ORIGINAL RESEARCH

Comparison of Immediate Adverse Effects of COVID-19 Vaccine (COVAXIN BBV152) in Pregnant vs Nonpregnant Women

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Abstract

Aims and objectives: The aim of this study was to compare the immediate adverse effects of the coronavirus disease 2019 (COVID-19) vaccine (COVAXIN) in a pregnant woman with that of a nonpregnant woman.

Materials and methods: It is a prospective observational study done at Vanivilas Hospital, Bangalore Medical College & Research Institute (BMCRI) for 2 months. The sample size was 100 pregnant and 100 nonpregnant women. Telephonically, patients were followed-up, and details of the side/adverse effects were collected in a proforma after 2 and 14 days. Data collected from both groups were analyzed using the Chi-square test or Fisher's exact test.

Results: The majority of women were in the age group of ≤25 years (64.0% and 36.0%, respectively) with a mean age of 25.01 ± 3.71 years among the pregnant and 28.52 ± 6.00 years among nonpregnant women. About 25.0% of pregnant women and 38.0% of nonpregnant women reported side effects. About 15.0% and 22.0% had taken treatment for side effects among pregnant women and nonpregnant women, respectively. Among the pregnant women, the common side effects reported were injection site pain (17) followed by fever (5), fatigue (4), and myalgia (03). Whereas among the nonpregnant women, the common side effects reported were injection site pain (28) followed by fever (6), myalgia (3), headache (2), and fatigue (1).

Conclusion: Side effects reported following the administration of Covaxin in pregnant and nonpregnant women are fever, fatigue, injection site pain, myalgia, and headache. The proportion of side effects was not significantly different in the pregnant and nonpregnant women following Covaxin administration.

Clinical significance: Covaxin is an inactivated killed vaccine against COVID-19 by Bharat Biotech. The vaccine has been recommended for pregnant women by the Government of India during corona pandemic. Studies are lacking regarding the difference in adverse events in pregnant versus nonpregnant women, after vaccine administration.

Keywords: Adverse events, SARS COV 2, Vaccination.

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Introduction

Pregnant women are prone for severe illness compared to nonpregnant because of COVID-19 infection. Severe illness includes need for hospitalization, requiring oxygen and ventilatory support, sometimes maternal death also. Pregnant women affected with COVID-19 are at risk of preterm delivery, leading to adverse perinatal outcome.[1] A study by Umashankar et al.[2] showed pregnant and postpartum women affected with COVID-19 are at risk of maternal death, when presented with symptoms of severe acute respiratory illness. The study by Kapadia et al.[3] showed that majority of the cases of pregnancy with COVID-19 had mild disease without acute respiratory distress syndrome (ARDS), which responded to supportive treatment. Preventive measures for COVID-19 infection are COVID appropriate behavior and vaccine.

Covaxin, vaccine against COVID-19, was developed by Bharat Biotech, along with collaboration with the Indian Council of Medical Research (ICMR)—National Institute of Virology (NIV). Vaccine developed from inactivated killed virus. Recommended doses are two doses in 4 weeks gap. The administration of vaccine is through intramuscular route. As per the manufacturer's manual expected side effects are injection site pain/swelling/redness/itching, headache, fever, malaise/body ache, nausea, vomiting, and rashes. The Ministry of Health also mentions about the similar mild side effects following COVID-19 vaccination.

Getting a COVID-19 vaccine during pregnancy can protect pregnant women from severe illness following COVID-19 infection. Side effects can occur after receiving any of the available

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COVID-19 vaccines. Solicited local and systemic reactions that were reported were similar among persons who were pregnant and nonpregnant women according to U.S. surveillance review of the safety of mRNA COVID-19 vaccines during pregnancy.[4] In India, now the Government of India has approved the use of vaccines during pregnancy.[5] There is a limited experience with the use of the vaccine in pregnant women. The Royal College of Obstetricians and Gynecologists (RCOG) states that pregnant women should be offered the vaccine as the general population.[6]

Most of the side effects with COVAXIN (BBV152) occur on the day of vaccination (6–8 hours later) and resolve within 2–3 days. These are uncommon on day 5–7 after vaccination, indicating that these effects are self-limiting and of short duration. Adverse reactions are relatively less after the second dose as compared to the first dose. In our study, we wanted to know if pregnant women behave differently to COVID vaccine compared to nonpregnant women.

Aims and Objectives

The aim of this study is to compare the immediate adverse effects of COVID-19 vaccine (COVAXIN) in pregnant woman with that of nonpregnant women.

Materials and Methods

It is a prospective observational study done for a period of 2 months, from August 1, 2021 to September 30, 2021. The study was conducted at Vanivilas Hospital, BMCRI. The sample size was 100 pregnant and 100 nonpregnant women.

Inclusion Criteria

The inclusion criteria were:

- Low-risk pregnant women who are willing to take Covaxin at Vanivilas Hospital in the age group of 18–45 years.
- Nonpregnant women in the age group of 18–45 who are coming for COVID-19 vaccination (Covaxin) at Vanivilas Hospital without any medical risk factors (like diabetes, hypertension, cardio vascular disease, neuromuscular disease, epilepsy, etc.).

Exclusion Criteria

The inclusion criteria were:

- Pregnant and nonpregnant women not willing to get vaccinated/participate in the study.
- High-risk pregnant women (current pregnancy with medical risk factors like diabetes or hypertension, cardiovascular disease, and renal disease).
- Nonpregnant women with comorbidity or medical risk factors (as mentioned in the inclusion criteria).

After obtaining approval and clearance from the institutional ethics committee (Letter number: BMCRI/PS/147/2021-22), the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent. Pregnant women who were vaccinated at Vanivilas Hospital, BMCRI were recruited for the study. Participants were counseled about benefits and risks associated with the vaccine. Vaccine chosen was voluntary by the women. Vaccine vials are not matched. Demographic and obstetric details were collected in the proforma. Telephonically, patients were followed-up, and details of the side/adverse effects were collected in a proforma after 2 and 14 days.

Similar group of patients who were nonpregnant were also followed-up in a similar way, and incidence of adverse effects was compared. Variables that were matched in pregnant and nonpregnant group are age, sex, and no known co-morbidities in both groups. Side effects known like injection site pain, headache, fatigue, fever, body ache, abdominal pain, nausea and vomiting, dizziness-giddiness, tremor, sweating, and injection site swelling, or if any, were noted down. Side effects were treated symptomatically. The Covaxin vaccine (BBV152) is an inactivated vaccine. The manufacturer/developer is Bharat Biotech, India. The route of administration was intramuscular injection.

Statistical Analysis

The data were entered into Microsoft Excel and were analyzed using SPSS (version 20.0 for Windows; SPSS Inc., Armonk, NY: IBM Corp). The continuous data were expressed in mean and standard deviation, and the categorical data were expressed in proportions. The association between the reported side effects and pregnancy status was assessed using the Chi-square test or Fisher's exact test. The difference in proportions of overall side effects among pregnant and nonpregnant women was compared using *Z*-test for difference in proportions. A *p*-value of <0.05 was considered statistically significant.

Results

Among the pregnant and nonpregnant women, the majority of them were in the age group of ≤25 years (64.0% and 36.0%, respectively) with the mean age of 25.01 ± 3.71 years among the pregnant women and 28.52 ± 6.00 years among nonpregnant women. About 59.0% and 64.0%, respectively, had a gap of ≤6 weeks between the two doses of COVID-19 vaccine.

Among the study subjects, 25.0% of the pregnant women had side effects, whereas 38.0% of nonpregnant women had side effects. About 15.0% and 22.0% had taken treatment for side effects among pregnant women and nonpregnant women, respectively. None of the study subjects had previous history of allergy (Table 1).

Among pregnant women, 19.0% were in the first trimester, 35.0% in the second trimester, and 46.0% in the third trimester.

Table 1: Socio-demographic and clinical details of the patients

Variables	*Pregnant n = 100 (%)*	*Nonpregnant n = 100 (%)*
Age group in years		
≤25	64 (64.0)	36 (36.0)
26–30	28 (28.0)	31 (31.0)
>30	08 (08.0)	33 (33.0)
Gap between the two doses		
≤6 weeks	59 (59.0)	64 (64.0)
>6 weeks	41 (41.0)	36 (36.0)
Side effects		
Yes	25 (25.0)	38 (38.0)
No	75 (75.0)	62 (62.0)
Treatment given		
Yes	15 (15.0)	22 (22.0)
No	85 (85.0)	78 (78.0)

According to gravida status, 50.0% were primigravida, 33.0% were gravida 2, 16.0% were gravida 3, and 1.0% were gravida 4, depicted in Figure 1. Previous history of abortion and neonatal death were reported among 9.0% and 1.0% of pregnant women, respectively, illustrated in Figure 2.

Among the pregnant women, the common side effects reported were injection site pain (17) followed by fever (5), fatigue (4), and myalgia (3). Whereas among the nonpregnant women, the common side effects reported were injection site pain (28) followed by fever (6), myalgia (3), headache (2), and fatigue (1). The side effects are tabulated in Table 2.

The association of the presence of side effects according to the day of vaccination was studied. Among pregnant and nonpregnant women, the proportion of side effects for the first dose on day 2 was 35.9% and 64.1%, and on day 14, it was 100.0% and 0.0%, respectively. After the second dose, on day 2, 43.5% (pregnant) and 56.5% (nonpregnant) had reported side effect but on day 14, none of them reported side effects. However, there was no statistical association between reported side effects and pregnancy status ($p > 0.05$), as depicted in Table 3.

The total number side effects was calculated among both groups. A total of 200 doses of COVID-19 vaccine were administered considering two doses per study subjects per group ($n = 100$). The total number of reported side effects was more in the nonpregnant women group when compared to the pregnant women group, but the difference in the reported side effects was not statistically significant ($Z = -1.78$, $p = 0.08$). The comparison of side effects and significance is shown in Table 4.

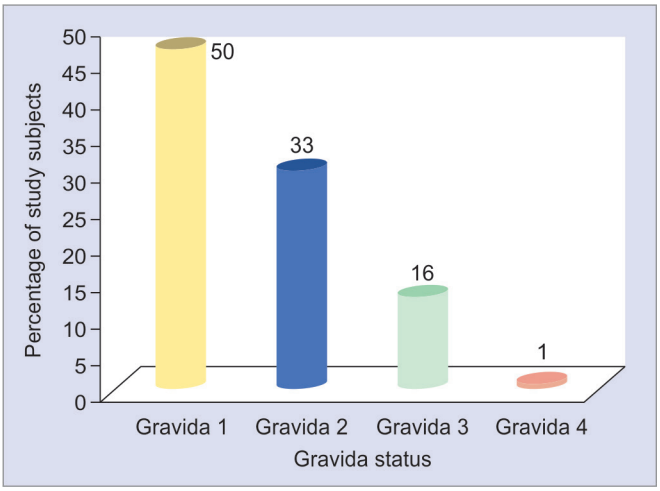

Fig. 1: Distribution of study subjects based on obstetric history ($n = 100$) and gravida status

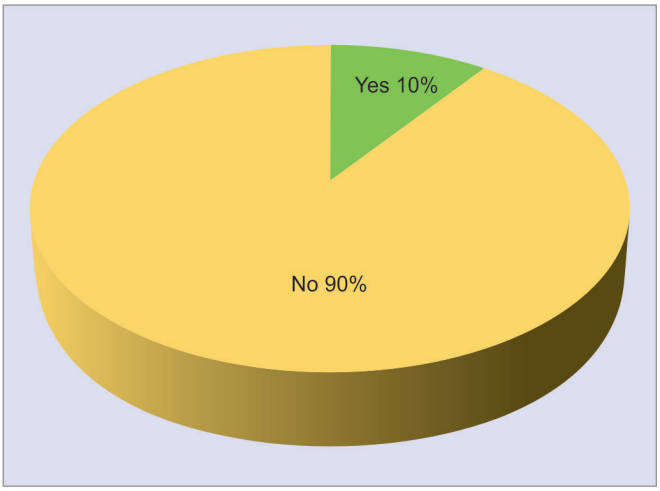

Fig. 2: Reported history of previous abortions or neonatal death

Discussion

In this study, we have evaluated the immediate side effects among 100 pregnant and 100 nonpregnant women following Covaxin. The majority of the women were in the age group of less than 25 years.

Table 3: Association of reported side effects according to the day of vaccination among the study subjects

Variables	*Pregnant n =100 (%)*	*Nonpregnant n = 100 (%)*	
Side effects on the first dose, day 2			
Yes	14 (35.9)	25 (64.1)	3.85 (0.05)
No	86 (53.4)	75 (46.6)	
Side effects on the first dose, day 14			
Yes	01 (100.0)	00 (00.0)	(1.00)*
No	99 (49.7)	100 (50.3)	
Side effects on the second dose, day 2			
Yes	10 (43.5)	13 (56.5)	0.44 (0.51)
No	90 (50.8)	87 (49.2)	

*Fisher's exact test

Table 2: Frequency of reported side effects according to the day of vaccination among the study subjects

	Pregnant women (n = 100)					*Nonpregnant women (n = 100)*				
	First dose		*Second dose*			*First dose*		*Second dose*		
Side effect	*D2*	*D14*	*D2*	*D14*	*Total*	*D2*	*D14*	*D2*	*D14*	*Total*
Fatigue	01	00	03	00	04	01	00	00	00	01
Fever	04	00	01	00	05	03	00	03	00	06
Injection site pain	09	01	07	00	17	18	00	10	00	28
Myalgia	02	00	01	00	03	03	00	00	00	03
Headache	00	00	00	00	00	01	00	01	00	02

Few patients reported multiple side effects

Table 4: Comparison of total side effects of the COVID-19 vaccines among pregnant and nonpregnant women

Groups	*No. of doses*	*No. of side effects (%)*	*Z-value*	*p-value*
Pregnant women (*n* = 100)	200	25/200 (12.5)	−1.78	0.08
Nonpregnant women (*n* = 100)	200	38/200 (19.0)		

The gap between two doses was less than 6 weeks in the majority of women. In the present study subjects, 25.0% of the pregnant women had side effects whereas 38.0% of nonpregnant women had side effects.

Among pregnant women, 19.0% were in the first trimester, 35.0% in the second trimester, and 46.0% in the third trimester. According to gravida status, 50.0% were primigravida, 33.0% were gravida 2, 16.0% were gravida 3, and 1.0% were gravida 4.

Most common side effects in both groups were injection site pain. Other side effects were fever, myalgia, fatigue, and headache. Side effects were more in nonpregnant women compared to a study by Parida et al.[7] In all studies, the majority of the side effects were mild. Women with side effects received paracetamol tablet.

The results are applicable to the study done in our center. These results cannot be generalized, and the study needs to be conducted in a larger population.

Conclusion

The side effects reported following the administration of Covaxin in pregnant and nonpregnant women are fever, fatigue, injection site pain, myalgia, and headache. The proportion of side effects were not significantly different in the pregnant and nonpregnant women following Covaxin administration.

Acknowledgments

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