Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Adverse effects of COVID-19 messenger RNA vaccines among pregnant women: a cross-sectional study on healthcare workers with detailed self-reported symptoms

OBJECTIVE: Pregnant patients with COVID-19 are at an increased risk for severe illness when compared with nonpregnant patients.[1] None of the COVID-19 messenger RNA (mRNA) vaccines that were approved under the emergency use authorization have been tested in pregnant individuals during the initial vaccine trials despite the support offered by several agencies.[2] Although recent studies revealed more detailed side effects for both mRNA vaccines, there are limited data and literature that specifically focus on pregnant women.[3,4]

The objective of this study was to analyze and compare the detailed side-effect profile of the mRNA vaccines among pregnant healthcare workers (HCWs) with that of nonpregnant HCWs using a self-reported online survey questionnaire consisting of a systematic review of organ systems independent of information collected through the Vaccine Adverse Event Reporting System (VAERS).[5]

STUDY DESIGN: A cross-sectional study was conducted after obtaining institutional review board approval using an independent online survey questionnaire (Survey Monkey, San Mateo, CA). Anonymous responses about the side effects were collected from HCWs representing various parts of the country during the early phase of COVID-19 vaccination. Informed consent was obtained from the study participants. The responses were received from 1452 HCWs

TABLE
Comparison of the side-effect profile among pregnant and nonpregnant women

	Group that received the mRNA vaccine		
Adverse event or side effect	**Pregnant ($n_1 = 38$)**	**Nonpregnant ($n_2 = 991$)**	***P* value (Fisher exact test)**
Sore arm or pain	37/38	894/991	.2517
Fatigue	22/38	643/991	.3905
Headache	19/38	519/991	.8689
Chills	18/38	424/991	.6183
Myalgia	13/38	488/991	.0714
Nausea	11/38	211/991	.313
Fever	6/38	279/991	.0999
Sweating	6/38	135/991	.6342
Feelings of joy, relief, or gratitude	4/38	67/991	.3265
Rash	4/38	67/991	.3265
Joint pains	3/38	206/991	.0625
Swelling	3/38	94/991	1
Flushing	3/38	84/991	1
Brain fogging or reduced mental clarity	3/38	76/991	1
Itching	2/38	94/991	1
Decreased appetite	2/38	88/991	.7669
Decreased sleep quality	2/38	74/991	1
Palpitations or increased heart rate	2/38	64/991	1
Heat or cold intolerance	2/38	53/991	1

Kadali. Adverse effects of COVID-19 messenger RNA vaccines among pregnant women. Am J Obstet Gynecol 2021. *(continued)*

TABLE
Comparison of the side-effect profile among pregnant and nonpregnant women *(continued)*

Adverse event or side effect	Group that received the mRNA vaccine		*P* value (Fisher exact test)
	Pregnant ($n_1 = 38$)	Nonpregnant ($n_2 = 991$)	
Anxiety	2/38	34/991	.3876
Heartburn	2/38	19/991	.1799
Muscle spasm	1/38	103/991	.1676
Nasal congestion	1/38	64/991	.5073
Increase in sleep	1/38	39/991	1
Vomiting	1/38	22/991	1
Seizures[a]	1/38	0/991	.0369
Diarrhea	0/38	61/991	.1624
Shortness of breath	0/38	23/991	1
Cough	0/38	20/991	1
Decrease in memory	0/38	14/991	1
Hives	0/38	11/991	1
Depression	0/38	8/991	1
Psychological stress	0/38	7/991	1
Swelling of lips or oral cavity	0/38	5/991	1
Atopic eczema	0/38	5/991	1
Hay fever	0/38	3/991	1
Asthma exacerbation	0/38	3/991	1
Behavioral changes	0/38	1/991	1

mRNA, messenger RNA.

[a] The participant with a report of seizure has a known history of seizure disorder and her anticonvulsant blood level was reported as borderline low; [b] The pregnancy-related adverse events were very rarely reported (gestational hypertension [1 in 38], threatened labor [1 in 38], miscarriage [1 in 38], and premature delivery [1 in 38]) from the Pfizer-BioNTech vaccine group and none were reported from the Moderna group.

Kadali. Adverse effects of COVID-19 messenger RNA vaccines among pregnant women. Am J Obstet Gynecol 2021.

(who received 1 of the 2 mRNA-based COVID-19 vaccines) during the postvaccination period. Out of 1452 HCWs, 1029 were women and 38 were pregnant. Only the complete responses were included in the final analysis of this study. A statistical analysis was performed using Fisher exact tests to compare the side-effect profile between pregnant and nonpregnant groups.

RESULTS: Among the 1029 HCW women, 38 were pregnant, 20 of whom received the Pfizer-BioNTech vaccine and the remaining 18 received the Moderna vaccine. About 81.58% (31 of 38) of the pregnant HCWs received both doses of the mRNA vaccine. The Table shows the detailed adverse events report among pregnant and nonpregnant women. No significant statistical differences were found between the groups for all of the symptoms reported for both groups (however, the participant with a report of seizure has a known history of seizure disorder and borderline low anticonvulsant blood levels). Most of the symptoms reported were within the early postvaccination phase of the vaccine and, consequently, the latent effects of these vaccines were not studied. No specific data about the initial timing of onset and duration of symptoms after vaccine administration were obtained during this study.

CONCLUSION: The side-effect profile obtained from a detailed systematic review of organ systems among pregnant women who received either of the mRNA vaccines in the immediate or early postvaccination period were nonlife threatening and they appeared to be similar (with no significant statistical difference) when compared with nonpregnant women. The pregnancy-related adverse events were very rarely reported (see "b" below the Table). There is high acceptance of the second vaccine dose, which is an encouraging aspect for future pregnant vaccine recipients. Pregnant individuals should be educated to participate and be encouraged to be compliant with their report to VAERS after COVID-19 vaccination to a have more longitudinal follow-up for the evaluation of latent effects. As the vaccination continues among pregnant women, we

recommend monitoring further reports from the Centers for Disease Control and Prevention. ■

Renuka Ananth Kalyan Kadali, MD, MS
Department of Internal Medicine
Central Harnett Hospital, Cape Fear Valley Health System
Campbell University Jerry M. Wallace School of Osteopathic Medicine
215 Brightwater Dr
Lillington, NC 27546
Renuka.Kadali@harnetthealth.org
dr.kadali1982@gmail.com

Ravali Janagama, MD, MS
Department of Pediatrics
Kidzcare Pediatrics
Sanford, NC

Sharanya R. Peruru, MS
Department of Statistics
North Carolina State University
Raleigh, NC

Shailaja Racherla, MBBS
Department of Pathology and Laboratory Medicine
University of California Davis School of Medicine
Sacramento, CA

Radhika Tirumala, MD
Department of Obstetrics and Gynecology
Atrium Health
Charlotte, NC

Rajasekhar R. Madathala, MD
Department of Internal Medicine
Mayo Clinic
Rochester, MN

Viswanath Gajula, MD
Division of Pediatric Critical Care Medicine
Department of Pediatrics
The University of Mississippi Medical Center
Jackson, MS

R.A.K.K. and R.J. contributed equally.

The authors report no conflict of interest.

This study received no funding.

The opinions expressed in this article are those of the authors and do not necessarily reflect the views of their institutions, pharmaceutical companies, vaccine manufacturing companies, or the Centers for Disease Control and Prevention, National Institute of Allergy and Infectious Diseases, National Institute of Health, and Department of Health and Human Services.

The approval for the parent study was obtained from the institutional review board at Cape Fear Valley Health System, Fayetteville, North Carolina.

REFERENCES

1. Ellington S, Strid P, 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, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769–75.
2. Stafford IA, Parchem JG, Sibai BM. The coronavirus disease 2019 vaccine in pregnancy: risks, benefits, and recommendations. Am J Obstet Gynecol 2021;224:484–95.
3. Kadali RAK, Janagama R, Peruru S, Malayala SV. Side effects of BNT162b2 mRNA COVID-19 vaccine: a randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers. Int J Infect Dis 2021;106:376–81.
4. Kadali RAK, Janagama R, Peruru S, et al. Non-life-threatening adverse effects with COVID-19 mRNA-1273 vaccine: a randomized, cross-sectional study on healthcare workers with detailed self-reported symptoms. J Med Virol 2021;93:4420–9.
5. Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. N Engl J Med 2021. [Epub ahead of print].

 https://doi.org/10.1016/j.ajog.2021.06.007