Covid-19 Induced Neonatal Immunity

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Abstract – December 2019 a few cases of severe pneumonia was detected in Wuhan, China The patients were exhibiting symptoms like fever, dry cough, sore throat, breathlessness, and fatigue. investigation employing next generation sequencing and phylogenetic analysis led to the identification of the causative agent of this respiratory disease, a novel coronavirus 2019 [1]. As more cases started to appear around the world, on February 11, 2020, the World Health Organization assigned a name, Corona Virus Disease 2019 or COVID-19, to the disease and declared it a pandemic on March 11, 2020. The virus was renamed from 2019-nCoV to SARS-CoV-2 by the International Committee on Taxonomy of Viruses on the basis of its genetic similarity to a previously known coronavirus, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) [2].

Coronavirus 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome SARS-CoV-2, has resulted in more than six million deaths and has infected over 500 million people as of July 19, 2022 [3]. SARS-CoV-2 infected pregnant women are at increased risk of severe COVID-19 than non-pregnant women and have a higher risk of adverse pregnancy outcomes like intrauterine/fetal distress and preterm birth.

The most severe outcomes of COVID-19 have been documented in geriatric individuals and pregnant women with chronic diseases, including hypertension, diabetes, and cardiopulmonary problems [4]. Newborn protection from infection is primarily dependent on neonatal innate immune responses and maternally derived, transplacentally acquired antibodies. The extent to which maternal antibodies produced in response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy cross the placenta is important for understanding potential neonatal protection from coronavirus disease 2019 (COVID-19.

We investigated humoral responses to SARS-CoV-2 in maternal and cord blood paired samples in the case of natural infection during late second and third trimesters of pregnancy recruited at TSMU Department of Obstetrics and Gynecology TSMU First University Clinic. Georgia, Tbilisi. Maternal nasopharyngeal swabs were collected for SARS-CoV-2 detection by rate-PCR for confirmation of viral infection at the admission to the hospital. We measured IgG to spike (S) receptor-binding domain and nucleocapsid (N) Sixty-eight pregnant women SARS-CoV-2 positive by rRT-PCR were included in our study. Serology samples of maternal and cord blood has been collected immediately after delivery. For study design we have determined inclusion and exclusion criteria's. General medical data of patients included in the study have been collected from medical records and Informed written consent was obtained from all the patients involved in the study. SARS-CoV-2, IgG has been detected by ELISA method.

infected mothers had increased levels of virus-specific antibodies maternal IgG levels showed positive correlations with their counterparts in cord blood. PCR positive mothers showed stronger effect when infection was closer to delivery.

Our results show that SARS-CoV-2 infection during the second and third trimester of pregnancy induces antibody response at delivery and causes lower level of the SARS-CoV-2-specific IgG trans placental transfer, when the infection is closer to delivery.

Keywords – Covid-19, Pregnancy, Immunity.

I. INTRODUCTION

December 2019 a few cases of severe pneumonia was detected in Wuhan, China The patients were exhibiting common symptoms like fever, dry cough, sore throat, breathlessness, and fatigue. investigation employing next generation sequencing and phylogenetic analysis led to the identification of the causative agent of this respiratory disease, a novel coronavirus 19 [1]. As more cases started to appear around the world, on February 11, 2020, the World Health Organization assigned a name, Corona Virus Disease 2019 or COVID-19, to the disease and declared it a pandemic on March 11, 2020. The virus was renamed from 2019-nCoV to SARS-CoV-2 by the International Committee on Taxonomy of Viruses on the basis of its genetic similarity to a previously known coronavirus, Severe Acute Respiratory Syndrome Coronavirus (SARS-Cov-19) [2].

Coronavirus 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome SARS-CoV-2, has resulted in more than six million deaths and has infected over 500 million people as of July 19, 2022 [3]. SARS-CoV-2 infected pregnant women are at increased risk of severe COVID-19 than non-pregnant women and have a higher risk of adverse pregnancy outcomes like intrauterine/fetal distress and preterm birth.

The most severe outcomes of COVID-19 have been documented in geriatric individuals and pregnant women with chronic diseases, including hypertension, diabetes, and cardiopulmonary problems, or with some other respiratory viral infections [4].

The immune status of pregnant women adapts to tolerate the fetus by changing the cellular composition and the functions of immune cells. T cell-mediated immunity and humoral responses are suppressed [5], As a consequence, pregnant women are at increased risk of morbidity and mortality from respiratory viral infections [6–7]. Several studies show that pregnant women with COVID-19 are more likely to be hospitalized and have increased rates of ICU admissions and mechanical ventilation compared with non-pregnant women with COVID-19, resulting in a higher risk of mortality [8–9]

Newborn protection from infection is primarily dependent on neonatal innate immune responses and maternally derived, transplacentally acquired antibodies. The extent to which maternal antibodies produced in response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy cross the placenta is important for understanding potential neonatal protection from coronavirus disease 2019 (COVID-19. The maternal inflamatory response induced by SARS-CoV-2 infection may also have deleterious effects on the offspring. Although vertical transmission has been hardly observed in SARS-CoV-2 to date [10].

Maternal infection may also alter the ability of antibodies to transfer across the placenta as has been shown for other infections like HIV, Zika [11] and recently in COVID-19 [12]

II. AIM OF THE STUDY

was determine the pattern of transplacental transfer of viral specific immunoglobulins, IgG to spike (S) receptor-binding domain and nucleocapsid (N) from naturally infected mothers to neonate via umbilical cord blood. The paper presents preliminary results of the study proceeded in the department.

III. MATERIAL AND METHODS

Sixty-eight pregnant women naturally infected with SARS-CoV-2 infection during different gestational age have been included in the study. All patients participating in this study were SARS-CoV-2 positive by PCR during admission to the hospital in their late second and/or third trimester of the pregnancy. The patients had voluntarily included in our study. Informed written consent was obtained from all the patients involved in the study. General medical data of patients included in the study have been collected from medical records and are shown in the Table N1. Collection of the maternal and umbilical cord blood has been done immediately after delivery by professional midwife after instructions from laboratory responsible for testing.

Inclusion criteria:1) women with a positive SARS-CoV-2 PCR; 2) symptoms consistent with SARS-CoV-2 infection (high temperature, fatigue, muscular pain, diarrhea, taste and smell loss, cough, diveficult breathing, pneumonia).

Table 1. General medical data of patients included in the study

Mean age	28 years
Extra genital diseases	1 case – Diabetes, hypertension, osteochondrosis
	1 case – hypothyroidism and coxarthrosis
	1 case – idiopathic thrombocytopenia, ovarian drilling, diabetes, hypothyroidism
	1 case – nephrolithiasis
	1 case – salpingectomy due to ectopic pregnancy
Parity	18 cases of primiparity
	31 cases of multiparty
Covid -19 infection during pregnancy	All of the cases
Way of delivery vaginal/CS	12 cases of caesarian section
	37 cases of vaginal uncomplicated delivery
Gestation during delivery	46 cases of term delivery
	3 cases of preterm delivery 36 w
Neonatal gender	21 females
	28 males
Neonatal weight	48 cases of normal weight
	1 case -2200 gr
Need for NIC	1 case of referral to NICU
Gestation singleton/multiply	All singleton

IV. RESULTS

We have assessed the effect of the SARS-CoV-2 infection on the IgG transplacental transfer. In observed samples IgG levels in cord blood showed differences depending on the maternal PCR status during the third trimester and the time gap between viral infection and delivery. The PCR positive mothers during the third trimester or near to the delivery revealed transfer of fewer anti-SARS-CoV-2 IgG to cord blood. Lower anti-SARS-CoV-2 IgG levels observed in cord blood in recent compared to past infections reveals that interval between infection and anti-SARS-CoV-2 IgG transplacental transfer plays important role.

Our study has revealed that the IgG transfer at birth is lower for third trimester infection as compared to second-trimester infections as effective production of specific IgG takes longer time from the moment of esquire the infection. This could be because the mother has been seropositive for a shorter period, therefore maternal antibody levels may have not reached the peak and there has been less time for transfer of antibodies through the cord blood.
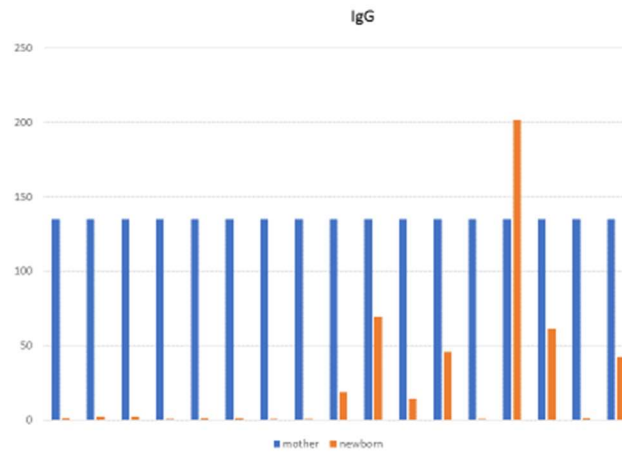
As a conclusion of our study we suggest that SARS-CoV-2 infections closer to term have a stronger negative impact on the IgG transplacental transfer. Thus maternal infection closer to the delivery provides poor immune defense of neonate from SARS-CoV-2 infection.

REFERENCE

[1] Zhou P, Yang X-L, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. (2020) 579:270–3. doi: 10.1038/s41586-020-2012-7

[2] Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. (2020) 395:565–74. doi: 10.1016/S0140-6736(20)30251-8

[3] WHO. WHO coronavirus disease (COVID-19) dashboard . Available at: https://covid19whoint/ (Accessed 11 April 2021).

[4] Kumar R, Yeni CM, Utami NA, Masand R, Asrani RK, Patel SK, et al. SARS- CoV-2 infection during pregnancy and pregnancy-related conditions: Concerns, challenges, management and mitigation strategies-a narrative review. J Infect Public Health [Internet] (2021) 14(7):863–75. doi: 10.1016/j.jiph.2021.04.005

[5] Aghaeepour N, Ganio EA, Mcilwain D, Tsai AS, Tingle M, van Gassen S, et al. An immune clock of human pregnancy. Sci Immunol (2017) 2(15):eaan2946. doi: 10.1126/sciimmunol.aan2946

[6] Jamieson DJ, Honein MA, Rasmussen SA, Williams JL, Swerdlow DL, Biggerstaff MS, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. Lancet. (2009) 374(9688):451–8. doi: 10.1016/S0140-6736(09)61304-0

[7] Mullins E, Evans D, Viner RM, O'Brien P, Morris E. Coronavirus in pregnancy and delivery: rapid review. Ultrasound obstetrics gynecology (2020) 55 (5):586–92. doi: 10.1002/uog.22014

[8] Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - united states, January 22-June 7, 2020. MMWR Morb Mortal Wkly Rep (2020) 69(25):769–75. doi: 10.15585/mmwr.mm6925a1

[9] WAPM. Maternal and perinatal outcomes of pregnant women with SARS- CoV-2 infection. Ultrasound Obstet Gynecol (2021) 57(2):232–41. doi: 10.1002/ uog.23107

[10] Perlman JM, Salvatore C. Coronavirus disease 2019 infection in newborns. Clin Perinatol (2022) 49(1):73–92. doi: 10.1016/j.clp.2021.11.005

[11] Castanha PMS, Souza W v, Braga C, de Arau̇jo TVB, Ximenes RAA, Albuquerque MdeFPM, et al. Perinatal analyses of zika- and dengue virus- specific neutralizing antibodies: A microcephaly case-control study in an area of high dengue endemicity in Brazil. PLoS Negl Trop Dis (2019) 13(3):e0007246. doi: 10.1371/journal.pntd.0007246

[12] Edlow AG, Li JZ, Collier ARY, Atyeo C, James KE, Boatin AA, et al. Assessment of maternal and neonatal SARS-CoV-2 viral load, transplacental antibody transfer, and placental pathology in pregnancies during the COVID-19 pandemic. JAMA Netw Open (2020) 3(12):e2030455. doi: 10.1001/ jamanetworkopen.2020.30455