

## Vaccination and immunological profile for COVID-19: a cohort among pregnant women treated at two Basic Health Units in the state of Goiás, between 2021 and 2022

### Vacinação e perfil imunológico para Covid-19: uma coorte entre gestantes atendidas em duas Unidades Básicas de Saúde no estado de Goiás, entre 2021 e 2022

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#### Abstract

**Objective:** this study aimed to analyze the vaccination and immunological profile for COVID-19 in pregnant women treated at Basic Health Units in Goiânia, GO, Brazil, between May 2021 and July 2022. **Methods:** this is a prospective cohort study. The participants were selected by convenience, signed a consent form, answered a questionnaire, and had blood samples collected for anti-SARS-CoV-2 (immunochromatography). This procedure was repeated up to three times throughout the pregnancy. After delivery, new samples were collected from the postpartum woman and the newborn for analysis. **Results:** the seroprevalence for IgG anti-SARS-CoV-2 among the 66 pregnant women monitored was 83.3%. It was ascertained that two or three doses of a COVID-19 vaccine produce a more effective immune response than just one dose. More than 75% of newborns presented SARS-CoV-2 IgG antibodies. **Conclusion:** these data are relevant to encourage vaccination of pregnant women, following the complete vaccination schedule, and breastfeeding.

**Keywords:** Pregnant women; COVID-19; SARS-CoV-2; Immunization; Infants; Maternal and child health.

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## Resumo

**Objetivo:** este estudo teve como objetivo analisar o perfil vacinal e imunológico para Covid-19 em gestantes atendidas em Unidades Básicas de Saúde em Goiânia-GO, entre maio de 2021 e julho de 2022. **Métodos:** trata-se de um estudo de coorte prospectivo. As participantes foram selecionadas por conveniência, assinaram um termo de consentimento, responderam a um questionário e realizaram coleta de amostras de sangue para análise de anticorpos anti-SARS-CoV-2 (imunocromatografia). Esse procedimento foi repetido até três vezes ao longo da gestação. Após o parto, novas amostras foram coletadas da puérpera e do recém-nascido para análise. **Resultados:** a soroprevalência de IgG anti-SARS-CoV-2 entre as 66 gestantes acompanhadas foi de 83,3%. Verificou-se que a aplicação de duas ou três doses da vacina contra a Covid-19 gera uma resposta imune mais eficaz do que apenas uma dose. Mais de 75% dos recém-nascidos apresentaram anticorpos IgG anti-SARS-CoV-2. **Conclusão:** esses dados são relevantes para incentivar a vacinação de gestantes, a adesão ao esquema vacinal completo e a amamentação.

**Palavras-chave:** Gestantes; Covid-19; SARS-CoV-2; Imunização; Recém-nascidos; Saúde materno-infantil.

## Introduction

Infectious diseases remain a leading preventable cause of maternal mortality worldwide, particularly in low-resource settings. Effective interventions for prevention, diagnosis, and treatment could significantly reduce pregnancy-related deaths linked to these conditions.<sup>(1)</sup> In December 2019, several cases of pneumonia from unknown causes emerged in the city of Wuhan, China. It was found to be a new betacoronavirus, called SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), which causes COVID-19 (Coronavirus Disease 2019).<sup>(2)</sup> According to the Ministry of Health,<sup>(2)</sup> pregnant and puerperal women are among the groups at increased individual risk of serious outcomes for COVID-19. Pregnancy itself causes physiological changes in the respiratory tract, such as edema and increased lung expansion, which already makes pregnant women more susceptible to lung infections. SARS-CoV-2 infection during pregnancy causes increased inflammatory processes and induces dysfunction of the pulmonary endothelium. These changes occur mainly in the first and third trimesters, making cases severe, with outcomes such as hypertensive syndromes, maternal deaths, and premature births.<sup>(3-12)</sup>

Immunization through vaccines is one of the main and most important public health inter-

ventions in Brazil, whose main objectives are the control, eradication, and elimination of vaccine-preventable diseases. The National Immunization Program (PNI) in Brazil, which has been in existence for almost 50 years, is responsible for coordinating the entire national vaccination policy.<sup>(13)</sup> Given the seriousness and proportions of COVID-19, educational institutions and pharmaceutical industries in several countries have worked hard to develop safe and effective vaccines against this disease.<sup>(14)</sup> In Brazil, there are four vaccines authorized for use: Sinovac/Butantan, Janssen, AstraZeneca/Fiocruz, and Pfizer/Wyeth.<sup>(15)</sup> Pregnant and postpartum women were included in the priority vaccination groups, due to the higher risk of developing serious illness in this group and the high lethality rate of COVID-19 in pregnant women in Brazil (8.4%), compared to the general population (1.9%).<sup>(12,15-17)</sup>

Although there is no evidence or reasonable biological mechanisms that indicate an increased risk of serious adverse events caused by vaccines during pregnancy or breastfeeding,<sup>(18-23)</sup> there is resistance among the population to receiving the vaccine. A study by Stock *et al.*<sup>(10)</sup> showed that serious complications from COVID-19 in pregnant women were more common in those who were not vaccinated. In addition, scientific evidence indicates that the antibodies stimulated by the vaccine reach

the umbilical cord blood and breast milk, benefiting infants.<sup>(24)</sup> Another study on the 'vaccination of pregnant women using mRNA vaccines was able to link this to a lower risk of hospitalization for their respective infants due to COVID-19.<sup>(25)</sup> Based on the data presented, this study aimed to analyze the vaccination and immunological profile for COVID-19 in pregnant women attending Basic Health Units (UBS), as well as to assess associated risk factors, in the municipality of Goiânia-GO, Central-Western Brazil, between May 2021 and July 2022.

## Methods

The study was approved by the Comitê de Ética do Hospital das Clínicas da Universidade Federal de Goiás - UFG (nº. 4.342.339) and by the Escola Municipal de Saúde Pública de Goiânia (046/2020). Pregnant women were selected by convenience sampling and provided informed consent in accordance with applicable regulations. This is a quasi-experimental study, carried out as a prospective cohort, from May 2021 to April 2022.

The study was carried out in two Basic Health Units (UBS) in Central region of Goiânia. The participants were all interviewed individually and face-to-face while waiting for their prenatal appointments. The questions were read aloud, and the answers were written down by the researcher, without giving any options. Also in the first stage, the pregnant women were given information on how to prevent the disease, as well as other important information about the disease, and were given leaflets (prepared by the author) containing the same information. Vaccination data — including whether patients were vaccinated (and if so, which vaccine was administered and when) — were collected directly from "Meu SUS Digital", a digital health solution that facilitates access to health information. The vaccines used by pregnant women were those authorized for use in Brazil until the time of the last collection: Sinovac/Butantan (inactivated virus), Janssen (serotype 26 adenovirus vectors), AstraZeneca/Fiocruz (recombinant

adenovirus vector), and Pfizer/Wyeth (synthetic messenger RNA).<sup>(15)</sup>

In the second stage, blood samples were taken from the pregnant women taking part in the study before delivery. Peripheral blood samples were collected by syringe and stored in vacuum tubes containing EDTA anticoagulant. After plasma separation, samples were stored at -20 °C until serological testing. Following collection, blood samples were transported to the Laboratory of Parasite-Host Relationship Studies at the Institute of Tropical Pathology and Public Health, Universidade Federal de Goiás. In the laboratory, samples were centrifuged, and after separation, plasma was stored in cryotubes and maintained in a freezer at -20 °C.

In the third stage, samples were taken from the puerperal woman and her infant, to confirm the data found during the pregnancy follow-up. None of the children had received COVID-19 vaccinations at the time their blood samples were taken. Peripheral blood samples were collected, and, after processing, the plasma was stored at -20 °C until the serological tests were carried out.

The samples were collected at the following intervals: first collection, as soon as the pregnant woman agreed to take part in the study, answered the questionnaire and signed the informed consent form; second collection, 8 weeks after the first collection; third collection, eight weeks after the second collection; when possible, an interval of three months was established between collections, to monitor the entire pregnancy.

The parameters for estimating the sample size were: a prevalence of 5.5% for COVID-19 in pregnant women in Goiânia, a reliability level (type I error) of 5%, and precision level of 5%, resulting in several 80 pregnant women. The sample was chosen by convenience, with all pregnant women present at the research sites during the period from May 2021 to April 2022 being invited to take part in the study. There was no restriction on the gestational age limit for the first collection. The following were excluded from the study: pregnant women who had diseases that made pregnancy

risky and would need to go to a referral unit to continue prenatal care; pregnant women who stopped prenatal care at the health units participating in the study, as this would make it impossible to follow up subsequent stages.

All the samples collected were tested for IgM and IgG anti-SARS-CoV-2 antibodies using immunochromatography tests from Nutriex® and Biomanguinhos. The data obtained from the questionnaires and the analyses of the samples collected were entered into the REDCap® (Research Electronic Data Capture) platform. The study evaluated behavioral factors potentially associated with SARS-CoV-2 exposure, including working outside the home, hand hygiene practices after bathroom use or before meals, use of public transportation, face mask adherence, attendance at crowded enclosed spaces, frequency of touching the eyes or nose, and household/close contact with confirmed COVID-19 cases. Using the sample results from each participant, the IgM and IgG results from the different phases investigated were compared using the IBM® Statistical Package for the Social Sciences® (SPSS®), version 17.0, software. Acute SARS-CoV-2 infection was defined as a positive RT-PCR (real-time polymerase chain reaction) test. The RT-PCR results were self-reported by participants and not conducted by the study team. For the comparison of categorical variables, Pearson's chi-square test ( $p < 0.05$ ) and Fisher's exact test ( $p < 0.05$ ) were used when the assumptions of the chi-square test were not met.

## Results

During the follow-up period, 128 pregnant women were interviewed in the two health units that took part in the study, of which four (3.1%) were excluded because they did not meet the inclusion criteria previously described. Of the 124 pregnant women included, 66 (52.8%) had their collections completed (at least one collection from the pregnant woman during prenatal care — some of them had 2 or 3 collections — one after delivery

and one from the infant, adding up to a minimum of 198 samples), and 58 (47.2%) had started follow-up but had not completed it, for different reasons.

The first collection and the collection after childbirth were carried out on all participants, while the second and third collections were only carried out on pregnant women who were available at the health units at the time of collection. The final collections were carried out after delivery (approximately 45 days after delivery), where blood samples were also taken from the respective infants.

About the sociodemographic and serological profile of the pregnant women, it was observed that the majority were aged between 21 and 30 (53%; 35/66) (ranging from 15 to 40 years old with an average of 27.6 years old), had already had at least one pregnancy (51.5%; 34/66), were in the first or second trimester of pregnancy (34.8%; 23/66), had never had an abortion (93.9%; 62/66), had between two and five consultations (53%; 35/66), were in a stable relationship (married or living as married) (69.7%; 46/66), had completed high school (50%; 33/66), had a monthly family income of one to two minimum wages (75.7%; 50/66) and declared themselves to be brown (62.1%; 41/66).

Behavioral habits were assessed as they could influence positivity for the disease. Only working outside was associated to the presence of IgG anti-SARS-CoV-2 antibodies (Table 1). The prevalence found for COVID-19 was 83.3% (55/66). In the samples collected from the infants, only one of them (1.5%) was IgM positive for COVID-19. Since the RT-PCR testing was not conducted in our laboratory but rather self-reported by the patient, we do not have this specific data point available for analysis. When it came to detecting IgG, 77.3% (51/66) of the infants reacted to anti-SARS-CoV-2 IgG. The presence of IgG anti-SARS-CoV-2 antibodies in the mother was associated to the presence of the same antibodies in her infants. Regarding the detection of anti-SARS-CoV-2 antibodies in the samples analyzed, it is important to note the influence of vaccines on the presence or absence of these antibodies.

**Table 1** – Distribution of pregnant women attending two basic health units in Goiânia-GO, from May 2021 to July 2022, regarding behavioral habits related to COVID-19.

Behavioral habits	n=51 (%)	COVID-19 IgG+ n (%)	COVID-19 IgG- n (%)	OR (IC 95%)	p-value
<i>Works outside home?</i>					
Yes	28 (54,9)	23 (82,1)	5 (17,5)	2,45 (0,67-8,94)	0,168 <sup>a</sup>
No	23 (45,1)	15 (65,2)	8 (34,8)		
<i>Washes hands after bathroom use/before meals?</i>					
Yes	50 (98,0)	38 (76)	12 (24)	9,25 (0,35-241,5)	0,255 <sup>b</sup>
No	1 (2,0)	0	1 (100)		
<i>Uses public transportation?</i>					
Yes	23 (45,1)	18 (78,5)	5 (21,7)	1,44 (0,40-5,21)	0,577 <sup>a</sup>
No	28 (54,9)	20 (71,4)	8 (28,6)		
<i>Uses face mask?</i>					
Yes	50 (98,0)	37 (74)	13 (26)	0,93 (0,03-24,13)	> 0,999 <sup>b</sup>
No	1 (2,0)	1 (100)	0		
<i>Frequents crowded enclosed spaces?</i>					
Yes	17 (33,3)	15 (88,2)	2 (11,8)	3,59 (0,69-18,51)	0,175 <sup>b</sup>
No	34 (66,7)	23 (67,6)	11 (32,4)		
<i>Frequently touches eyes/nose?</i>					
Yes	30 (58,8)	22 (73,3)	8 (26,7)	0,86 (0,24-3,12)	0,818 <sup>a</sup>
No	21 (41,2)	16 (76,2)	5 (23,8)		
<i>Household member/close contact with COVID-19?</i>					
Yes	24 (47,1)	19 (79,2)	5 (20,8)	1,6 (0,44-5,79)	0,472 <sup>a</sup>
No	27 (52,9)	19 (70,4)	8 (29,6)		

**Caption:** a: chi-square test ( $p < 0,05$ ); b: Fisher's exact test ( $p < 0,05$ ).

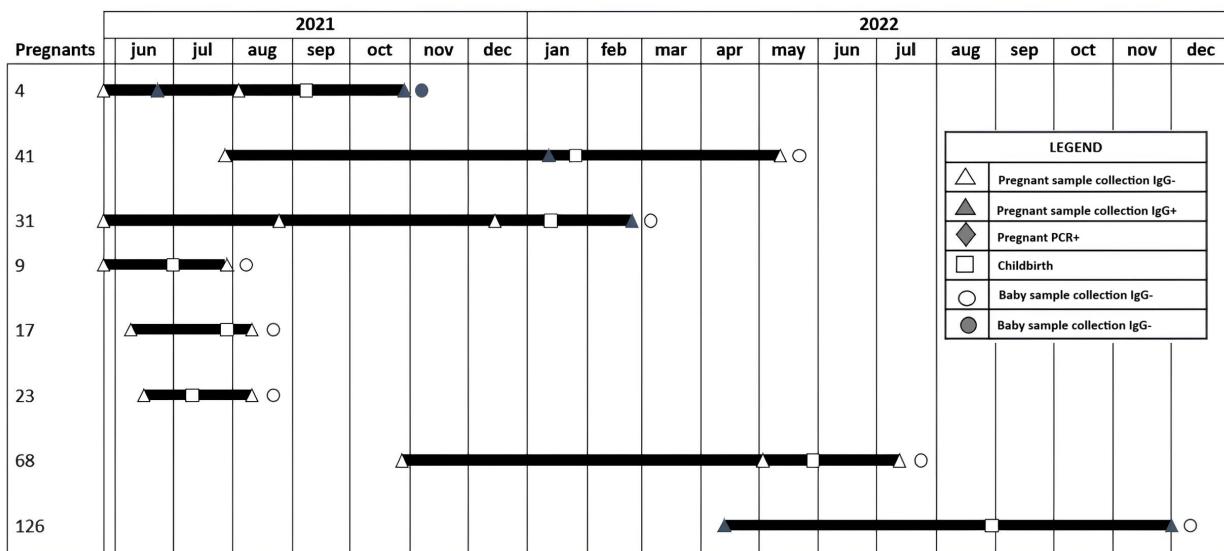
**Source:** the authors.

The pregnant women were divided into groups according to their vaccination and immunological profile for COVID-19, to better assess the presence of anti-SARS-CoV-2 antibodies: Group I — pregnant women who did not receive any doses of the vaccine; Group II — pregnant women who received the vaccine before giving birth, but did not produce antibodies; Group III — pregnant women who presented antibodies from the first collection after at least one dose of the vaccine (before giving birth); Group IV — pregnant women who received

the vaccine before giving birth, but only produced antibodies after two or three doses of the vaccine and Group V — pregnant women who were only vaccinated after giving birth.

Group I represent 12.1% (8/66) of all pregnant women, of whom one showed antibodies in the first collection, three showed antibodies to COVID-19 in the last or penultimate collection, and only one declared a diagnosis by RT- PCR who also had antibodies present in her infant (Figure 1, below).

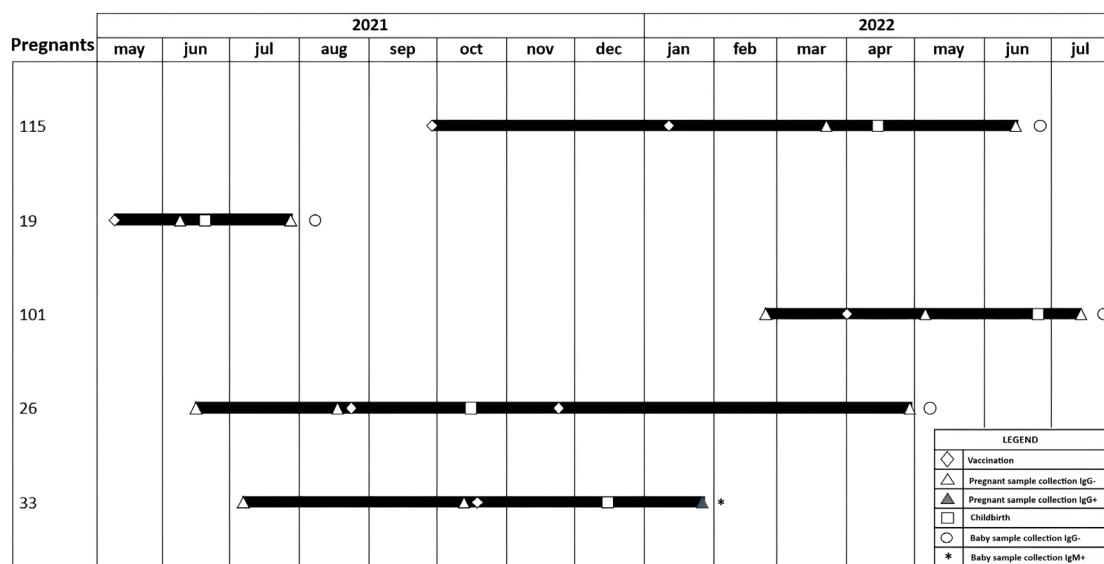
**Figure 1** – Timeline of the follow-up of a group of eight unvaccinated pregnant women and their respective newborns seen at two primary healthcare units in Goiânia-GO, from May 2021 to July 2022.



Source: the authors.

Group II is made up of five pregnant women (7.6%; 5/66). Only one of the pregnant women was IgG positive for COVID-19, while her infant was IgM positive for COVID-19 (Figure 2).

**Figure 2** – Timeline of the follow-up of a group of 5 vaccinated pregnant women and their respective newborns who did not show IgG anti-SARS-CoV-2 antibodies after at least one dose of vaccine, attended at two primary health care units in Goiânia-GO, from May 2021 to July 2022.



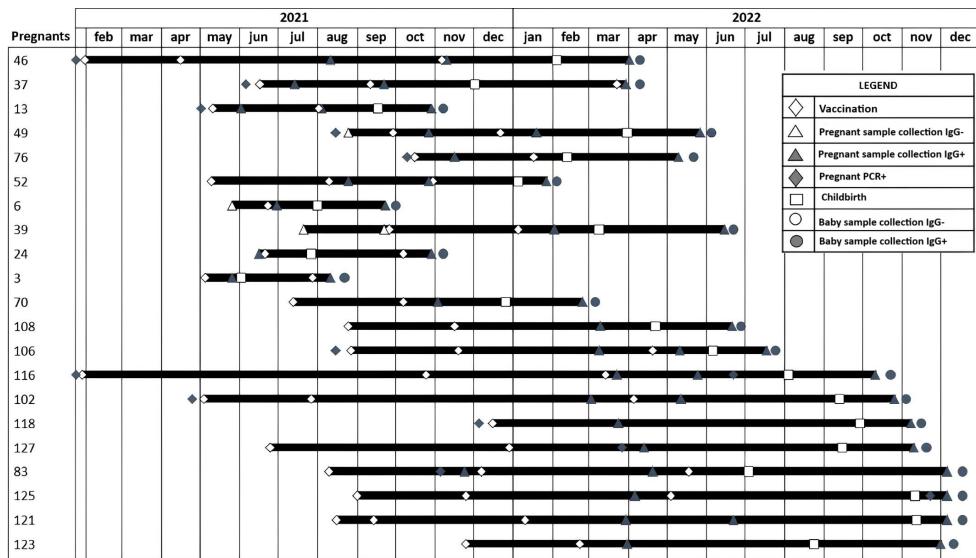
Source: the authors.

Group III is made up of 21 pregnant women (31.8%; 21/66). Of these, 12 (57.1%; 12/21) had a positive RT- PCR diagnosis (patient-reported), and one had a positive IgG result for COVID-19 at the

very first collection, before any dose of the vaccine had been administered. All the pregnant women

and infants in this group had positive IgG antibodies to COVID-19 at the last collection (Figure 3).

**Figure 3** – Timeline of the follow-up of a group of 21 vaccinated pregnant women who were IgG positive for COVID-19 at the first collection after administration of at least one dose of the vaccine and their respective newborns, attended at two primary health care units in Goiânia-GO, from May 2021 to July 2022.

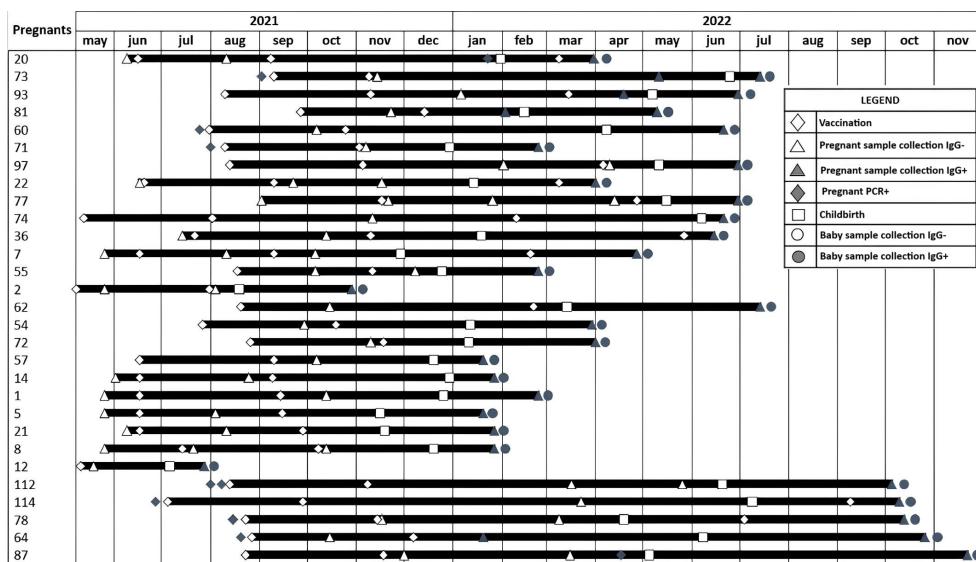


Source: the authors.

In group IV (43.9%; 29/66), all mothers and infants had positive IgG for COVID-19 in the final

collection (after delivery), as can be seen in Figure 4 below.

**Figure 4** – Timeline of the follow-up of a group of 29 vaccinated pregnant women and their respective newborns who had IgG anti-SARS-CoV-2 antibodies after two or three doses of vaccine, attended at two primary health care units in Goiânia-GO, from May 2021 to July 2022.

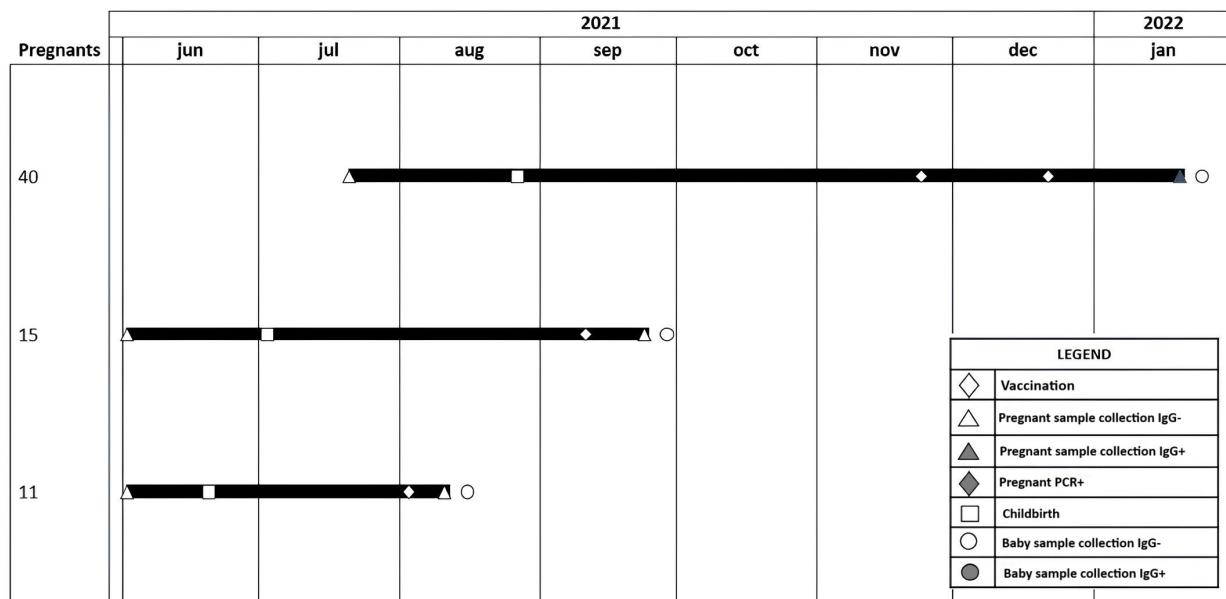


Source: the authors.

Group V is made up of only three pregnant women (4.5%; 3/66). Only one of them was IgG

positive for COVID-19, and none of the infants had the presence of these antibodies (Figure 5).

**Figure 5** – Timeline of the follow-up of a group of 3 pregnant women vaccinated only after delivery and their respective newborns, attended at two basic health units in Goiânia-GO, from May 2021 to July 2022.



Source: the authors.

Among the 66 pregnant women, 23 (34.8%) were RT-PCR positive for COVID-19 (patient-reported).

## Discussion

In the face of an epidemic such as that experienced between 2019 and 2023, it is necessary to protect the population to control morbidity and mortality, induced by immunization through vaccines. Risk groups have been prioritized for health-care actions, including pregnant women. The data presented showed that the pregnant women who had anti-SARS-CoV-2 IgG were those who had been vaccinated or who have not been vaccinated and have had the infection (positive RT-PCR), and there was no significant association between any of the sociodemographic characteristics analyzed and the presence of these antibodies.

A study carried out in Georgia (USA), which assessed sociodemographic characteristics and risk

factors for SARS-CoV-2 infection in obstetric patients, found a relationship between COVID-19 infection and a high neighborhood density.<sup>(26)</sup> This fact is in line with global risk factors, which state that crowds of people favor viral spread.<sup>(27)</sup> This finding is in line with what was detected in the present study, in which pregnant women who worked outside were more likely to have anti-SARS-CoV-2 IgG, since this condition increases the chances of contact with a larger volume of people.

Analyzing the relationship between the presence of IgG anti-SARS-CoV-2 antibodies in mothers and infants, it was found that the presence of antibodies in mothers was associated with the presence of antibodies in infants. This is considered a desirable consequence, as these antibodies can provide temporary protection for infants, and there is no provision for vaccinating children under 6 months.<sup>(21,28)</sup>

To assess the presence of antibodies in patients and their infants, the vaccination profile of

each patient must be considered. Looking at the pregnant women who were not vaccinated during the study (group I), only one of them reported having had COVID-19 during pregnancy. She and her infant had antibodies at the last vaccination, certainly due to the transfer of antibodies produced by the mother during pregnancy through the placenta.<sup>(13)</sup>

Still in the group of unvaccinated pregnant women, three others showed anti-SARS-CoV-2 IgG during follow-up, which was probably due to contact with the virus. In one of them, the antibodies were detected in the collection before delivery but were not detected in the final collection (after delivery) or the pregnant woman's infant. It's important to keep in mind that the collection with the positive IgG result took place 120 days apart.

The third and eighth pregnant women in this group had IgG anti-SARS-CoV-2 antibodies in the last collection, but their infants did not have these antibodies. The third pregnant woman may have had the disease very close to the end of her pregnancy, which was insufficient time for her to produce IgG and transfer it vertically to the infant since the last collection before delivery was 28 days before this event, and she didn't have any anti-SARS-CoV-2 antibodies. Another fact that could explain the two infants without antibodies is what was found in the study by Shook *et al.*<sup>(28)</sup> The study found that infants of mothers vaccinated against COVID-19 had antibodies that persisted for up to 6 months, while infants of mothers who had the disease no longer had antibodies at that age, indicating that titers drop dramatically during this interval.

Group II of pregnant women corresponds to those who received one or two doses of the vaccine but had no detectable antibodies in any of the samples. This can be explained by the decline in vaccine efficacy over time and reinforces the importance of the third dose for an effective immune response against SARS-CoV-2.<sup>(29)</sup> Only one pregnant woman in this group showed anti-SARS-CoV-2 IgG in the last collection, which was probably a response to contact with the virus, as this

patient's infant was the only one in the study to show anti-SARS-CoV-2 IgM, which reveals a recent infection with the virus.

Group III of pregnant women is made up of those who had received at least one dose of the vaccine and showed antibodies even before giving birth, at the very first test. Some of these pregnant women had a positive diagnosis (by RT-PCR) for COVID-19 before starting follow-up, which may also have influenced the production of antibodies. Only one pregnant woman in the group had IgG antibodies even before the first dose of the vaccine, which indicates that she had contact with the SARS-CoV-2 virus. All these pregnant women and their infants showed antibodies in the final collection, reaffirming the importance of vaccination during pregnancy.

Among the pregnant women who were vaccinated, those in group IV showed detectable antibodies only after two or three doses of the vaccine. This corroborates the study by Thompson *et al.*<sup>(29)</sup> who found that vaccine efficacy increased considerably after the third dose. All the patients in this group and their respective infants had IgG anti-SARS-CoV-2 antibodies in the final collection. This could be explained either by transplacental transfer during pregnancy or by breast milk during breastfeeding. It has already been reported that IgG antibodies induced by mRNA vaccines against COVID-19 can persist for at least six months in milk, and the viral neutralizing power of these antibodies persists for at least three months. This could provide children who are breastfed (even milk from milk banks, since the antibodies resist pasteurization) with some kind of transient protection against the SARS-CoV-2 virus.<sup>(21,30)</sup>

Group V was vaccinated only after giving birth. Of these pregnant women, only one received two doses of the vaccine, and she was also the only one to show IgG antibodies in the last collection. However, none of the infants in this group showed antibodies. This reinforces the importance of vaccinating pregnant women during pregnancy so that these antibodies can be transferred vertically, or even through breastfeeding (information we

don't have about the individuals being monitored), which is also an option for passive immunization of these infants.<sup>(21,30)</sup>

The seroprevalence of SARS-CoV-2 among the pregnant women monitored was 83.3% (55/66). The group of pregnant women who were vaccinated before giving birth corresponds to a total of 55 pregnant women, of whom 100% (55/55) had IgG anti-SARS-CoV-2 antibodies at the last collection, as well as 92.7% (51/55) of the infants, highlighting the importance of vaccinating pregnant women as a strategy to prevent COVID-19 during pregnancy and in infants.

While this study contributes valuable data regarding immune responses to COVID-19 vaccination in pregnant women, certain limitations warrant consideration. The primary limitation stems from the small sample sizes in specific subgroups, particularly Group II (n=5) and Group V (n=3). Further research with larger, multicenter cohorts will be essential to validate these preliminary findings across diverse populations of pregnant women with varying immunization response profiles. Considering the results observed, it is possible to infer that two or more doses of COVID-19 vaccine produce a more effective immune response than just one dose. In addition, the study produced information on COVID-19, vaccination, and prenatal care that will serve as a basis for further studies and will directly contribute to actions and decisions by managers in the development of actions, especially in primary care, to prevent this disease.

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