CASE REPORT

Maternal transfer of anti-SARS-CoV-2 antibodies through immunization and breastfeeding for 12 months

Transferência materna de anticorpos anti-SARS-CoV-2 por meio de imunização e amamentação por 12 meses

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ABSTRACT

In February 2023, according to the World Health Organization, there had been more than 700 million cases of COVID-19 worldwide. Maternal immunization has become a hotspot in research on the transplacental transfer of antibodies to the fetus. Vaccinations administered during pregnancy are intended to protect the mother from serious illness. **Case presentation:** In this report, we describe a case wherein the transfer of anti-SARS-CoV-2 antibodies to the fetus, baby, and infant was observed through immunization and breastfeeding. Maternal antibodies were detected in the umbilical cord at birth, in breast milk for up to 10 mo after birth, and in the child's blood for up to 1 y of age, which suggests the importance of vaccination during pregnancy as well as maternal and neonatal protection. **Conclusion**: When an vaccine was administered to the pregnant patient, effective immunological results were obtained in terms of both placental transfer and breastfeeding, for up to 1 y of age.

Keywords: COVID-19 vaccines, Immunity, Maternally-acquired, Breastfeeding, Pregnancy.

RESUMO

Em fevereiro de 2023, a Organização Mundial da Saúde apontou que foram confirmados mais de 700 milhões de casos de COVID-19 em todo o mundo. A imunização materna tornou-se um ponto importante na pesquisa sobre a transferência transplacentária de anticorpos para o feto. As vacinas administradas durante a gravidez destinam-se a proteger a mãe de doenças graves. **Apresentação do caso:** Neste relato, descrevemos um caso em que foi observada a transferência de anticorpos anti-SARS-CoV-2 para o feto, recém-nascido e lactente por meio de imunização e amamentação. Anticorpos maternos foram detectados no cordão umbilical ao nascimento, no leite materno até 10 meses após o nascimento e no sangue da criança até 1 ano de idade, o que sugere a importância da vacinação durante a gravidez, bem como proteção materna e neonatal. **Conclusão**: Quando uma vacina foi administrada à paciente grávida, resultados imunológicos efetivos foram obtidos em termos de transferência placentária e amamentação, até 1 ano de idade.

Palavras-chave: Vacina contra COVID-19, Imunidade materno-adquirida, Amamentação, Gravidez.

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INTRODUCTION

In February 2023, the World Health Organization confirmed that there were approximately 757,264,511 cases of coronavirus disease (COVID-19) worldwide, of which 6,850,594 resulted in death[1]. Initially, severity was believed to be related to the elderly and immunodeficient populations[2]. With the emergence of variants, increased risk has been reported in younger people[3], including pregnant women who, before the introduction of immunization, had increased susceptibility to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection as well as greater complications[4,5].

Maternal immunization is one of the hotspots in research on the transplacental transfer of maternal antibodies to the fetus, and findings related to this area will help protect the mother against serious diseases, as well as the fetus and newborn[6]. Transplacental transport of IgG class antibodies from the mother to the fetus begins to occur at approximately 13 wk of gestation, and it occurs continuously over the months, with greater transfer seen in the last trimester[7]. Occasionally, fetal IgG values may exceed those of the mother[8].

Accumulating evidence confirms the efficacy and safety of immunization against COVID-19 in pregnant women[6,9-12] , in addition to being crucial in controlling the disease and reducing morbidity and mortality during and after pregnancy. Given this scenario, we herein describe a case of transplacental transfer of anti-SARS-CoV-2 antibodies from the mother to the fetus, baby, and infant through immunization and breastfeeding, and follow-up for 12 mo postpartum.

Case presentation

On February 8, 2021, I. B. A. S, a 32-y-old nurse, received the first dose of the monovalent immunizer (0.5 mL; Fiocruz-Covishield™; AstraZeneca Rio de Janeiro, Brazil) containing a single recombinant chimpanzee adenovirus vector replication--deficient (ChAdOx1) that expresses the SARS-CoV-2 glycoprotein S. The second dose was administered with the same immunizer, on May 31, 2021, wherein the patient was at 12 wk of gestation (G2 A0 P1). On October 14, 2021, the patient, who was at 37 wk of gestation, received a booster dose (third dose) of the immunization Comirnaty® (Pfizer-BioNtech-Puurs, Belgium) containing single-stranded mRNA (mRNA) embedded in lipid nanoparticles with a highly purified 5-cap structure, using in vitro cell--free transcription of the corresponding DNA templates encoding the S protein (spike) of SARS-CoV-2. On February 26, 2022, 2 mo after childbirth, the patient received the fourth dose of the immunizing Comirnaty®

During prenatal care, the patient attended 11 consultations without clinical manifestation of SARS-CoV-2 infection and without intercurrences and/or complications. As a healthcare worker, she was at high risk of exposure to SARS-CoV-2 but had no history of infection. During her pregnancy, she gained weight (7.6 kg), and at the time of delivery, she weighed 60.6 kg and was 160 cm tall. She had a normal delivery at 40 wk and 1 d, at 2h30min am on December 10, 2021, in the city of Dourados/Mato Grosso do Sul/Brazil. The baby was female, weighed 3,160 kg, was 50-cm long, and had a head circumference of 34 cm. Upon complete physical examination, the patient was clinically healthy and had

no abnormalities. She was breastfed in the first hour after birth and was maintained under exclusive breastfeeding until the sixth month of life. The Apgar scores at 1 and 5 min were 9 and 10, respectively.

At the time of delivery, a cord blood sample was collected and evaluated using the 2019-nCoV IgG/IgM Combo Test Card rapid test (MP Biomedical® 07RDCOV19, Germany), where the antibodies were found to be induced by the mother's immunizations (IgG positive and IgM negative). A peripheral blood sample was collected from the infant at 6 mo of age, together with samples of blood and breast milk, and submitted to the same test, given that IgG was positive and IgM was negative. The patient underwent follow-up serological tests every 15 d for antibody control, with all tests maintaining positive IgG and negative IgM results. Upon completing 12 mo from the date of delivery, the child's peripheral blood sample was collected; despite having no prior immunization against COVID-19, the peripheral blood and breast milk samples were assessed with the same serological test, maintaining anti-SARS-CoV-2 antibody positivity in all samples (IgG positive and IgM negative). No clinical manifestations of SARS-CoV-2 infection were observed in the infant/child during the study period. The study involving a human participant was reviewed and approved by the Research Ethics Committee of the Universidade Federal da Grande Dourados, protocol number 5.809.315. The patient signed an informed consent form to participate in this study. Written informed consent has been obtained from the individual for the publication of any potentially identifiable data included in this relate.

DISCUSSION

This case highlights the importance of vaccination during pregnancy for both maternal and baby protection. Passive immunization acquired through maternal vaccination against COVID-19 administered to the patient during pregnancy and during breastfeeding resulted in the transfer of antibodies and protection until the child was 12 mo old.

In Brazil, the National Immunization Program is considered one of the largest programs in the world and is an example of public health policies; it includes 19 routinely offered vaccines and 45 immunobiologicals, available for all age groups and vaccination campaigns. Through immunization, diseases such as smallpox and polio have been eradicated in the country[13]. For pregnant women, vaccines against diphtheria, tetanus, hepatitis B, pertussis, influenza, and COVID-19 are recommended[14].

In April 2021, vaccination against COVID-19 in pregnant and postpartum women was authorized by the Ministry of Health, and vaccines authorized for this priority population in Brazil included the inactivated virus antigen through CoronaVac® (Sinovac Life Sciences/Butantan, Beijing-China/São Paulo/Brazil), containing mRNA with Comirnaty® (Pfizer-BioNtech-Puurs, Belgium) and replicating adenovirus with AstraZeneca/Fiocruz, but vaccine administration is temporarily interrupted owing to possible maternal complications associated with the vaccine[15].

One of the most important obstacles to nonadherence to immunization against COVID-19 is safety, especially for the fetus and baby. Safety and protection against in-

fection and the serious effects of COVID-19 are stimuli for adherence to vaccine administration during pregnancy[16-18]. As with vaccination against H1N1, the use of vaccines against COVID-19 has raised concerns regarding vaccination in pregnant women. In the USA, between December 14, 2020, and May 8, 2021, the Center for Disease Control and Prevention, along with eight health organizations, identified 135,968 pregnant women and only 11.1% completed the vaccination schedule, with greater adherence in Asian and White pregnant women and lower adherence among Hispanics and Blacks[17]. In the United Kingdom, in a study conducted between March 1 and July 4, 2021, a total of 28.7% of pregnant women adhered to the vaccination schedule, with lower adherence in young pregnant women, with high levels of deprivation and Afro-Caribbean or Asian ethnicity. Moreover, adherence to vaccination against COVID-19 in pregnant women remains low, which is mainly due to the lack of scientific evidence related to protection, safety, and efficacy[18].

No maternal and fetal/infant problems have been reported after maternal vaccination. In Canada, a study of 97,590 women showed no significant difference in terms of risk and complications among pregnant women who were vaccinated during pregnancy when compared with women who were not vaccinated or who received the vaccine after pregnancy[19]. In a study conducted in pediatric hospitals in the United States (US), a 61% reduction was observed in the potential for hospitalizations in children with COVID-19 when mothers were vaccinated during pregnancy[20], showing the relevance of immunization and protection of both the mother and the child. In another study, no significant difference was observed in immunological outcomes of vaccination between pregnant and lactating women when compared with nonpregnant women[21]. Information from US safety monitoring systems reported no serious complications attributable to COVID-19 vaccination in pregnant women in the last trimester or in the newborn[22]. In view of the facts, the benefits of immunization against COVID-19 in pregnant women outweigh the risks and complications.

The patient received vaccination before pregnancy, at the 12 wk and 37 wk of gestation and 2 mo after birth, and the presence of IgG was detected in the umbilical cord, breast milk, and in the infant/child up to the 12 mo of life. Some studies have shown that most women who received the vaccine had a transplacental transfer of antibodies to their newborns, and the IgG levels were practically equal to or higher than those determined in the mother[8,17,19]. Antibodies have been detected in umbilical cord blood, conferring immunity from the maternal vaccine[9,24,25]. Currently, vaccination against COVID-19 is recommended at any stage of pregnancy[10,11]. The transport of IgG class antibodies against SARS-CoV-2 acquired from the mother to the fetus begins at the end of the first trimester and increases over the months, with the greater transfer being observed in the last trimester[7]. The vaccines received by the mother in the first and third trimesters of pregnancy, as well as during breastfeeding, provided protection to the infant/child up to the 12 mo of life.

The patient received recombinant adenovirus vaccination before pregnancy and in the first trimester before discontinuation of the vaccine by the Ministry of Health; the patient then received the mRNA-containing vaccine in the third trimester of pregnancy and 2 mo after the birth of the infant. Maternal vaccination with vaccines containing the inactivated viral antigen, such as

CoronaVac®, has led to the transfer of antibodies from the mother to the fetus, conferring immunity to the fetus and newborn[12], demonstrating safety and efficacy in the induction of neutralizing antibodies[26].

One study assessed influenza and tetanus vaccines, which contain the inactivated viral antigen, and the results suggest that maternal vaccination in the second or third trimester of pregnancy may occasionally stimulate immunoglobulin M (IgM) production in the fetus[27]. In the case reported here, the baby's umbilical cord blood sample was not positive for IgM antibodies, which may be attributed to the fact that the patient, vaccinated at the end of pregnancy, had received the mRNA-containing immunizer against COVID-19.

Vaccination during pregnancy with mRNA-containing vaccines strongly stimulates the production of neutralizing antibodies, and IgG levels in the fetus were practically equal to those detected in the mother[8,13], which may reach up to 30% more in newborns[7]. The booster dose administered during pregnancy showed significantly greater immunity in pregnant women and umbilical cord, even to the variant Omicron BA.1., than in pregnant women who received only two doses[6].

SARS-CoV-2 infection during pregnancy also produces an extended period of maternal and fetal immunity[21]. However, another study demonstrated that maternal immunization, when compared with infection, elicits higher levels of immunoglobulins[24]. A study conducted in Boston reported that 6-mo-old infants born to mothers vaccinated with an mRNA-containing immunizer maintained persistent anti-Spike antibodies when compared with infants born to mothers infected with SARS-CoV-2[28].

Both the inactivated adenovirus–containing vaccine and the mRNA-containing vaccine culminated in the production of antibodies in the mother, which were transferred to the fetus/baby/child.

Antibodies were detected in breast milk samples up to the 10th month after the patient's last vaccination as well as in children up to the 12 mo of life. Antibodies have also been detected in breast milk samples collected after immunization[9,24,25]. The results for the presence of antibodies in the breast milk samples of postpartum women immunized with mRNA-containing vaccines suggest protection against COVID-19 for the baby, but the extent of benefits remains unknown[29,30]. Although the kit used for antibody detection is not standardized for milk, following the principle of the test, we observed the importance of carrying out the analysis and the result was positive in all samples. In Israel, women vaccinated with two doses of Pfizer-BioNTech vaccine and who were exclusively or partially breastfeeding had high secretion of SARS-CoV-2–specific IgA and IgG antibodies in breast milk samples for 6 weeks after vaccination[29].

Our case report where protection extended until the child was 12 mo old, highlights the importance of vaccination during pregnancy for both maternal and neonatal protection. This finding should motivate the maintenance of the group of pregnant women among the priorities in immunization. The COVID-19 vaccines that were administered to the patient during pregnancy demonstrated effective placental transfer of antibodies and yielded effective immunological results. However, further studies are needed to assess the late safety of the vaccine.

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