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SARS-Cov-2 Spike Protein Antibody Titers In Cord Blood After Vaccination Against Covid-19 During Pregnancy

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Abstract – In the early months of the COVID-19 pandemic, pregnant patients faced uncertain risks associated with severe acute respiratory syndrome SARS-CoV-2 viral infection. Aim of the study was to determine the titer of specific maternal and umbilical cord antibodies against SARS-CoV-2 viral protein S receptor domain after maternal antenatal vaccination. The paper presents preliminary results of the study proceeded in the department. 13 patients vaccinated during different gestational age have been included in the study. All patients participating in this study were vaccinated with two doses of BNT162b2 mRNA COVID-19 vaccine between the 4 to 31 week of gestation. The in vitro qualitative and quantitative determination of antibodies against SARS-CoV-2 viral protein S receptor domain in serum samples was performed by using an electrochemiluminescence immunoassay. Study results demonstrated that, vaccination against SARS-Cov-2 viral infection during pregnancy is accompanied with adequate production of antibodies that probably may defense neonates from severe infection at least within 6 month of life. Study has revealed positive correlation between time interval of vaccination and delivery for the presence of high titers of SARS-Cov-2 viral protein S receptor domain antibodies in neonatal cord blood, which may allow future determination of the optimal timing of COVID-19 vaccination in pregnant women although this problem need more future studies.

Keywords – Covid-19, Pregnancy, Vaccination, Immunity.

I. INTRODUCTION

In the early months of the COVID-19 pandemic, pregnant patients faced uncertain risks associated with severe acute respiratory syndrome SARS-CoV-2 viral infection Coronavirus -19 infection in pregnancy results in a spectrum of asymptomatic to critical maternal disease (1). According to immunologic and cardiopulmonary adaptations occurring during pregnancy, the risk of severe illness from respiratory infections typically increases. More than 73,600 infections and 80 maternal deaths have occurred in pregnant women in the United States alone as of March 1, 2021. Severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) infection is more severe in pregnant women compared with their nonpregnant counterparts, with an increased risk of hospital admission, intensive care unit stay, and death. (2)

A systematic review of 60 studies on SARS-CoV-2 viral infection in pregnancy reported that severe illness occurred in up to 18% of pregnant patients and critical disease complicated up to 5% of the cases, comparable to rates observed in the general population (3,4,5,). Nevertheless, despite recommendations from public health advocates for pregnant women including the Center for Disease Control and Prevention (CDC), the American College of Obstetricians and Gynecologists (ACOG), and the American Academy of Pediatrics, pregnant or breastfeeding women have been excluded from clinical trials during the

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development of existing COVID-19 vaccines. This causes large gaps in understanding the safety and efficacy of these vaccines in this population. The first vaccine trial began in pregnant women in February 2021 (6-12). According to the recommendations issued by the American College of Obstetricians and Gynecologists, the Center for Disease Control and Prevention, and the Royal College of Obstetricians and Gynecologists, COVID-19 vaccination should not be withheld in pregnant patients (13).

Antibodies, such as IgM and IgG, are among the primary mechanisms of the immune response to SARS-CoV-2 viral infection. IgG antibodies produced after an antenatal vaccination with such vaccines as DTP or influenza, cross the placenta and provide passive immunity in children up to three months after birth (14).

Coronavirus genomes encode four main structural proteins: spike (S), membrane (M), envelope (E), and nucleocapsid (N). The S protein forms the characteristic superfacial spikes of coronaviruses. The aim of this study was to determine the titers of maternal and newborn- specific antibodies against SARS-CoV-2 viral protein S receptor domain after antenatal vaccination.

II. Aim of the Study

Tto determine the titer of specific maternal and umbilical cord antibodies against SARS-CoV-2 viral protein S receptor domain after maternal antenatal vaccination. The paper presents preliminary results of the study proceeded in the department.

III. Material and Methods

13 patients vaccinated during different gestational age have been included in the study. All patients participating in this study were vaccinated with two doses of BNT162b2 mRNA COVID-19 vaccine between the 4 to 31 week of gestation. First dose was administered between 4 to 28 weeks and second dose between 6 to 31 weeks of gestation. The patients had voluntarily received vaccinations against COVID-19 during pregnancies. Vaccine has been injected intramuscularly, following all recommendations of use and preservation provided by manufacturer. General medical data of patients included in the study have been collected from medical records and are shown in the Table N1. Informed written consent was obtained from all the patients involved in the study. Collection of the maternal and umbilical cord blood has been done during delivery by professional midwife after instructions from laboratory responsible for testing.

Table N. General medical data of patients included in the study

Mean age	30 years
Extra genital diseases	1 case – cervical cancer 1 case – pregnancy after strumectomy and nonsevere mitral regurgitation 1 case - migraine
Parity	5 cases of primiparity 8 cases of multipartiy
Covid -19 infection during pregnancy	9 cases
Gestation during first dose of vaccination	1st trimester-3 cases 2nd trimester – 6 cases 3 rd trimester – 4 cases
Gestation during second dose of vaccination	1st trimester-3 cases 2nd trimester – 6 cases 3 rd trimester – 4 cases
Interval between second dose and delivery	From 6 to 31 weeks

Way of delivery vaginal/CS	6 cases of caesarian section 7 cases of vaginal uncomplicated delivery
Gestation during delivery	12 cases of term delivery 1 case of preterm delivery 35 w
Neonatal gender	3 female 10 male
Neonatal weight	12 cases normal weight 1 case -2300 gr
Need for NIC	No need of referral to NICU
Gestation singleton/multiply	All singleton

Inclusion criteria: vaccination by two doses of BNT162b2 mRNA COVID-19 vaccine.

Exclusion criteria: vaccination terminated before pregnancy

IV. Laboratory Methods

In our study, the in vitro qualitative and quantitative determination of antibodies against SARS-CoV-2 viral protein S receptor domain in serum samples was performed by using an electrochemiluminescence immunoassay.

The Eclia ® Anti-SARS-CoV-2 assay (Roche Diagnostics Switzerland) was used to detect the presence of antibodies against SARS-CoV-2 viral protein S receptor domain. Assays were performed according to the manufacturer's instructions. Chemiluminescent emission was measured using a photomultiplier Cobas e immunoassay analyzer (Cobas e411, Roche Diagnostics Switzerland). The results from Eclia® was quantified using the software automatically by comparing the electrochemiluminescence signal generated from the sample reaction product with the reference range level signal previously derived by calibration and defined as positive if >0,9.

V. Results

In a current study all pregnant woman vaccinated during pregnancy by BNT162b2 mRNA COVID-19 vaccine have revealed significant positive correlation between maternal and umbilical cord antibody titer, both specimens revealed significantly high titer of antibodies from reference range with unremarkable differences between maternal and cord antibody titers. Antibodies against SARS-CoV-2 protein S receptor domain were identified in all maternal and neonatal cord samples (n=13). All samples revealed titer significantly higher than reference range data (>0.9 positive). The mean maternal blood sample antibody titer against SARS-CoV-2 protein S receptor domain was 1879 (>0.9 positive). The mean umbilical cord blood sample antibody titer against SARS-CoV-2 viral S protein was 1672. The mean interval between the second dose of the vaccine and delivery was 18 weeks.

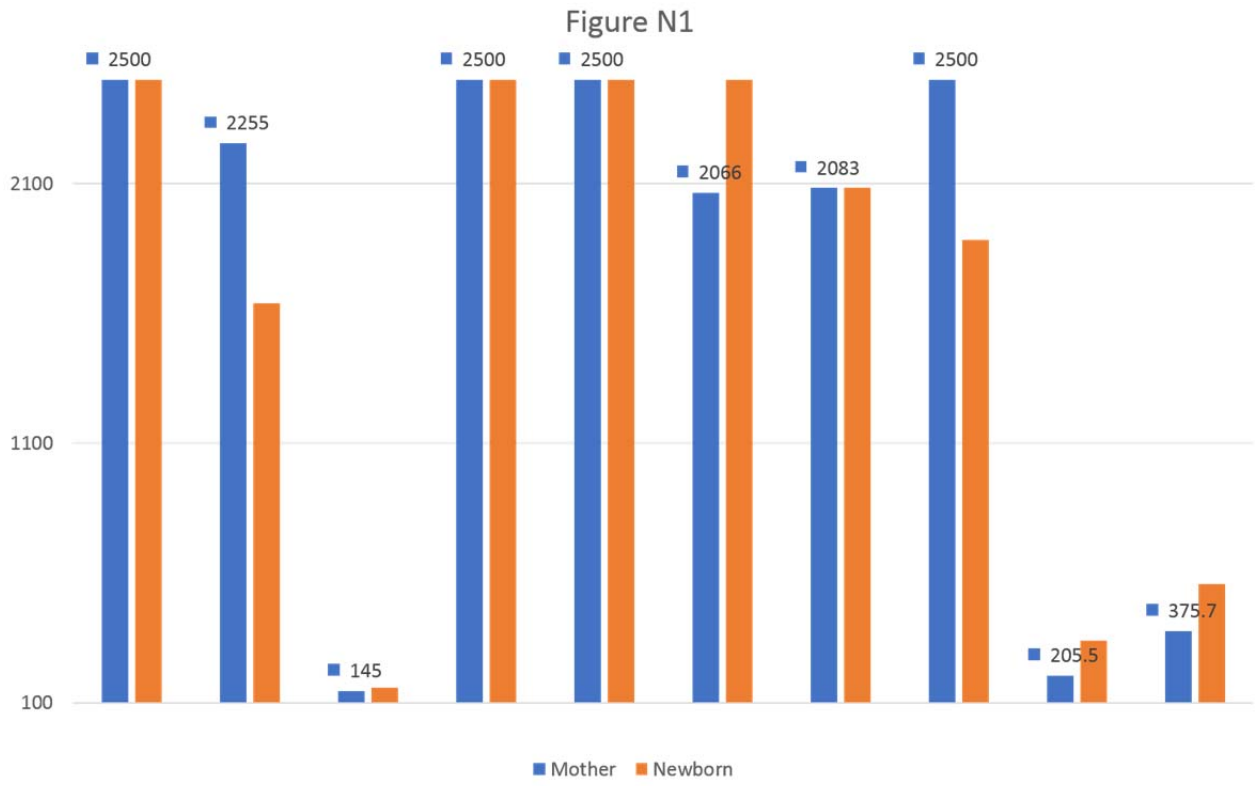

Figure 1

It is important to note that the correlation coefficient of the number of weeks from the second dose to delivery as − 0.7. That showed statistically insignificant data. Better correlation between maternal and neonatal antibody titer has been found in the cases of antenatal vaccination in the late second and/or early third trimester vaccination. No significant variations were reported in anti-S antibody titers based on maternal age, extragenital diseases and/or the interval between vaccine doses.

VI. Discussion

In all maternal serum specimen antibodies against Sars-Cov-2 viral protein S receptor domain was significantly high than reference range. Study results revealed strong correlation between maternal and cord blood antibodies titer, both were significantly high from reference range with unremarkable differences of the titers. Figure N 1.

The results of our study reveal high titers of antibodies against Sars-Cov-2 viral protein S receptor domain in cord blood collected after birth, suggesting that maternal immunization may provide protection to newborns through the trans placental transfer of antibodies that provide immunity against COVID-19in newborns but requires farther investigations. The American College of Obstetricians and Gynecologists, the Centers for Disease Control and Prevention, and the Society for Maternal-Fetal Medicine published statements supporting COVID-19 vaccine administration to pregnant individuals (6-12). Cord serum samples from all newborns included in our study showed the presence of specific antibodies against SARS-CoV-2 viral protein S domain and good correlation between weeks of gestation on vaccination and delivery for the production of fetal antibodies. Similar study results have been published by Vilajeliu et al. vaccination performed in the late second or third trimester of pregnancy, were associated to the presence of post-vaccination antibodies in 94% of newborns (15).

VII. Conclusion

In our study vaccination against SARS-Cov-2 viral infection during pregnancy is accompanied with adequate production of antibodies that probably may defense neonates from severe infection. Study has revealed positive correlation between time interval of vaccination and delivery for the presence of high titers of SARS-Cov-2 viral protein S receptor domain antibodies in

neonatal cord blood, which may allow future determination of the optimal timing of COVID-19 vaccination in pregnant women although this problem need more future studies.

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