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

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1 **Adverse effects of COVID-19 mRNA vaccines among pregnant women: A cross-sectional**
2 **study on healthcare workers with detailed self-reported symptoms**

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61 BACKGROUND:

62 Corona virus disease (COVID-19) patients with pregnancy are at increased risk of severe illness
63 when compared to non-pregnant patients.¹ None of the COVID-19 mRNA vaccines that were
64 approved under emergency use authorization (EUA) have been tested in pregnant individuals
65 during initial vaccine trials despite the support offered by several agencies.² Although recent
66 studies revealed more detailed side effects with both mRNA vaccines, there are limited data and
67 literature that specifically focus on pregnant women.^{3,4}

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70 OBJECTIVE:

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

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78 METHODS

79 A cross-sectional study was conducted after obtaining institutional review board approval using
80 an independent online survey questionnaire (Survey Monkey). Anonymous responses about side
81 effects were collected from HCWs representing various parts of the country during the early
82 phase of COVID-19 vaccination. Informed consent was obtained from the study participants.
83 The responses were obtained from 1452 HCWs (who received one of the two mRNA-based

84 COVID-19 vaccines) during the post-vaccination period. Out of 1452, 1029 were female HCWs,
85 of which 38 were pregnant. Only the complete responses were included in the final analysis of
86 this study. A statistical analysis was performed using Fisher exact tests to compare the side effect
87 profile between pregnant and non-pregnant groups.

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90 **RESULTS**

91 Among 1029 women, 38 were pregnant, 20 of which received Pfizer-BioNTech vaccine and
92 remaining 18 received Moderna vaccine. About 81.58% (31/38) of the pregnant HCWs received
93 both doses of mRNA vaccine. **Table 1** shows the detailed adverse event report among pregnant
94 and non-pregnant women. No significant statistical differences were found with almost all of the
95 symptoms reported between two groups (although for a participant with report of seizure has
96 known history of seizure disorder and borderline low anticonvulsant blood level). Most of the
97 symptoms reported were within the early post-vaccination phase of the vaccine, therefore the
98 latent effects of these vaccines were not studied. No specific data about the initial timing of onset
99 and duration of symptoms after vaccine administration were obtained during this study.

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102 **CONCLUSIONS**

103 The side effect profile obtained from detailed systematic review of organ systems among
104 pregnant women who received either of the mRNA vaccines in immediate or early post
105 vaccination were non-life threatening and they appear to be similar (with no significant statistical
106 difference) when compared with non-pregnant women. The pregnancy related adverse events

107 were very rarely reported [†]. There is high acceptance for the second dose of vaccine, which is an
108 encouraging aspect for future pregnant vaccine recipients. Pregnant individuals should be
109 educated to participate and be encouraged to be compliant with their report to VAERS after
110 COVID-19 vaccination to have more longitudinal follow-up for evaluation of latent effects. As
111 the vaccination continues among pregnant women, we recommend monitoring further reports
112 from Centers for Disease Control and Prevention.

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116 pharmaceutical companies, vaccine manufacturing companies, or the CDC, NIAID, NIH, and
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119 **Institutional Review Board (IRB) approval:** The approval for the parent study was obtained
120 from the Institutional Review Board at Cape Fear Valley Health System, 1638 Owen Drive,
121 Fayetteville, NC 28304.

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123 **Authors' Contributions:** All authors contributed significantly to this work. Conceptualization
124 and proposal writing was done by RAKK and RJ. RJ, VG and RAKK supervised data collection.
125 RAKK, SRP and SR performed statistical analysis. RAKK, RJ managed the data and wrote the
126 manuscript. RT, VG, RRM and SR performed critical review of the manuscript. All authors have
127 read and approved the manuscript.

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130 **REFERENCES:**

131

132 1. Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with
133 Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States,
134 January 22-June 7, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(25):769-775.

135 Published 2020 Jun 26. doi:10.15585/mmwr.mm6925a1

136 2. Stafford IA, Parchem JG, Sibai BM. The coronavirus disease 2019 vaccine in pregnancy: risks,
137 benefits, and recommendations. *Am J Obstet Gynecol.* 2021;224(5):484-495.

138 doi:10.1016/j.ajog.2021.01.022

139 3. Kadali RAK, Janagama R, Peruru S, Malayala SV. Side effects of BNT162b2 mRNA COVID-19
140 vaccine: A randomized, cross-sectional study with detailed self-reported symptoms from
141 healthcare workers. *Int J Infect Dis.* 2021;106:376-381. doi:10.1016/j.ijid.2021.04.047

142 4. Kadali RAK, Janagama R, Peruru S, et al. Non-life-threatening adverse effects with COVID-19
143 mRNA-1273 vaccine: A randomized, cross-sectional study on healthcare workers with detailed
144 self-reported symptoms. *J Med Virol.* 2021;93(7):4420-4429. doi:10.1002/jmv.26996

145 5. Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary Findings of mRNA Covid-19 Vaccine
146 Safety in Pregnant Persons [published online ahead of print, 2021 Apr 21]. *N Engl J Med.*

147 2021;NEJMoa2104983. doi:10.1056/NEJMoa2104983

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155 **TABLE 1: Comparison of side effect profile among pregnant and non-pregnant women**

| Adverse event/side effect | Group that received the mRNA vaccine | | p-value (Fisher's exact test) |
|--------------------------------------|--------------------------------------|------------------------------------|----------------------------------|
| | Pregnant (n ₁ =38) | Non pregnant (n ₂ =991) | |
| Sore arm/pain | 37/38 | 894/991 | 0.2517 |
| Fatigue | 22/38 | 643/991 | 0.3905 |
| Headache | 19/38 | 519/991 | 0.8689 |
| Chills | 18/38 | 424/991 | 0.6183 |
| Myalgia | 13/38 | 488/991 | 0.0714 |
| Nausea | 11/38 | 211/991 | 0.313 |
| Fever | 6/38 | 279/991 | 0.0999 |
| Sweating | 6/38 | 135/991 | 0.6342 |
| Feelings of joy/relief/gratitude | 4/38 | 67/991 | 0.3265 |
| Rash | 4/38 | 67/991 | 0.3265 |
| Joint pains | 3/38 | 206/991 | 0.0625 |
| Swelling | 3/38 | 94/991 | 1 |
| Flushing | 3/38 | 84/991 | 1 |
| Brain fogging/reduced mental clarity | 3/38 | 76/991 | 1 |
| Itching | 2/38 | 94/991 | 1 |
| Decreased appetite | 2/38 | 88/991 | 0.7669 |
| Decreased sleep quality | 2/38 | 74/991 | 1 |
| Palpitations/increased heart rate | 2/38 | 64/991 | 1 |
| Heat or cold intolerance | 2/38 | 53/991 | 1 |
| Anxiety | 2/38 | 34/991 | 0.3876 |
| Heartburn | 2/38 | 19/991 | 0.1799 |
| Muscle Spasm | 1/38 | 103/991 | 0.1676 |
| Nasal congestion | 1/38 | 64/991 | 0.5073 |
| Increase in sleep | 1/38 | 39/991 | 1 |
| Vomiting | 1/38 | 22/991 | 1 |
| *Seizures | 1/38 | 0/991 | 0.0369 |
| Diarrhea | 0/38 | 61/991 | 0.1624 |
| 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/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 |

156 *The participant with report of seizure has known history of seizure disorder and her anticonvulsant blood level was
157 reported as borderline low

158 †The pregnancy related adverse events were very rarely reported [(gestational hypertension (1/38), threatened labor
159 (1/38), miscarriage (1/38), premature delivery (1/38)] from the Pfizer-BioNTech vaccine group and none were
160 reported from the Moderna group

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