

**REVIEW ARTICLE**

# Prioritizing pregnant women for COVID-19 vaccination

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**Abstract**

Despite emerging evidence on safety and efficacy, most countries do not offer COVID-19 vaccines to pregnant women even though they are at higher risk of complications from COVID-19. We performed a web search of COVID-19 vaccination policies for pregnant women under two categories: countries bearing a high burden of COVID-19 cases and countries with a high burden of maternal and under-five mortality. Of the top 20 countries affected by COVID-19, 11 allow vaccination of pregnant women, of which two have deemed it safe to vaccinate pregnant women as a high-risk group. In contrast, only five of the 20 countries with high under-five mortality and maternal mortality allow vaccination of pregnant women and none of these countries has included them as part of a high-risk group that should be vaccinated. India and Indonesia, with one-fifth of the world's population, fall under both categories but do not include pregnant women as a priority group for COVID-19 vaccination. To prevent COVID-19 from further aggravating the already heavy burden of maternal and under-five mortality, there is a strong case for including pregnant women as a high-priority group for COVID-19 vaccination. We recommend including COVID-19 vaccination in routine antenatal care in all countries, particularly India and Indonesia in view of their high dual burden.

**KEYWORDS**

COVID-19, dual burden of disease, maternal mortality, pregnancy, under-five mortality, vaccination

## 1 | INTRODUCTION

The coronavirus disease (COVID-19) pandemic has accentuated problems in countries that face an already high burden of under-five mortality, with 5.2 million under-fives dying before their fifth birthday, and half of these deaths occurring within the first 28 days of life.<sup>1</sup> This comes as a push-back to Sustainable Development Goal 3.2 which aims to achieve by 2030 an end to preventable deaths of newborns and children under-five. Worryingly, this appeared unreachable even before the pandemic. Similarly, more than 300 000 women died from pregnancy-related causes in 2015<sup>2</sup> and achievement of Sustainable Development Goal 3.1—to reduce the global maternal mortality ratio to less than 70 maternal deaths per

100 000 live births by 2030—was appearing unlikely at the start of pandemic.

Pregnancy is a time of increased demands on the body and lowered immune response which increases the risk of complications from infections. Pregnant women are known to be at significantly higher risk of severe COVID-19 related complications compared with non-pregnant women.<sup>3,4</sup> Hence, protecting pregnant women against COVID-19 is critical. Vaccination has emerged as a reliable protective measure against severe COVID-19 infection.<sup>5,6</sup> At present, pregnant women are either not included for COVID-19 vaccination or the policies are ambiguous with the decision often left to the woman.<sup>7</sup> Evidence is emerging of the safety and efficacy of COVID-19 vaccines including the benefits of protection passed to

the newborn<sup>8</sup> which supports including pregnant women in the high-priority group for COVID-19 vaccination. However, it is not known if there is overlap between countries facing a high burden of COVID-19 cases and those with a high burden of maternal and under-five child mortality. Moreover, policies on administration of COVID-19 vaccines for pregnant women across countries globally have not been documented.

The aim of the present article was to identify the countries bearing a high burden of COVID-19 cases and search their policies on vaccination during pregnancy. A similar exercise was performed for countries with a high burden of maternal and under-five mortality. Countries appearing on both lists were identified. Our findings are presented along with an argument for priority vaccination of pregnant women.

## 2 | MATERIALS AND METHODS

We accessed publicly available data on total COVID-19 cases, total COVID-19 deaths, vaccination rates, burden of maternal and under-five mortality from "Our World in Data" (<https://ourworldindata.org/>). We sorted countries by burden of COVID-19 cases, and under-five deaths. We also searched the web for policies on vaccination during pregnancy in high burden countries. The results are presented

in two tables listing total COVID-19 cases and maternal and under-five deaths, including level of vaccination and policy environment.

## 3 | RESULTS

The top 20 countries by total COVID-19 cases carry a disproportionately large burden of cases (79%) and COVID-19 deaths (81%) globally (Table 1). These countries also harbor 19% of all maternal deaths and 24% of under-five deaths. Most of these countries have achieved a reasonable level of vaccination against COVID-19 with an average of 13%, with USA topping the list with 40%. Of the top 20 countries affected by COVID-19, two (USA and UK) have guidelines in place that recommend vaccination of pregnant as a high-risk group,<sup>9</sup> and nine others (Brazil, France, Italy, Argentina, Spain, Mexico, Turkey, Netherlands and recently India) allow COVID-19 vaccination for pregnant women.

The top 20 countries with the highest burden of under-five mortality (Table 2) account for 74% of all under-five deaths and also a similar proportion of global maternal deaths. These countries had 19% of all COVID-19 cases, and 12% of COVID-19 deaths globally. Most of these countries have very low levels of vaccination against COVID-19 (average: 0.88%), with a maximum of 3.7% in Indonesia and 3% in India. None of the high maternal and under-five mortality

**TABLE 1** Top 20 countries with a high burden COVID-19 cases and their policies on COVID-19 vaccination in pregnant women (as of May 29, 2021)

Country	COVID-19 cases	COVID-19 deaths	Persons fully vaccinated per 100 population	Maternal deaths per year	Under-five child deaths per year	Pregnant women included for COVID-19 vaccination
USA	33 217 995	593 288	39.7	550	26 867	Yes, on priority
India <sup>a</sup>	27 555 457	318 895	3.07	45 000	989 167	Yes
Brazil	16 342 162	456 674	10.13	1300	43 278	Yes
France	5 697 076	109 327	15.3	66	3235	Yes
Turkey	5 220 549	46 970	14.5	210	14 979	Yes
Russia	4 977 332	117 990	7.89	450	13 777	No
UK	4 489 552	128 020	35.42	74	3487	Yes, on priority
Italy	4 205 970	125 793	18.53	18	1646	Yes
Germany	3 673 990	88 192	16.32	42	2687	No
Argentina	3 663 215	76 135	5.57	390	7793	Yes
Spain	3 663 176	79 888	18.43	21	1239	Yes
Colombia	3 319 193	86 693	6.28	480	10 841	No
Iran	2 875 858	79 384	0.48	340	19 562	No
Poland	2 869 652	73 440	16.67	12	1679	No
Mexico	2 405 772	222 661	9.24	890	30 973	Yes
Ukraine	2 251 242	52 088	0.27	120	4130	No
Peru	1 942 054	68 816	3.18	420	9133	No
Indonesia	1 797 499	49 907	3.74	6400	125 213	No
Netherlands	1 664 708	17 866	15.56	12	706	Yes
Czechia	1 659 980	30 059	12.75	5	358	No

<sup>a</sup>Decision to allow vaccination of pregnant women in India was taken on June, 25, 2021.

TABLE 2 Top 20 countries with high maternal and under-five mortality and their policies on COVID-19 vaccination in pregnancy (as of May 29, 2021)

Country	COVID-19 cases	COVID-19 deaths	Persons fully vaccinated per 100 population	Maternal deaths per year	Under-five child deaths per year	Pregnant women included for COVID-19 vaccination
India <sup>a</sup>	27 555 457	318 895	3.07	45 000	989 167	Yes
Nigeria	166 191	2071	0	58 000	714 188	Yes
Pakistan	913 784	20 607	0.69	9700	403 638	No
Democratic Republic of Congo	31 279	781	NA	22 000	299 985	No
Ethiopia	270 527	4127	NA	11 000	188 690	No
China	91 096	4636	NA	4400	155 576	Yes
Indonesia	1 797 499	49 907	3.74	6400	125 213	No
Tanzania	509	21	NA	8200	113 824	No
Bangladesh	794 985	12 480	2.48	5500	99 608	No
Angola	33 607	745	0.6	5400	96 345	NA
Uganda	44 594	361	0.01	5700	84 968	Yes
Niger	5406	192	0.03	5400	82 322	No
Sudan	34 889	2600	0.2	4100	81 825	No
Mozambique	70 673	834	0.24	5300	80 562	No
Mali	14 259	514	0.07	4400	80 332	No
Somalia	14 647	768	NA	3400	77 644	Yes
Afghanistan	68 366	2869	0.29	4300	77 300	No
Cote d'Ivoire	47 146	301	NA	5400	76 571	No
Chad	4926	173	NA	5400	75 761	No
Cameroon	77 982	1270	0.03	5100	70 649	No

<sup>a</sup>Decision to allow vaccination of pregnant women in India was taken on June, 25, 2021.

burden countries have guidelines for preferential vaccination of pregnant women as a high-risk group, while only five (Nigeria, China, Uganda, Somalia and recently India) allow vaccination of pregnant women.

Two countries, India and Indonesia—with one-fifth of the world's population—fall into both groups, contributing 17% of COVID-19 cases, 11% of COVID-19 deaths, 17% of maternal mortality, and 21% of under-five deaths globally. To date, neither country has allowed priority COVID-19 vaccination of pregnant women, thereby accentuating the already high risk to survival of mothers and children aged under five years. Anecdotal reports suggest that more pregnant women are dying from COVID-19 during the present wave of the pandemic in India than the earlier wave.<sup>10</sup>

#### 4 | WHY PRIORITIZE PREGNANT WOMEN FOR COVID-19 VACCINATION?

The arguments for vaccination of pregnant women against COVID-19 are as follows:

1. Pregnant women experience more severe COVID-19 disease than non-pregnant women.<sup>11</sup> They are more likely to require hospitalization, admission to the intensive care unit (ICU), and receive invasive ventilation and extra-corporeal membrane oxygenation compared with non-pregnant symptomatic women.<sup>11</sup> There is a 70% increased risk of death among symptomatic pregnant women compared with non-pregnant symptomatic women.<sup>12</sup> Physiological changes of pregnancy which include increased heart rate and oxygen consumption, edema of the respiratory tract, decreased lung capacity, increased chances of thromboembolic disease and altered immune functions place pregnant women at a higher risk of all viral infections, including COVID-19.<sup>13</sup> Women who become infected with COVID-19 while pregnant experience higher maternal and neonatal morbidity and mortality compared with pregnant women without COVID-19 infection.<sup>14</sup> These include higher incidence of pregnancy induced hypertension, pre-eclampsia, eclampsia, infections requiring antibiotics, more frequent referrals to higher centers, higher caesarean section rates, more chance of admission to the ICU and high dependency unit, and longer hospital stay.<sup>14</sup> Preterm birth, neonatal ICU stay for 7 days or longer, and neonatal death before discharge from hospital are all higher in the COVID-positive pregnancy group.<sup>4</sup> Thus, there is a compelling need to protect pregnant women against COVID-19.
2. Regarding the safety of vaccines against COVID-19, there have been no preauthorized clinical trials involving pregnant women so far, since they were consciously excluded for ethical reasons. However, there are reasons to believe that COVID-19 vaccines are safe in pregnancy. Among more than 128 000 pregnant women in the United States alone, who indicated they were pregnant at the time they received COVID-19 vaccination, the analyses did not identify any safety concerns for pregnant women who were vaccinated or for their babies.<sup>15</sup> None of the vaccines contain live virus and hence it is extremely unlikely that a vaccine virus could replicate and cross the placenta and infect the fetus. Studies done on pregnant laboratory animals in developmental and reproductive toxicity (DART) studies have not provided any concerning results for the Pfizer-BioNTech, Moderna, Johnson & Johnson/Janssen, and Oxford-AstraZeneca vaccines.<sup>16</sup> A study on 3958 pregnant women who received mRNA COVID-19 vaccines did not show obvious safety signals.<sup>14</sup> Adverse pregnancy and neonatal outcomes among women who received mRNA COVID-19 vaccines were similar to those reported in other studies involving pregnant women before the pandemic.<sup>17</sup> The mRNA vaccines appear to be safe for pregnant women, based on currently available data. Two adenovirus vaccines (Johnson & Johnson/Janssen<sup>18</sup> and Oxford-AstraZeneca)<sup>19</sup> have been found to be associated with a serious clotting disorder, thrombosis with thrombocytopenia syndrome, in recipients under 50 years of age.<sup>9,10</sup> However, this adverse effect is very rare, with incidence ranging from 1 case per 26 000 to 1 case per 127 000 doses.<sup>20</sup> Compared with the enormous protection that the vaccine offers against COVID-19, this risk is very small; therefore, vaccination of pregnant women is being recommended.<sup>21</sup> However, where mRNA vaccines are available, as in the USA and UK,<sup>22,23</sup> women are being given the option to choose these vaccines. The Australian government has also recommended that it is preferable for pregnant women to receive the Pfizer COVID-19 vaccine.<sup>24</sup>
3. COVID-19 vaccines are as effective in pregnant women as the general population. It has been shown that pregnant women elicit a robust humoral immune response after vaccination with immunogenicity and reactogenicity that is equivalent to that in non-pregnant women.<sup>25</sup> Vaccine-induced immune response is higher than that elicited in response to natural COVID-19.<sup>25</sup> To break the cycle of virus transmission, mass-scale immunization is necessary in a region, which would eventually make the region disease free. Most epidemiologists believe that a threshold of 70% protection by vaccination or infection would provide herd immunity in a population.<sup>26</sup> This has happened in Israel, where life has returned to near normal after 58% of its population has been vaccinated.<sup>27</sup> Wide immunization coverage in Israel included vaccination of pregnant women.<sup>28</sup> COVID-19 infection after vaccination is known, but the viral load in such cases is substantially lower, as well as onward transmission of the virus.<sup>29</sup>
4. COVID-19 vaccination in pregnancy has dual benefit: both the mother and newborn get antibodies, which have been demonstrated in cord blood and breast milk.<sup>25</sup> High immunoglobulin A levels in early milk<sup>8</sup> compared to later milk makes a case for vaccination during pregnancy rather than in lactation. At present, children aged under 5 years are not offered COVID-19 vaccines; however, young people are becoming increasingly susceptible to newer variants, for example the P.1 variant in Brazil.<sup>30</sup> Israel has placed pregnant women on the high priority list for COVID-19 vaccination<sup>31</sup> backed by studies in the country that show efficient

maternofetal transplacental transfer of anti COVID-19 spike antibodies.<sup>32</sup>

5. In view of the higher risk of severe COVID-19 in pregnant women, the World Health Organization (WHO) recommends that pregnant women with a history of underlying medical conditions be vaccinated during pregnancy, after consulting their healthcare provider.<sup>16</sup> Since pregnancy is a factor that leads to increased risk of severe illness with COVID-19, the Centers for Disease Control and Prevention (CDC) and the American College of Obstetricians and Gynecologists (ACOG) have recommended including pregnant women as eligible to receive COVID-19 vaccination.<sup>21,22</sup> Pregnant women are advised to discuss with their healthcare provider and make an informed decision regarding vaccination.<sup>21</sup> In the UK, the Joint Committee on Vaccination and Immunization (JCVI) has recommended that COVID-19 vaccines should be offered to pregnant women at the same time as the rest of the population, based on their age and clinical risk group.<sup>33</sup> The European Medicines Agency also recommends that vaccination in pregnant women may be considered on a case-by-case basis.<sup>34</sup> In India, the Federation of Obstetric and Gynaecological Societies of India (FOGSI)<sup>35</sup> and the National Technical Advisory Group on Immunization (NTAGI)<sup>36</sup> have recommended that pregnant women may be offered the choice to receive any COVID-19 vaccine. Amid rising concerns voiced by health professionals, gender experts, researchers, and the press, the government of India on June 25, 2021, allowed COVID-19 vaccination for pregnant women<sup>37</sup>; however, pregnant women are not included in the priority group and COVID-19 vaccination is not included as part of antenatal care.
6. Some parts of the world have a high burden of COVID-19 infection-related morbidity and mortality and also moderate coverage of vaccination against the disease (Table 1). Other countries have both high maternal and neonatal mortality (Table 2), which have worsened during the pandemic owing to the added burden of COVID-19 infection as well as lockdowns that hamper the utilization of health services.<sup>38</sup> Two countries—India and Indonesia—fall into this category, where the impact of COVID-19 infection is high, maternal and under-five deaths are substantial, and the proportion of the population vaccinated against COVID-19 is low. These countries have been hardest hit by the pandemic and are in urgent need of higher vaccination coverage, including pregnant women as a high priority group. The challenge is to implement immunization of pregnant women against the virus as well as improve utilization of antenatal services, while the social constraints and risk of infection posed by the pandemic continue to persist.

## 5 | DISCUSSION

COVID-19 infection in pregnant women places them at higher risk both in terms of severity of infection as well as the course and outcome of pregnancy. Lingering fears exist that the virus could be

passed to the baby during pregnancy or after birth during breastfeeding or taking care of the newborn.<sup>39</sup> It also paralyzes family dynamics, as self-isolation becomes difficult.

If a breastfeeding mother contracts COVID-19, it poses a dilemma over whether the baby should be kept close-by to continue breastfeeding or whether the mother should isolate herself. However, the WHO has recommended that rooming-in of baby with an infected mother and breastfeeding should be continued with COVID-19 appropriate precautions due to the established role of breast milk in child development and survival.<sup>40</sup> If the vaccine is administered during pregnancy, the mother would have sufficient antibodies in breastmilk to protect the baby. Therefore, it is of utmost importance that pregnant women are immunized during pregnancy. Although COVID-19 vaccination is recommended for all lactating women in India,<sup>41</sup> pregnant women are still not included as a priority group.

An efficient way to vaccinate pregnant women against COVID-19 is to include vaccinations in routine antenatal care, the same as tetanus immunization and iron and folic acid supplementation. Antenatal care registration has fallen due to fear of COVID-19 and mandatory lockdowns. Converging antenatal care with COVID-19 vaccination will maximize coverage, with positive effects on maternal and child outcomes. The setback due to COVID-19 on maternal and under-five health could be offset and the pandemic used as an opportunity to further the survival revolution for under-fives across the globe. To strike the right balance between optimal antenatal care and restricting movements out of the home, at least four face-to-face antenatal contacts have been recommended during the pandemic.<sup>42</sup> Integrating COVID-19 vaccination into antenatal care protocol would reduce two extra visits for vaccination and naturally improve compliance with both. The timing of vaccination should be such that it elicits maximum antibody response in cord blood and colostrum/early milk, and its administration does not interfere with immune response to routine vaccination in pregnancy. However, both of these areas warrant further research.

The adverse effect of thrombosis reported with adenovirus vaccines, such as the Oxford-AstraZeneca vaccine currently administered by many countries globally,<sup>43,44</sup> has raised concerns about their safety, particularly during pregnancy which is a hypercoagulable state. In several countries, mRNA vaccines are not available as they require stringent cold chain conditions with sub-zero temperature. Neither Indonesia (Oxford-AstraZeneca and Sinovac's CoronaVac) nor India (Oxford-AstraZeneca's Covishield and Bharat Biotech's Covaxin) have mRNA vaccines. CoronaVac and Covaxin are inactivated vaccines and, even with the limited data available, are assumed to be safe in pregnancy.<sup>45,46</sup> In view of the obvious benefits of vaccination, rare nature of adverse events, and to contain the COVID-19 pandemic, all countries—in particular India and Indonesia—should use available vaccines for protecting pregnant women as a priority. Like all recipients, pregnant women should have access to information about the safety and efficacy of the vaccine, including information about data that are not available.

## 6 | CONCLUSION

Despite evidence supporting the safety and efficacy of COVID-19 vaccines and the need to protect pregnant women, only a few countries with a high burden of COVID-19 cases, high maternal mortality, and high under-five mortality have allowed vaccination of pregnant women. Countries like India and Indonesia with a high burden of COVID-19 cases and an existing burden of high maternal and under-five mortality should allow and prioritize vaccination of all pregnant women because of the protection it gives to the mother and through the transmission of antibodies in breast milk to the baby. We recommend that all countries should not only allow COVID-19 vaccination of pregnant women, but also prioritize this high-risk group. An effective and systematic way of achieving high coverage of pregnant women would be to include COVID-19 vaccination in the protocol for antenatal care (with an opt-out option). If this strategy is adopted, the devastating effects of the COVID-19 pandemic can be converted into an opportunity to increase coverage of routine antenatal care services, while protecting mothers and their unborn babies against COVID-19.

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### CONFLICTS OF INTEREST

The authors have no conflicts of interest.

### AUTHOR CONTRIBUTIONS

YS conceptualized the study, compiled information from web sources, and wrote the paper. TS performed the literature review and was a major contributor in writing the manuscript. RS tabulated the data and interpreted the data. All authors read and approved the final version of the manuscript.

### DECLARATIONS

All the data supporting the results reported in the article can be found freely online, mainly at: <https://ourworldindata.org/>

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