19th World Congress in Fetal Medicine

Serological and clinical response to SARS-CoV-2 infection and vaccination during twin pregnancies

Svirsky R, Landau Rabbi M, Abu Hamad R, Galoyan N, Sharabi-Nov A, Kuglar N, Sharon N, Gayer A, Yeger R, Baram O, Korach-Lev Zion O, Meiri H, Maymon R
Department of Obstetrics and Gynecology, Shamir (Assaf Harofeh) Medical Center, Zerifin, Israel

Objective

Complications of pregnant women infected by SARS-CoV-2 are usually accompanied by more severe disease compared to age-matched non-pregnant women, most likely due to many physio pathological consequences of increased body mass, reduced chest volume by the growing uterus, exacerbating the load on the infected lungs, and affecting the cardiac output; as well as increased immune tolerance during pregnancy. The above changes may increase the risk of maternal morbidity and mortality during advanced pregnancy. Twin pregnancies impose a higher challenge compared to singleton, because of larger placenta mass, larger body mass index, and other overload complications. In Israel, the authors of this study led the introduction of guidelines for pregnant women's vaccination during pregnancy when the vaccine became available after the first and second pandemic waves. Our objectives were to evaluate the temporal changes in the serological levels of Anti-Spike Protein IgG (Anti-S) in twin pregnancies immunized by the BNT162b2 Pfeizer/BioNTech vaccination before and during pregnancy and also to compare them to the levels in non-pregnant women.

Methods

The study covers the period after the first two waves of the pandemic and overlapped the third and fourth waves characterized mainly by infections with the Delta and Omicron viral variants. At the time of analysis, we had at Shamir Medical Center 77 women enrolled with twin pregnancy, 69 with di-chorionic and di-amniotic (DCDA) twins and 9 with monochorionic diamniotic (MCBA) twins who were enrolled as a part of the Pretwin Screen International Study (Erapermed JTC2019-61) with a special additional section added to the original study protocol. The enrolment started in December 2020 and the study included women enrolled until February 2022. The women donated blood at the first, second, and early third trimesters. Blood samples were processed to serum and analyzed at the hospital clinical chemistry laboratory for serological response. All serum samples were tested both for spike (S) and Nucleus (N) IgG antibodies to differentiate between the immune response to previous vaccinations and SARS-CoV-2 infections. Quantitative detection of IgG antibodies to SARS-CoV-2 spike glycoprotein (IgG S) was performed using the LIAISON® SARS-CoV-2 (DiaSorin, Saluggia, Italy). The sensitivity and specificity of this assay are 97.4% and 98.5%, respectively. Samples were considered negative for antibody titers <13AU/ml. Positive cases were diagnosed either by the Covid-19 Polymerase Chain Reaction (PCR) test at the time of disease using the FDA approved TaqPath Combo Kit, targeting the N2, ORF1Ab, and S genes; r or by a quantitative detection of the IgG antibodies to SARS-CoV-2 nucleoprotein (IgG N) that was performed using the Elecsys® immunoassay (Roche Diagnostics, Mannheim, Germany) according to the manufacturer instructions. The sensitivity and specificity of this assay are both >99%. Cut off index (COI) is defined as < 1.0 for non-reactive sample. Twin pregnant women were immunized either before pregnancy or during the second trimester with at least two BNT162b2 Pfeizer/BioNTech vaccination standard protocol. Our database included all details of patient demographic, medical, previous and current pregnancy information. SPSS-statistical package was used to conduct a-parametric Kruskal-Wallis's and Mahn-Whitney comparison among groups for continuous parameters and Chi-square for categorical values presented as n (%). $P<0.05$ was considered significant. An age matched hospital employee cohort of non-pregnant women who were tested according to the same testing procedures described above was also included. These women were tested immediately before, one month after, and 3 months after the third immunization with BNT162b2 Pfeizer/BioNTech vaccine.

Results

At the time of analysis, 4 women lost their pregnancy completely, 2 lost 1 fetus, and 5 underwent reduction to singleton due to genetic, structural, or both types of defects, and 50 already delivered twins. There were no significant differences between DCDA and MCDA in any of the parameters at the first, second, and third trimesters. We found that among women who were vaccinated at the end of the first trimester, the level of anti S-IgG b was halved when tested 10-14 weeks later, during the third trimester ($p=0.014$), which was significantly a faster decay ($p<0.001$) compared to women who were vaccinated before pregnancy or in comparison to non-pregnant women, where the antibody level increased 10-20 times above background before vaccination, and remained high for at least 4 to 14 weeks post-vaccination. We also found that in twin pregnancy the level of Anti-S IgG b among women immunized before pregnancy was ~ 5 times higher compared to the level among women immunized during pregnancy ($p<0.001$), while immunization before pregnancy generated a serological response that was not different compared to non-pregnant women and lasted for a similar duration. Eighteen of the women were diagnosed as infected with SARS-CoV-2 based on PCR/Anti-N IgG. The fraction of women who were diagnosed during pregnancy positive for infection by SARS-CoV-2 was higher among women who were vaccinated before becoming pregnant with twins. All immunized pregnant women who were infected by SARS-CoV-2 had very mild symptoms, and none were hospitalized. There were 13 women with a twin pregnancy who were not vaccinated at all, of which 3 were PCR positive, 1 before pregnancy, and 2 developed severe illness requiring hospital admission during pregnancy.

Conclusion

In twin pregnancies, the timing of the vaccination has a long-term impact on the level of a positive serological response to the spike antigen. The serological response to vaccination before pregnancy was not significantly different from non-pregnant women. In comparison, women who got immunized during pregnancy had a significantly lower increase in the serological response of anti-S antibodies, which was also decayed faster, indicating a potential for immune tolerance or a rapid uptake of the antibodies by the placenta and its transfer to the fetus. Interestingly, the higher serological level among pregnant women did not guarantee resistance to the viral infection, particularly during the third trimester, when additional factors such as increased body mass index, a lower lung volume, and the pregnancy load are increased. However, when immunized women with twin pregnancies are infected by the SARS-CoV-2 virus, they appeared to be protected from having severe complications and their disease remained mild.