



ORIGINAL RESEARCH PAPER

Obstetrics & Gynecology

CORD BLOOD IGG ANTIBODIES AGAINST SARS COV-2 IN PREGNANT WOMEN AT A RURAL TEACHING HOSPITAL

KEY WORDS: Covid- 19, SARS- Cov 2 Antibodies, Maternal, Neonatal

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ABSTRACT

Introduction: The significant risks posed to mothers and fetus by COVID-19 in pregnancy have sparked a worldwide debate surrounding the antenatal SARS-CoV-2 infection and vaccination. ACOG and CDC recognize pregnancy as a risk factor, Recent data demonstrated that pregnant women with COVID-19 infection are at increased risk for intensive care unit (ICU) admission, mechanical ventilation, and death, compared with properly matched nonpregnant women. Moreover, COVID-19 illness increases the risk for pregnancy complications such as preterm birth, pregnancy-induced hypertensive diseases, and thromboembolic diseases. Maternal IgG antibodies to SARS-CoV-2 were transferred across the placenta after asymptomatic as well as symptomatic infection during pregnancy. Proper transfer of neutralizing antibodies may be critical during pregnancy, as a greater proportion of neonates and infants have severe or critical illness upon COVID-19 infection than older pediatric counterparts. **Aims and Objectives:** To detect cord blood IgG antibodies against SARS CoV-2 in pregnant women. To assess the association between maternal and fetal SARS-CoV-2 specific antibodies. **Methods:** A brief questionnaire was administered to 42 antenatal women attending for delivery at Medicit Institute of Medical Sciences, Hyderabad, Telangana State. The questionnaire included information such as vaccination status, previous history of Covid infection, presence of any symptoms at the time of admission, comorbid conditions like DM, HTN, Thyroid disorders, etc. Following delivery, 2ml cord blood sample has been collected. Serum has been separated and used for detection of SARS CoV-2 IgG antibody titers by quantitative ELISA. **Results:** Among 42 antenatal cases, 4 were controls among them two were positive control and two were negative controls. Out of remaining 38, the SARS-CoV-2 IgG antibodies are detected in 14 cases. IgG was detected in the cord blood for 33.3% of the total cases. Among those detected positive for antibodies, 50% had preterm deliveries. **Conclusion:** IgG antibodies have been detected in the cord blood collected from the vaccinated women as well as the women affected with SARS-Co-2 and even increased the risk for pregnancy complications such as preterm birth, pregnancy-induced hypertensive diseases, Gestational Diabetes.

INTRODUCTION

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus^{1,7}. The significant risks posed to mothers and fetus by COVID-19 in pregnancy have sparked a worldwide debate surrounding the antenatal SARS-CoV-2 infection and vaccination. ACOG and CDC recognize pregnancy as a risk factor^{1,3}.

Physiological changes during pregnancy have a significant impact on the immune system, respiratory system, cardiovascular function, and coagulation. These may have positive or negative effects on COVID-19 disease progression¹⁶.

Nearly 48% of pregnant women affected with COVID-19 required ICU admission, pregnant women are at more risk of severe illnesses particularly in the third trimester which increases the mortality rate among pregnant women¹³. COVID-19 illness increases the risk for pregnancy complications such as preterm birth, pregnancy-induced hypertensive diseases, and thromboembolic diseases, still birth(0.4 to 0.6%), ruptured ectopic pregnancies, maternal depression, congenital anomalies, risk of miscarriage^{4, 14}.

Recent studies along with Ministry Of Health & Family welfare(MOHFW) and National Institute For Research In

Reproductive Health(NIRRH) demonstrated that vertical transmission seems to be uncommon and unaffected by mode of birth, feeding choice^{10,11,19}. Most of the new-borns of SARS-CoV-2 positive mothers have been born with good APGAR score, asymptomatic at birth². Early neonatal death was seen in 0.2 to 0.3%¹⁵.

The present study was to estimate the prevalence of transfer of SARS CoV-2 immunoglobulin (Ig) G to newborns who delivered at MediCiti Institute of Medical Sciences.

MATERIALS AND METHODS:

A brief questionnaire was administered to 42 antenatal women attending for delivery at MediCiti Institute of Medical Sciences Hyderabad, Telangana from November 2021 to December, 2021. The questionnaire included information such as vaccination status, previous history of Covid infection, presence of any symptoms at the time of admission, comorbid conditions like DM, HTN, Thyroid disorders, etc.

Following delivery, 2ml cord blood sample has been collected. Serum has been separated and stored it at -40 degree Fahrenheit and used for detection of SARS CoV-2 IgG antibody titers by quantitative ELISA (QUALISA).

Use Of Qualisa :-

QUALISATM COVID-19 IgG ELISA assay is intended for the qualitative in-vitro detection of novel coronavirus infected cases. The cases are screened based on the detection of human antibodies (IgG) specifically against new corona virus(SARS-CoV-2) in serum/plasma from COVID-19 suspected/infected person.

Principle Of Qualisa:-

QUALISATM COVID-19 IgG is an Enzyme Linked Immunosorbent Assay(ELISA) that employs purified recombinant antigens representing most conserved antigenic segments of S1 protein.

Microwell strips are coated with recombinant antigens representing Receptor Binding Domain(RBD) antigen of SARS-CoV-2. Samples along with positive and negative controls are added in the coated wells and incubated. The wells are washed to remove unbound components and anti-human IgG conjugated to horseradish peroxidase (HRPO) is added. After a short incubation wells are washed again and bound enzyme is detected by adding substrate. The reaction is stopped after specified time with acid and absorbance is determined for each well at 450nm with an ELISA reader. The cutoff value is calculated by the given formula and results are interpreted by calculating the Covid IgG Index.

Statistical Analysis:

Information collected was entered into MS-Office Microsoft excel 2010 spread sheet. This raw data was exported to SPSS version 16 for analysis. Descriptive data was presented in measured in percentages.

RESULTS:

Cord blood was collected from 42 women delivered at MediCiti Institute of Medical Sciences, Hyderabad. Four samples were taken as controls. SARS Cov 2 IgG antibodies were detected in 14 women with a prevalence of 33.3%. Among 14 women, one mother was partially vaccinated against COVID-19. Only one woman had a history of COVID - 19 infection in the first trimester. Asymptomatic infection was seen in 12 (85%) women. Table 1 shows characteristics of study population. Most of the women in the study population were less than 25 years of age as the study was conducted in a rural teaching hospital where women get married and conceive soon. However, 76.3% of women were literate and belonged to middle class. Normal weight was seen in 42% of women followed by overweight (31.5%). Sixty five percent of women delivered vaginally. There was a preponderance of male babies in the study. Among women who tested Ig G positive against SARS Cov 2, 50% had preterm deliveries. Gestational diabetes mellitus was seen in 25% of women and gestational hypertension in 13 % of women. Pie diagram shows the maternal complications.

DISCUSSION:

The protection of newborns from infection mainly depends on neonatal immune responses and maternally derived transplacentally acquired antibodies⁶. In the context of the ongoing COVID-19 pandemic, it is essential to know which maternally produced antibodies in response to either SARS-CoV-2 infection or SARS-CoV-2 vaccination cross the placenta during the pregnancy⁶. The knowledge will help establish maternal vaccination strategies. Maternal immunization protects both the mother and fetus from the morbidity of certain infections. It can also provide passive infant protection against vaccine-preventable infections acquired independently after birth.

Pathophysiology :-

Receptor Binding Domain (RBD) of spike protein binds to ACE-2 (entry receptor) which results in infection. IgG antibodies that bind to the RBD of the spike protein helps to determine the immune response to the virus. Our study evaluates presence of IgG antibody in cord blood of

newborns born to women delivered at MediCiti Institute Of Medical Sciences irrespective of the vaccination status and who contracted SARS-CoV-2 infection during pregnancy. The limitations of our study include the relatively small sample size, the low availability of the samples adequate for estimation of anti- SARS-CoV-2 antibodies and the lack of correlation to the presence of antibodies in breastmilk. And lack of quantification of antibody titers.

Recently, Flannery et al. conducted a study among the 83 SARS-CoV-2 seropositive pregnant women, anti-SARS-CoV-2 IgG antibodies were detected in 72 (87%) born babies' cord blood. And cord blood IgG concentrations were corelates positively with maternal IgG concentrations and that placental transfer ratios were more than 1 among mothers with asymptomatic SARS-CoV-2 infection or symptomatic infection. They also said that antibody transfer ratios increased with increasing time between the onset of maternal infection and delivery time⁶.

Lior Kashani-Ligumsky, Miriam Lopian, et al , have conducted a study on Titers of SARS CoV-2 antibodies in cord blood of neonates whose mothers contracted SARS CoV-2 (COVID-19) during pregnancy (group 1) and in those whose mothers were vaccinated with mRNA to SARS CoV-2 during pregnancy (group 2) and concluded that Antibodies against SARS-CoV-2 spike protein were detected in all samples from Group 1 and 2 And concluded that Neonates born to mothers vaccinated during pregnancy have higher antibody titers and may therefore have more prolonged protection than those born to women infected during pregnancy¹².

Paul Gilbert MD et al conducted a study on presence of Antibodies to SARS-CoV-2 detected in cord blood after maternal vaccination show that SARS-CoV-2 IgG antibodies are detectable in a newborn's cord blood sample even after a single dose of vaccination¹⁷.

Dustin D. Flannery, DO, MSCE et al done a study on Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios amd concludes that maternal IgG antibodies to SARS-CoV-2 were transferred across the placenta after asymptomatic as well as symptomatic infection during pregnancy⁶.

Isabel Villegas-Mota, Arredondo-Pulido et al conducted a study on Cord Blood SARS-CoV-2 IgG Antibodies and Their Association With Maternal Immunity and Neonatal Outcomes on 100 women in which 21 women who were seropositive at delivery and the newborn born to seropositive women 16 were tested positive for anti-SARS-CoV-2 IgG antibodies in cord blood⁸.

Megan E. Trostle, Maria E. Agüero-Rosenfeld et al, conducted a study on antibody levels in cord blood from pregnant women vaccinated against COVID-19 and concluded that transplacental passage of immunoglobulin (Ig) G antibodies to the SARS-CoV-2 virus occurs following natural infection and antibody transfer may even occur following COVID-19 messenger RNA (mRNA) vaccination¹⁸.

CONCLUSION:

Although 83.3% women had neither a history of SARS-COV-2 infection nor vaccination, 31.5% of the neonates had IgG antibodies against SARS-COV-2 probably suggesting an asymptomatic infection in the mother. Any symptoms of COVID 19 infection in infancy or childhood of neonates with positive IgG antibody, should raise a suspicion regarding asymptomatic infection in the mother.

Further studies are needed to determine if SARS-CoV-2 antibodies are protective against newborn infection; if so, at what concentration; and whether the transplacental kinetics of vaccine-elicited antibodies are similar to naturally

acquired antibodies. Additionally, serial total antibody measurements may be used to determine how long protection is expected which may help to determine when the best time would be to begin vaccination in newborns born to mothers who received a vaccine for SARS-CoV-2.

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Conflicts of interest: None declared

Table 1: Baseline characteristics of study population

Variables	Number
Age (Years)	
≤25	27 (71%)
25- 34	10 (26%)
35-45	1 (2%)
Literacy	
Illiterate	9 (23.6%)
Literate	29 (76.3%)
Socioeconomic status	
Lower, Lower middle	13 (34.2%)
Middle	14 (36.8%)
Upper, Upper Middle	10 (26.3%)
BMI (Kg/m ²)	
≤ 18.4	9 (23.6%)
18.5-22.9	16 (42.1%)
23-27.4	12 (31.5%)
≥ 27.5	1(2%)
Gravida	
Primi	14 (36.8%)
Multi	24(63.1%)
Gestational age in weeks at birth	
Preterm	19 (50%)
Term	19(50%)
Mode of delivery	
LSCS	13 (34.2%)
Vaginal	25(65.7%)
Sex of the neonate	
Female	16 (42.1%)
Male	22 (57.8%)

REFERENCES:

- 1) ACOG and SMFM Joint Statement on WHO Recommendations Regarding COVID-19 Vaccines and Pregnant Individuals. Accessed May 26, 2021. <https://www.acog.org/en/news/news-releases/2021/01/acog-and-smfm-joint-statement-on-who-recommendations-regarding-covid-19-vaccines-and-pregnant-individuals>.
- 2) Berghella V, Hughes B. COVID-19" pregnancy issues and antenatal care. Update May 14, 2021
- 3) Centers for Disease Control Prevention. Investigating the Impact of COVID-19 during Pregnancy. (2022). Available online at: <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/pregnancy-data-on-covid-19/what-cdc-is-doing.html> (accessed April 27, 2022).
- 4) Chmielewska B, Barratt I, Townsend R, Kalafat E, van der Meulen J, Gurole-Urganci I, O'Brien P, Morris E, Draycott T, Thangaratnam S, Le Doare K, Ladhani S, von Dadelszen P, Magee L, Khalil A. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. *Lancet Glob Health*. 2021 Mar 31;S2214-109X(21)00079-6. doi: 10.1016/S2214-109X(21)00079-6. Epub ahead of print. PMID: 33811827; PMCID:PMC8012052..
- 5) Dong L., Tian J., He S., Zhu C., Wang J., Liu C., Yang J. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. *Jama*. 2020;323(18):1846–1848. [PMC free article] [PubMed] [Google Scholar]
- 6) Flannery DD, Gouma S, Dhudasia MB et al. **Assessment of maternal and neonatal cord blood SARS-CoV-2 antibodies and placental transfer ratios**, *JAMA Pediatr*. 2021.
- 7) Government of India, Ministry of Health & Family Welfare, Directorate General of Health Services (EMR Division). Revised Guidelines on Clinical Management of COVID-19. [Online] March 31, 2020. Accessed on April 5, 2020.
- 8) Helguera-Repetto AC, Villegas-Mota I, Arredondo-Pulido GI, Cardona-Pérez JA, León-Juárez M, Rivera-Rueda MA, Arreola-Ramírez G, Mateu-Rogell P, Acevedo-Callegos S, López-Navarrete CE, Valdespino-Vázquez MY, Martínez-Salazar G, Rodríguez-Bosch M, Coronado-Zarco IA, Castillo-Cutiérrez MDR, Cuevas-Jiménez CA, Moreno-Verduzco ER, Espino-Y-Sosa S, Cortés-Bonilla M, Irlés C. Cord Blood SARS-CoV-2 IgG Antibodies and Their Association With Maternal Immunity and Neonatal Outcomes. *Front Pediatr*.

- 2022 Jun 29;10:883185. doi:
- 9) Hayakawa S., Komine-Aizawa S., Mor G.G. Covid-19 pandemic and pregnancy. *J. Obstet. Gynaecol. Res.* 2020;46(10):1958–1966. [PMC free article] [PubMed] [Google Scholar]
- 10) Lamouroux A, Attie-Bitach T, Martinovic J, Leruez-Ville M, Ville Y. Evidence for and against vertical transmission for SARS-CoV-2 (COVID-19). *Am J Obstet Gynecol*. [Internet]. 2020 [cited 2020 June 16]; DOI:10.1016/j.ajog.2020.04.039.14
- 11) Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. SARS-CoV-2 Infection in children. *NEJM*. 2020;382:1663-5 DOI:10.1056/NEJMc2005073
- 12) Lopian M, Cohen R, Senderovich H, Czeiger S, Halperin A, Chaim AB, Kremer I, Lessing JB, Somekh E, Neiger R. Correction to: Titers of SARS CoV-2 antibodies in cord blood of neonates whose mothers contracted SARS CoV-2 (COVID-19) during pregnancy and in those whose mothers were vaccinated with mRNA to SARS CoV-2 during pregnancy. *J Perinatol*. 2021 Nov;41(11):2696. doi: 10.1038/s41372-021-01272-7. Erratum for: *J Perinatol*. 2021 Nov;41(11):2621-2624. PMID: 34876672; PMCID: PMC864998.
- 13) Mahajan, Niraj N. MD; Pophalkar, Madhura MS; Patil, Sarika MPhil; Yewale, Bhagyashree MBBS; Chaithanya, Itta Krishna PhD; Mahale, Smita D. PhD; Gajbhiye, Rahul K. MBBS, PhD **Pregnancy Outcomes and Maternal Complications During the Second Wave of Coronavirus Disease 2019 (COVID-19) in India**, *Obstetrics & Gynecology*: July 7, 2021 - Volume - Issue - 10.1097/AOG.0000000000004529 doi: 10.1097/AOG.0000000000004529
- 14) Mullins E, Hudak ML, Banerjee J, Getzlaff T, Townson J, Barnette K, et al., PAN-COVID investigators and the National Perinatal COVID-19 Registry Study Group.
- 15) Pregnancy and neonatal outcomes of COVID-19: coreporting of common outcomes from PAN-COVID and AAP-SONPM registries. *Ultrasound Obstet Gynecol*. 2021 Apr;57(4):573-581. doi: 10.1002/uog.23619. PMID: 33620113; PMCID:PMC8014713
- 16) Pereira NZ, Oliveira LMDS, Gozzi-Silva SC, Sato MN. Pregnancy, viral infection, and COVID-19. *Front Immunol*. 2020;11:1672. doi: 10.3389/fimmu.2020.01672.
- 17) Paul G, Chad R. Newborn antibodies to SARS-CoV-2 detected in cord blood after maternal vaccination - a case report. *BMC Pediatr*. 2021 Mar 22;21(1):138. doi: 10.1186/s12887-021-02618-y. PMID: 33752624; PMCID: PMC7982334.
- 18) Trostle ME, Agüero-Rosenfeld ME, Roman AS, Lighter JL. High antibody levels in cord blood from pregnant women vaccinated against COVID-19. *Am J Obstet Gynecol* MFM. 2021 Nov;3(6):100481. doi: 10.1016/j.ajogmf.2021.100481. Epub 2021 Sep 22. PMID: 34562636; PMCID: PMC8455300.
- 19) Yang Z, Liu Y. Vertical transmission of severe acute respiratory syndrome Coronavirus 2: a systematic review. *Am J Perinatol*. [Internet]. 2020 [cited May 13]; DOI:10.1055/s-0040-1712161.15