

Presence of SARS-CoV-2 neutralizing and vaccine spike antibodies in amniotic fluid during the second trimester of pregnancy, detected by amniocentesis (Winner of the SIMP Award, in memory of Professor Giorgio Pardi)

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Objective. Thanks to the SARS-CoV-2 vaccination, pregnant women are protected from the complications of COVID-19 infection, but the benefits of this vaccination in preventing morbidity and mortality in the fetus are not yet clear: it is not well understood if and how these antibodies cross the placenta. Indeed antibodies made after a pregnant person has received an mRNA COVID-19 vaccine have been found in amniotic fluid and umbilical cord blood at term and represent a safer method of enhancing neonatal antibody levels than administration of immunoglobulin preparation to the infant. The aim of the study is to test the presence of neutralizing SARS-CoV-2 antibodies and spike antibodies in the amniotic fluid in the second trimester of pregnancy, and then to compare the antibodies level in maternal serum and amniotic fluid to evaluate their correlation.

Materials and Methods. This cohort study took place at the Department of Obstetrics and Gynecology of Messina at the AOU Policlinico G. Martino from September 2021 to February 2022; the study consisted of 22 pregnant women who had amniocentesis in the gestational period between 15 weeks plus 6 days and 18 weeks: we analyzed serum and amniotic fluid samples of women who contracted the SARS-CoV-2 infection, or who were vaccinated against the same virus, within one year, or never infected by SARS-CoV-2 or vaccinated against it. During the amniocentesis, all patients underwent a single sample of maternal serum and of amniotic fluid to evaluate SARS-CoV-2 neutralizing antibody and S1 receptor binding domain IgG antibody levels. Inclusion criteria were pregnant women with the need to undergo amniocentesis.

Results. 22 pregnant women were enrolled in the study: 10 of them were vaccinated with a mRNA COVID-19 vaccine; 12 women were not vaccinated, 4 of them had developed COVID-19 infection within one year before the collection and 2 of them developed the infection during pregnancy; the other 6 never developed the infection and have not been vaccinated, enrolled as comparators. Mann-Whitney test showed that vaccinated patients had significantly higher S1 receptor binding domain antibody levels both in amniotic fluid ($p < 0.006$) and maternal blood ($p < 0.005$) than not vaccinated women; also SARS-CoV-2 neutralizing antibody levels were higher in pregnant women who developed COVID-19 infection both in am-

niotic fluid ($p < 0.007$) and maternal blood ($p < 0.004$) than not vaccinated women. There was a significantly high correlation between the concentrations of spikes antibody levels in vaccinated pregnant women’s serum and amniotic fluid ($p = 0.000$), and of neutralizing antibody levels in serum and amniotic fluid of women who developed COVID-19 infection ($p = 0.000$).

Conclusions. To the best of our knowledge, the analysis of amniotic fluid and serum showed for the first time that all the vaccinated pregnant women samples had SARS-CoV-2 spikes immunoglobulins both in maternal blood and amniotic fluid. There is a very high correlation between maternal blood and amniotic fluid S1 receptor binding domain antibody levels in vaccinated women: this demonstrates that there is an early transplacental antibody transfer. Also neutralizing antibodies were found in the amniotic fluid of infected pregnant women, with high correlation between concentrations.

