5.2 years were not vaccinated. Physician's advise 104 (91.2%), vaccine safety and its effect on foetus 52(72.2%) were main determinants for vaccine uptake and refusal, repectively. Family and peer pressure was also responsible in

Table-1: Contextual factors and reasons for and against vaccination among pregnant women (n=186).

Variables	Frequency	Percentage (%)
Vaccination status		
Vaccinated	114	61.3
Unvaccinated	72	38.7
Number of doses (n=114)		
Single	77	67.5
Both	37	32.5
Type of vaccine (n=114)		
Sinopharm	35	30.7
Sinovac	44	38.6
Pfizer	8	7.0
AstraZeneca	1	0.9
Moderna	5	4.4
CanSino	21	18.4
Reason for vaccine uptake (n=114)		
Doctors advice	104	91.2
Media	4	3.5
Hospital registration	4	3.5
Others	2	1.8
Reason for Refusal (n=72)		
Harmful effect on pregnancy	52	72.2
Refused by family	19	26.4
Consent regarding vaccine safety	1	1.4
Time interval between vaccination and delivery (Mean ± SD)	45.9	30.4

19(26.4%) cases for vaccine refusal. The mean duration between vaccination and delivery was 45.9±30.4 days (Table 1).

Body mass index (BMI), parity, level of education, socioeconomic status, history of COVID-19 infection, booking status and presence of gestational diabetes mellitus (GDM) were significantly different between the vaccinated and unvaccinated groups (Table2).

Table-2: Demographic and maternal outcomes (n=186).

Variables	Vaccinated (n = 114)	Unvaccinated (n = 72)	p-value[a]
Mean Age (years)	27.9 ± 4.1	27.5 ± 5.2	0.522
Mean Body mass index, kg/m^2	24.6 ± 5.5	22.0 ± 3.2	0.003
Mean Parity	1.8 ± 1.2	2.7 ± 1.9	0.002
Mean Gestational age (weeks)	37.9 ± 1.9	37.6 ± 1.9	0.142
Level of education			
Primary	33 (28.9)	23 (31.9)	0.029
Secondary	67 (58.8)	48 (66.7)	
College/ University	14 (12.3)	1 (1.4)	
Socioeconomic status			
< 25000 PKR	11 (9.6)	14 (19.4)	0.056
≥ 25000 PKR	103 (90.4)	58 (80.6)	
History of COVID infection			
Yes	0 (0)	8 (11.1)	< 0.001
No	114 (100.0)	64 (88.9)	
Booking status			
Booked	110 (96.5)	60 (83.3)	0.002
Continue from previous Column..			
Un-booked	4 (3.5)	12 (16.7)	
Mode of delivery			
SVD	33 (28.9)	16 (22.2)	0.310
LSCS	81 (71.1)	56 (77.8)	
Preterm labour			
Yes	7 (6.1)	2 (2.8)	0.486
No	107 (93.9)	70 (97.2)	
Pregnancy Induced Hypertension			
Yes	5 (4.4)	2 (2.8)	0.708
No	109 (95.6)	70 (97.2)	
Gestational diabetes mellitus			
Yes	9 (7.9)	0 (0)	0.013
No	105 (92.1)	72 (100.0)	

Mean ±SD and n (%) are reported. ap-value was calculated by Independent t test/ Mann whitney test and Chi-square/ Fisher exact test, as appropriate. SVD: Spontaneous vaginal delivery, LSCS: Lower segment caesarean section.

Antibody titers and APGAR score at 1 minute were significantly higher in the group of vaccinated women (p<0.05) (Table 3).

Table-3: Neonatal outcomes (n=186).

Variables	Vaccinated (n = 114)	Unvaccinated (n = 72)	p-value[a]
Mean Weight of Body (kg)	2.9 ± 0.5	2.8 ± 0.5	0.777
Mean Antibody titers (U/mL)	580.8 ± 1209.5	143.1 ± 162.9	< 0.001
Gender			
Male	60 (52.6)	32 (44.4)	0.277
Female	54 (47.4)	40 (55.6)	
APGAR score at 1-min			
< 7	13 (11.4)	18 (25.0)	0.015
≥ 7	101 (88.6)	54 (75.0)	
APGAR score at 5-min			
< 7	4 (3.5)	5 (6.9)	0.312
≥ 7	110 (96.5)	67 (93.1)	
Foetal complication			
Alive	112 (98.2)	72 (100)	0.523
Stillbirth	2 (1.8)	0 (0)	

Mean ±SD and n (%) are reported. ap-value was calculated by Independent t test/ Mann Whitney test and Chi-square/ Fisher exact test, as appropriate.
APGAR: Appearance-Pulse-Grimace-Activity-Respiration.

Mean antibody titers were high in those newborns whose mothers were vaccinated with Pfizer vaccine, followed by Sinovac (Figure).

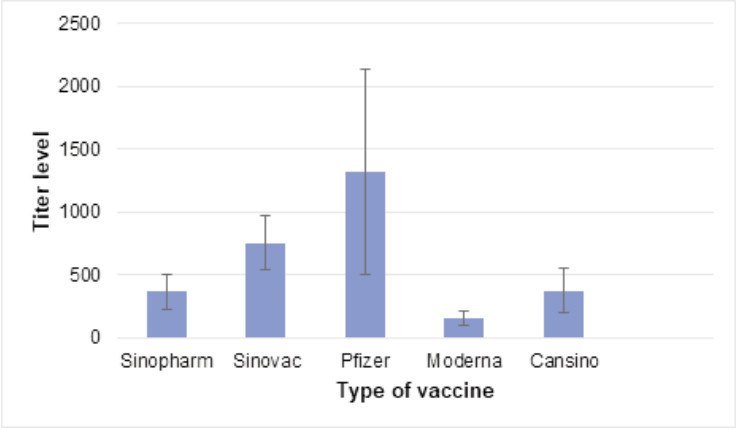

Figure: Mean antibody titers with standard errors by type of coronavirus disease-2019(COVID-19) vaccine.

Table-4: Odds ratio (OR) for high-level antibody titers (>236U/mL) by maternal and neonatal outcomes.

Variables	OR[a] (95% CI)	p-value
Vaccination status		
Unvaccinated	Ref	
Vaccinated	3.61 (1.69 - 7.68)	0.001
Level of education		
Primary	Ref	
Secondary	2.86 (1.29 - 6.36)	0.010
College/ University	0.43 (0.10 - 1.79)	0.245
Booking status		
Unbooked	Ref	
Booked	2.06 (0.58 - 7.28)	0.260
Mode of delivery		
SVD	Ref	
LSCS	0.49 (0.22 - 1.12)	0.091
Preterm Labour		
No	Ref	
Yes	4.61 (0.69 - 30.61)	0.113
Gestational diabetes mellitus		
No	Ref	
Yes	0.17 (0.03 - 0.99)	0.049
Baby weight, kg	0.73 (0.36 - 1.48)	0.386

OR[a]: Odds ratio adjusted for those variables whose p-values were < 0.25 at univariate analysis, CI: Confidence interval, SVD: Spontaneous vaginal delivery, LSCS: Lower segment caesarean section.

Multivariate anaysis showed that newborns of vaccinated mothers had 3.6 times higher odds of having high antibody titers than those mothers who were unvaccinated, and mothers with secondary level of education had 2.8 times higher odds of having newborns with high antibody titers compared to those who had primary level of education (Table 4).

Discussion

In the current study, only 114 (61.3%) women had been vaccinated against COVID-19 infection. A study in the United Kingdom reported a rate of 40% for pregnant women in the third trimester.[14]

In the unvaccinated group, 52(72.2%) women in the current study had refused vaccine due to safety concerns for pregnancy. In a Turkish cohort of more than 300 pregnant women, 48(43%) among those who wanted to get vaccinated showed concerns about vaccine safety during pregnancy compared to 169 (90%) women who did not want to get vaccinated.[9] In another survey of 341 pregnant and lactating women, inhibition against getting vaccinated was seen in 25% respondents.[15] The other major factor for not getting vaccinated in the current study was peer or family pressure 19(26.4%) which reflected the social values in Pakistani society. Also, among the vaccintaed group, medical advice by doctors was the main reason cited by 104(91.2%) subjects. The influence of healthcare providers in getting vaccinated has been identified in other studies as well.[16] A study identified reasons for and against COVID-19 vaccination among healthcare workers, and found that 43(80%) women of reproductive age were hesitant towards vaccine due to various reasons.[17] It is important that healthcare workers themselves have satisfactory knowledge about vaccination, besides getting vaccinated, in order to give confidence to the women who come to seek their professional help and opinion. In the current study, 67(58.8%) vaccinated women had secondary level of education. A scoping review found three main determinants for vaccine hesitancy and uptake; demographic factors (gender, education), environmental (media and politics), and vaccine-specific factors (safety concerns).[18]

Transplacental transfer of maternal antibodies, particularly immunoglobulin G (IgG) is a recognised phenomena. It is around 10% of maternal circulation at 17-22 weeks of gestation, rises to 50% in the second trimester, and becomes 20-30% greater than the maternal concentration in the third trimester.[19] The antibodies levels have been found to be higher in women who got vaccinated in the third trimester.[20] Hence, it is recommended that one should get vaccinated later in the pregnancy as antibodies appear in newborn as early as within 15 days of maternal vaccination. The current study observed no significant difference in maternal outcomes of preterm birth, and pregnancy-induced hypertension (PIH) among vaccinated and nonvaccinated women. This may be attributed to the small sample size.

The study found antibody titers higher in newborns of vaccinated compared to nonvaccinated women. The

presence of low levels of antibodies in newborn of unvaccinated women may be due to herd immunity or unrecognised mild infection of mother in the past.

The current study has limitations. It did not include all women during the study period due to logistical reasons, and only a small group of newborns were evaluated for the presence of antibodies after maternal vaccination. Also, it did not quantify them into IgM or IgG, and, instead, used the presence of total antibodies in the newborn. Due to logistical constraints, the study also did not pair it with maternal antibody levels.

Conclusion

Majority of factors for vaccine hesitancy and uptake identified were similar to those identified globally. Healthcare workers should provide knowledge to hesitant mothers to increase vaccine uptake. Obstetrical complications were not affected by vaccination status, and a higher APGAR score at 1 minute was seen in vaccinated mothers.

Acknowledgement: We are grateful to Dr Ghulam Fatima, Chief Consultant Pathologist at the Central Labpratory of Dr Ruth Pfau Civil Hospital, Karachi.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Hessami K, Homayoon N, Hashemi A, Vafaei H, Kasraeian M, Asadi N. COVID-19 and maternal, fetal and neonatal mortality: a systematic review. J Matern Fetal Neonatal Med 2022; 35: 2936-41.
2. JCVI issues new advice on COVID-19 vaccination for pregnant women [press release]. UK: Public Health England Press, April 2021 2021.
3. Ministry of National Health Services Regulations & Coordination. Government of Pakistan. [Online] [Cited 2022 April 26]. Available from: URL: https://nhsrc.gov.pk.
4. Freeman D, Loe BS, Chadwick A, Vaccari C, Waite F, Rosebrock L, et al. COVID-19 vaccine hesitancy in the UK: the Oxford coronavirus explanations, attitudes, and narratives survey (Oceans) II. Psychol Med 2022: 52: 3127-41.
5. Goldshtein I, Nevo D, Steinberg DM, Rotem RS, Gorfine M, Chodick G, et al. Association Between BNT162b2 Vaccination and Incidence of SARS-CoV-2 Infection in Pregnant Women. JAMA 2021; 326: 728-35.
6. Gray KJ, Bordt EA, Atyeo C, Deriso E, Akinwunmi B, Young N, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. Am J Obstet Gynecol 2021; 225: 303 e1- e17.
7. Zauche LH, Wallace B, Smoots AN, Olson CK, Oduyebo T, Kim SY, et al. Receipt of mRNA COVID-19 vaccines preconception and during pregnancy and risk of self-reported spontaneous abortions, CDC v-safe COVID-19 Vaccine Pregnancy Registry 2020-21. Res Sq 2021; rs.3.rs-798175.
8. Deruelle P, Couffignal C, Sibiude J, Vivanti AJ, Anselem O, Luton D, et al. Prenatal care providers' perceptions of the SARS-Cov-2 vaccine for themselves and for pregnant women. PloS one 2021; 16: e0256080.
9. Goncu Ayhan S, Oluklu D, Atalay A, Menekse Beser D, Tanacan A, Moraloglu Tekin O, et al. COVID-19 vaccine acceptance in pregnant women. Int J Gynaecol Obstet 2021; 154: 291-6.
10. OpenEpi, Version 3, open source sample size calculator. [Online] [Cited 2021 October 15]. Available from: URL: https://www.openepi.com/SampleSize/SSPropor.htm.
11. Nir O, Schwartz A, Toussia-Cohen S, Leibovitch L, Strauss T, Asraf K, et al. Maternal-neonatal transfer of SARS-CoV-2 immunoglobulin G antibodies among parturient women treated with BNT162b2 messenger RNA vaccine during pregnancy. Am J Obstet Gynecol MFM 2022; 4: 100492.
12. National Immunization Management System. [Online] [Cited 2022 April 15]. Available from: URL: https://nims.nadra.gov.pk/nims/certificate.
13. AMERICAN ACADEMY OF PEDIATRICS COMMITTEE ON FETUS AND NEWBORN; AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS COMMITTEE ON OBSTETRIC PRACTICE. The Apgar Score. Pediatrics 2015; 136: 819-22.
14. Rottenstreich M, Sela HY, Rotem R, Kadish E, Wiener-Well Y, Grisaru-Granovsky S. Covid-19 vaccination during the third trimester of pregnancy: rate of vaccination and maternal and neonatal outcomes, a multicentre retrospective cohort study. BJOG 2022; 129: 248-55.
15. Mohan S, Reagu S, Lindow S, Alabdulla M. COVID-19 vaccine hesitancy in perinatal women: a cross sectional survey. J Perinat Med 2021; 49: 678-85.
16. Hammer CC, Cristea V, Dub T, Sivelä J. High but slightly declining COVID-19 vaccine acceptance and reasons for vaccine acceptance, Finland April to December 2020. Epidemiol Infect 2021; 149: e123.
17. Masood FB, Nasim A, Saleem S, Jafarey AM. Covid 19 vaccine hesitancy among health service providers: a single center experience from Karachi, Pakistan. J Pak Med Assoc. 2022; 72: 1142-7
18. Biswas MR, Alzubaidi MS, Shah U, Abd-Alrazaq AA, Shah Z. A Scoping Review to Find Out Worldwide COVID-19 Vaccine Hesitancy and Its Underlying Determinants. Vaccines (Basel) 2021; 9: 1243.
19. Wilcox CR, Holder B, Jones CE. Factors Affecting the FcRn-Mediated Transplacental Transfer of Antibodies and Implications for Vaccination in Pregnancy. Front Immunol 2017; 8: 1294.
20. Flannery DD, Gouma S, Dhudasia MB, Mukhopadhyay S, Pfeifer MR, Woodford EC, et al. Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios. JAMA Pediatr 2021; 175: 594-600.