SYMPOSIUM ON VACCINES AND PREGNANCY

COVID-19 and the impact of the vaccine on maternal health during pregnancy: safety and efficacy

COVID-19 y el impacto de la vacuna sobre la salud materna en el embarazo: seguridad y eficacia

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ABSTRACT

Introduction. During the COVID-19 pandemic, pregnant women were one of the most affected populations, with a significant increase in the risk of complications and mortality. Objectives. To review the evidence on the safety and efficacy of COVID-19 vaccines in pregnant women and analyze their impact on maternal morbidity and mortality globally and in Peru. Methods. A narrative review of the scientific literature published in international databases and official public health reports was conducted, focusing on observational studies, systematic reviews, and relevant clinical guidelines. Results. COVID-19 vaccines, especially mRNA vaccines, have demonstrated a favorable safety profile during pregnancy, with no association with spontaneous abortion, congenital malformations, or preterm birth. They also showed significant efficacy in preventing severe disease and maternal mortality. In Peru, the inclusion of pregnant women in the national vaccination plan in 2021 was associated with a marked reduction in maternal mortality attributed to COVID-19. Conclusions. COVID-19 vaccination in pregnant women is a key public health tool with proven benefits in reducing maternal morbidity and mortality. Its implementation should continue to be a priority in pandemic and epidemic outbreak contexts.
Keywords: Pregnancy; COVID-19; Vaccines; Safety; Maternal mortality.

RESUMEN

Introducción: Durante la pandemia de COVID-19, las gestantes fueron una de las poblaciones más afectadas, con un aumento significativo del riesgo de complicaciones y mortalidad. Objetivos: Revisar la evidencia sobre la seguridad y eficacia de las vacunas contra la COVID-19 en gestantes, y analizar su impacto en la morbimortalidad materna a nivel global y en Perú. Métodos: Se realizó una revisión narrativa de la literatura científica publicada en bases de datos internacionales y reportes oficiales de salud pública, enfocada en estudios observacionales, revisiones sistemáticas y guías clínicas relevantes. Resultados: Las vacunas contra la COVID-19, en especial las de ARNm, han demostrado un perfil de seguridad favorable durante el embarazo, sin asociación con aborto espontáneo, malformaciones congénitas ni parto prematuro. Asimismo, mostraron una eficacia significativa para prevenir enfermedad grave y mortalidad materna. En Perú, la inclusión de las gestantes en el plan nacional de vacunación en 2021 se asoció con una reducción marcada de la mortalidad materna atribuida a COVID-19. Conclusiones: La vacunación contra la COVID-19 en gestantes constituye una herramienta clave de salud pública, con beneficios comprobados en la reducción de la morbimortalidad materna. Su implementación debe continuar siendo prioritaria en contextos pandémicos y de brotes epidémicos.
Palabras clave: Embarazo; COVID-19; Vacunas; Seguridad; Mortalidad materna.

Introduction

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, pregnant women have been recognized as a particularly vulnerable population. Multiple studies have described the association between COVID-19, specifically in moderate and severe clinical presentations, with an increased risk of hypertensive disorders of pregnancy, preterm delivery, and admission to intensive care units. Furthermore, the risk of mortality is significantly higher in the pregnant population than in the non-pregnant population of women of reproductive age[1-3].

In Peru, the impact of the pandemic was particularly alarming. Prior to 2019, the maternal mortality rate had been declining. In 2020, there was a 45% increase in the maternal mortality rate compared to the previous year. In 2021, COVID-19 became the leading cause of maternal death nationwide, reaching its highest level in 15 years. It was the first time during this period that an indirect cause was the leading cause, surpassing direct obstetric causes such as postpartum hemorrhage and hypertensive syndromes of pregnancy[4,5]. (Table 1)

This phenomenon occurred not only in Peru but also around the world. The INTERCOVID study, which included 18 countries, many in Latin America, showed that pregnant women infected with SARS-CoV-2 have a 22 times higher risk of maternal mortality compared to uninfected pregnant women[2]. The Pan American Health Organization reported increases of 30 to 60% in the maternal mortality rate in the region[6].

Despite multiple reports and studies demonstrating the vulnerability of pregnant women, the implementation of vaccination strategies for pregnant women faced many obstacles. One of the main obstacles was the exclusion of pregnant women from vaccine clinical trials, which raised doubts among both health professionals and the patients themselves[7].

In South America, Peru was one of the first countries to authorize vaccination of pregnant women, while other nations such as Chile, Colombia, Ecuador, and Bolivia did not yet formally recommend it at that time. With regard to Peru, two crucial decisions were made. The first was not to exclude pregnant patients from the frontline staff vaccination program. The second was, in mid-2021, to consider pregnant women as a vulnerable group and therefore recommend priority access to the vaccine. This public health decision had a significant impact on maternal mortality from COVID-19 in the country, which decreased from 40.9% to 8.8% in the second half of 2021, and subsequently to 0.4% in 2023, according to data from the Ministry of Health[5,8].

Table 1: Maternal mortality in Peru from 2019 to 2023.

Year	Materbal deaths	Anual variation (%)	Main cause of maternal death
2019	302	–	Obstetric hemorrhage
2020	439	+45.4%	COVID-19 (as indirectal cause)
2021	493	+12.3%	COVID-19 (indirect cause surpassed direct obstetric causes)
2022	291	-41.0%	Preeclampsia and eclampsia
2023	262	-10.0%	Hypertensive disorders of pregnancy

In this context, the present article aims to review the available scientific evidence on the safety and efficacy of COVID-19 vaccines in pregnant women, as well as to analyze their impact on maternal morbidity and mortality at the global and national levels, with an emphasis on the Peruvian experience.

Methods

A narrative review of the scientific literature published in international databases (PubMed, Scopus, and Google Scholar) and in official reports from public health agencies was conducted, covering the period from the start of the pandemic to June 2025. Systematic reviews, observational studies, and relevant clinical guidelines on the safety and efficacy of COVID-19 vaccines in pregnant women, both globally and in Peru, were included.

No statistical tests were applied, as this was not an original study but a synthesis of existing evidence.

In terms of ethical considerations, this work did not involve experiments on humans or animals, nor the use of individual patient data, so informed consent or approval from an institutional ethics committee was not required.

The authors declare that no artificial intelligence tools were used. The critical analysis of the literature, interpretations, and conclusions were developed exclusively by the authors.

Results

Vaccine safety during pregnancy

Since the start of COVID-19 vaccination in pregnant women, numerous observational studies and international surveillance systems have shown that the vaccines are safe. Initially, most of the information published was based on messenger RNA technology (Pfizer-BioNTech and Moderna). In the following years, no evidence has been found to suggest an increased risk to

the mother and/or fetus. No increase in the risk of miscarriage, congenital malformations, premature birth, or other obstetric complications associated with vaccination has been reported[9,10]. The CDC developed the "v-safe" monitoring system, which provided robust data supporting these findings, even when vaccination occurs during the first weeks of pregnancy[11]. A recent systematic review included 177 studies with 638,791 participants from 41 countries and aimed to evaluate the safety of various COVID-19 vaccine platforms in pregnant women. Of the eleven types of vaccines included in this systematic review, the most frequently used were mRNA vaccines (87% of published data), followed by viral vector and inactivated virus vaccines.

The evidence, although of low to very low certainty due to the methodology used in these studies, suggests that vaccination during pregnancy does not have a significant impact on adverse maternal or neonatal safety outcomes, with variations ranging from 26 fewer events to 17 more events per 1,000 pregnant women, and between 13 fewer events to 9 more events per 1,000 newborns[12]. The side effects and symptoms of these vaccines are similar to those in the non-pregnant population, including nausea, chills, myalgia, and fever[13,14]. It should be noted that studies evaluating the safety of the vaccine depending on the time of administration found no association with spontaneous abortion or congenital malformations, so it is considered safe in any trimester[15-17].

Vaccination efficacy

COVID-19 vaccination in pregnant women has been shown to be highly effective in reducing symptomatic infection (especially moderate to severe), hospitalizations, and maternal mortality associated with COVID-19[9,18]. Ciapponi et al. reported statistically significant reductions in COVID complications in both maternal and neonatal health. Vaccination during pregnancy with mRNA vaccines was associated with a 72% reduction in severe cases or hospitalizations due to COVID-19 in pregnant women (95% CI: 42–86) and a 78% reduction in symptomatic cases (95% CI: 21–94). Specifically, when combining data across variants, the vaccine's effectiveness in reducing severe cases and hospitalizations was estimated at 72% (95% CI: 42–86) with messenger RNA vaccines, 49% (95% CI: 0–74) with viral vector vaccines, and 61% (95% CI: 0–93) with inactivated vaccines, regardless of the vaccination schedule.

In addition, pregnant women vaccinated with mRNA vaccines had a 9% decrease in emergency cesarean sections, and those vaccinated with mRNA or viral vector platforms showed a 75% to 83% reduction in the incidence of fetal deaths[12].

In infants, although the evidence is low, there was also a 64% reduction in severe cases or hospitalizations (95% CI: 37–80) and a 66% reduction in laboratory-confirmed infections (95% CI: 37–81).

Impact on maternal morbidity and mortality

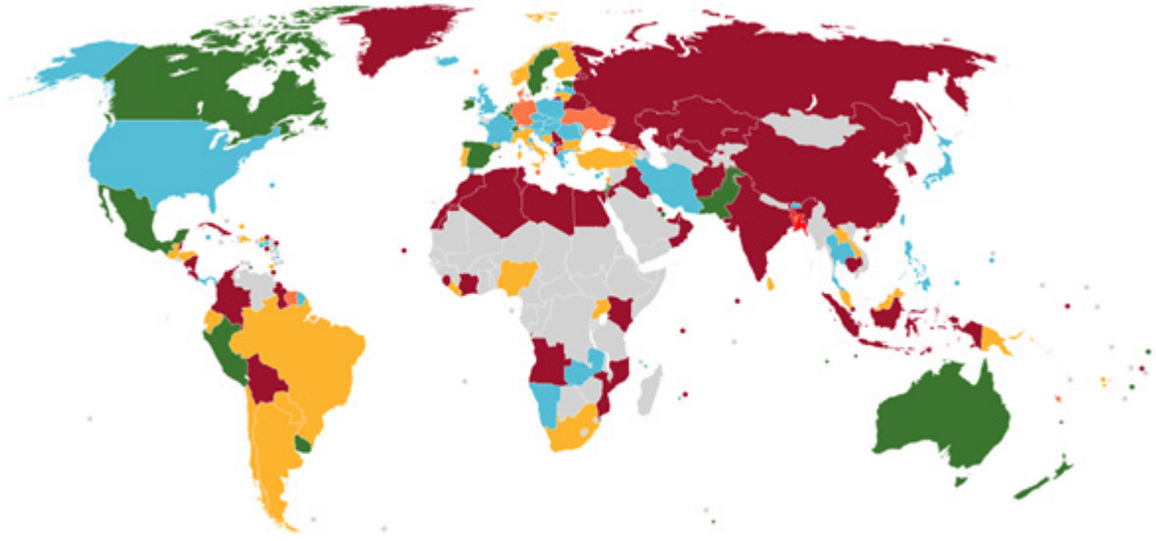
The pandemic revealed a significant increase in COVID-19-related maternal morbidity and mortality worldwide, particularly among pregnant women hospitalized with confirmed infection[11,19].

In Peru, there was a considerable increase in maternal mortality from indirect causes related to COVID-19 during 2020 and 2021[5,20]. The prioritization of vaccination for pregnant women since mid-2021 coincided with a dramatic reduction in maternal mortality due to COVID-19, from 40.9% in the first half of the year to 8.8% in the second half, reaching 0.4% in 2023[5]. Peru was one of the first countries to recommend vaccination for pregnant women (Figure 1). These data demonstrate the effectiveness of the public health policies implemented and constitute an outstanding example not only in the Latin American region but also worldwide[3,21].

Discussion

In the years following the pandemic, high-quality evidence has been reported, reinforcing the idea that COVID-19 vaccination during pregnancy is safe, effective, and has had a significant impact on reducing maternal morbidity and mortality. These findings have been published both globally and in the Peruvian context. They are so consistent that the recommendations issued by leading international organizations, such as the World Health Organization (WHO)[22], the Centers for Disease Control and Prevention (CDC)[11], and the American College of Obstetricians and

Figure 1: COVID-19 vaccination during pregnancy, June 2021.



Green. Recommended for some or all, Blue. Allowed, Yellow. Allowed with conditions, Orange. Not recommended, but with exceptions, Red. Not recommended, White. No official stance found, Gray. No official stance found

Gynecologists (ACOG)[23], agree on prioritizing pregnant women as a risk group in the design of COVID-19 immunization strategies.

Regarding vaccine safety during pregnancy, multiple retrospective studies and surveillance databases have shown that there is no evidence of an increase in relevant adverse events following administration of COVID-19 vaccines during pregnancy, especially mRNA vaccines[9]. Serious obstetric events, including spontaneous abortion, preterm birth, intrauterine growth restriction, congenital malformations, and preeclampsia, occurred at a frequency comparable to that expected in the general pregnant population[14,17]. It is important to emphasize that this safety profile in pregnancy holds true even when vaccination is administered during the first trimester of gestation, reinforcing the idea of its safety during embryogenesis[10,15,16].

The effectiveness of vaccination in pregnant women in reducing severe cases and hospitalizations has been widely demonstrated in systematic reviews and population studies[12,19]. Immunization against COVID-19, especially mRNA vaccines, has shown a significant reduction in the risk of symptomatic infection, hospitalization, admission to intensive care units, and maternal death associated with COVID-19[12,18]. Added to this is the consistent finding of a robust maternal immune response after vaccination, with the generation of adequate titers of neutralizing antibodies that are also efficiently transferred to the fetus through the placenta. The presence of anti-SARS-CoV-2 IgG in umbilical cord blood suggests passive neonatal protection that could contribute to reducing the burden of disease in the first months of life[21]. This dual benefit, both maternal and neonatal, positions vaccination in pregnant women as a high-value public health strategy.

The evidence also points to a clear positive impact on maternal morbidity and mortality following the implementation of vaccination in this population[12]. Internationally, a sustained decline in the rate of maternal deaths attributable to COVID-19 has been documented, with marked differences between vaccinated and unvaccinated women[18, 21]. In countries such as the United Kingdom, population data show that the vast majority of severe cases and deaths occurred in unvaccinated pregnant women[19]. Similarly, reports from the United States confirmed that more than 95% of severe cases and deaths from COVID-19 in pregnant women occurred in unvaccinated women, reaffirming the preventive nature of immunization in this group[21].

In the Peruvian context, the magnitude of the impact of COVID-19 was particularly severe. The pandemic abruptly reversed the progress made in reducing maternal mortality in previous decades, with more than 40% of maternal deaths in 2021 attributed to this infection (4, 20). Official reports confirmed this change in the causes of maternal mortality, placing COVID-19 above direct obstetric causes such as hemorrhage or hy-

pertensive disorders[5,6]. However, following the policy recommendation for vaccination in pregnant women in June 2021, a rapid and sustained reduction in these figures was observed[4, 5].

During the COVID-19 pandemic, the Peruvian Society of Obstetrics and Gynecology (SPOG) played a decisive role in identifying pregnant women as a particularly vulnerable population to SARS-CoV-2, advocating for their priority inclusion in vaccination strategies[24, 25]. Through official communications, letters to the Ministry of Health, and the publication of specific clinical guidelines[24], as well as statements issued in 2021 recommending vaccination with safe platforms[25], the SPOG provided technical guidance based on the best available evidence and promoted a more equitable health response. These actions not only supported decision-making by health personnel, but also served to counter misinformation and build confidence in the safety and efficacy of vaccination during pregnancy.

Despite these achievements, it is necessary to recognize the persistent challenges. Misinformation, vaccine resistance, and lack of equitable access to health services continue to limit vaccination coverage in some sectors of the pregnant population[6,7]. In Peru, structural inequalities in access to prenatal care, coupled with mistrust of health institutions, may explain the regional gaps observed in vaccination coverage[6,8]. It is essential to strengthen health education, evidence-based communication strategies, and surveillance systems to promote informed decisions by pregnant women and their families[6].

Finally, the impact and management of the pandemic showed the importance of consolidating public policies based on scientific evidence[6,21]. The case of Peru demonstrates that timely and well-targeted health interventions can reverse a trend of high maternal mortality in a health crisis context[4,5]. In this regard, COVID-19 vaccination in pregnant women should remain a priority in the design of responses to future pandemics, as well as in the planning of routine immunization programs for other emerging diseases[6, 21].

Limitations

This study has some limitations. As it is a narrative review, it does not include a systematic analysis or meta-analysis of published data, which may lead to a certain bias in the selection of the studies discussed. In addition, most of the available evidence on COVID-19 vaccination in pregnant women comes from observational studies and surveillance registries, which are less methodologically robust than clinical trials. However, the consistency of results across different contexts and countries, together with the magnitude of the benefit observed in Peru, lend consistency and value to the conclusions presented.

Conclusions

The scientific evidence reviewed conclusively demonstrates that COVID-19 vaccines, particularly those formulated with messenger RNA technology, are safe and effective when administered during pregnancy. Their use is not associated with an increase in adverse obstetric or perinatal events, and has been shown to significantly reduce the risk of severe disease, hospitalization, and maternal death associated with infection.

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