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Estimation of SARS-COVID antibody level in mother and newborn baby among mothers affected by covid during the antenatal period

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ABSTRACT

Background: Severe acute respiratory syndrome-coronavirus-2 infection increases the incidence of severe coronavirus disease-19 (COVID-19) in pregnant women. An increased risk of stillbirth and problems such as preeclampsia, preterm birth, and neonatal intensive care unit hospitalization may be caused by COVID-19 during pregnancy which might lead to an increased risk of COVID-19 mortality, admission to an intensive care unit, and mechanical ventilation. **Aims and Objectives:** To estimate SARS-COVID antibody level in mother and newborn baby among mothers affected by covid during the antenatal period. **Materials and Methods:** This is a prospective cross-sectional study conducted at Sri Ramachandra Institute of Higher Education and Research from June 2021 to September 2021. A total of 30 women, affected with SARS-COVID during the antenatal period, confirmed with reverse transcription-polymerase chain reaction testing were included in this study. Blood samples were collected from mothers at the time of delivery and cord blood sample was used for antibody detection in mothers and neonates respectively. **Results:** Severe infection was noted in 5 women (16.6%) who required oxygen supplementations, and 2 of them required heparin therapy. Women with severe illness showed decreased antibody levels-total antibody (≤500–100%), and neutralizing antibody (≤1000–60%), but statistical significance was not proved. Hence, antibody levels did not correlate with the severity of illness. **Conclusion:** The current study has demonstrated that women who were pregnant during the COVID-19 pandemic had good knowledge, attitudes, and practices. It is thought that these positive aspects will be beneficial to expectant mothers who are going through pregnancy while still adhering to health protocols or advice from medical professionals on how to carry a pregnancy safely amid this COVID-19 epidemic.

Key words: Coronavirus; Coronavirus disease-19; Pregnancy; Severe acute respiratory syndrome-coronavirus-2

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INTRODUCTION

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection increases the incidence of severe coronavirus disease-19 (COVID-19) in pregnant women. An increased risk of COVID-19 mortality, admission to an intensive care unit, and mechanical ventilation are linked to pregnancy.[1] An increased risk of stillbirth and problems such as preeclampsia, preterm birth, and neonatal intensive care unit hospitalization may be caused by COVID-19 during pregnancy.[2,3] Infants are at risk of hospitalization due to SARS-CoV-2 infection, even though newborns appear to have a lower risk of developing severe COVID-19. There have also been accounts of serious neonatal infections and deaths that can be attributed to them.[4-8] SARS-COV-2 is a group of coronaviruses which cause COVID-19. It has been causing a lot of morbidity and mortality, especially after the second wave to the most vulnerable group the pregnant women. It has been seen to affect multiple systems including respiratory, gastrointestinal, and nervous systems. Transmission is mainly by respiratory route.[9] The clinical feature ranges from fever, sore throat, myalgia to

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breathlessness, acute respiratory distress, and diarrhea.[10] The laboratory findings include lymphopenia, elevated C-reactive protein, erythrocyte sedimentation rate, D-dimer, Sr. ferritin, and fibrinogen. Specific diagnosis is made by detecting viruses in the oropharyngeal using PCR. Computed tomography also detects infection to a larger extent when the lungs are involved.[11] Symptomatic women are found to have poorer outcomes including abortions, preterm labor, preeclampsia, eclampsia, and intrauterine death when there is a necessity of intensive care for mother.[12] Transplacental route of transmission of SARS-COVID-19 is rare in early pregnancy as the fetus does not exhibit ACE 2 receptor. However, the placenta has ACE 2 receptor which had shown a positive of SARS-COVID-19 in affected mothers in the last trimesters. Most of the affected neonates were delivered before term; however, most of the neonates are found to be asymptomatic or with mild disease.[13] Transplacental transmission of Immunoglobulin G (IgG) is observed in neonates of SARS-COVID-19-infected mothers during pregnancy. In some neonates, IgM is also elevated. Being a macromolecular structure it usually does not cross the placenta. Hence this represents the transmission of the virus through the placenta.[14] About 87% transmission of antibodies is seen from COVID-affected mothers to neonates. The transmission is not related to the severity of COVID infection in mothers. The early the onset of infection during the antenatal period, higher the chances of transmission of antibodies to the neonates. The infants were found to have protection against SARS-COVID-19 when compared to other infants.[15] IgG antibodies from the vaccinated mother are transferred through the placenta. The antibody titer is high in antenatal mothers who received two doses of the vaccine when compared to antenatal mothers who received one dose of vaccine.[16]

Aims and objectives

Our study aims to estimate SARS-COVID antibody level in mother and newborn baby among mothers affected by covid during the antenatal period.

MATERIALS AND METHODS

This is a prospective cross-sectional study conducted at Sri Ramachandra Institute of Higher Education and Research from June 2021 to September 2021 A sample size of 30 was required to get a mean of 4.69, standard deviation of 1.45 with 12% relative precision, 95% confidence level. The sample size was calculated based on my parent article, based on IgG values. Mother who is affected by SARS-COVID-19 6 weeks before delivery and new-born of those mothers were included in this study. Mothers who had SARS-COVID-19 during their antenatal period confirmed with reverse transcription-polymerase chain reaction (RT-PCR) testing formed the study population. Their duration and severity of symptoms, need for hospitalization, and treatment given were noted. They were followed up during their antenatal period for other secondary outcomes during pregnancy. At the time of delivery, 2 mL of cord blood samples of the newborn and venous blood samples of mother were collected in red vacutainers. The samples were sent to the microbiology laboratory, where the blood samples were tested for SARS-COVID-19 antibodies. The samples were assessed for neutralizing antibodies with Abbott's ARCHITECT antibody test using Chemiluminescent Microparticle Immunoassay technique, where >50 is positive. The titers were observed and the results were tabulated.

Inclusion criteria

- Mothers affected by SARS-COV-19 in the antenatal period including first, second, and third trimesters, 6 weeks before delivery
- Newborn of COVID-affected mothers
- Mothers delivering after 28 weeks of gestation.

Exclusion criteria

- Mothers who are vaccinated either during or before pregnancy
- Mothers who are affected by SARS-COVID-19 within 6 weeks of delivery
- Women <18 years.

Statistical analysis

The ratios were obtained by dividing the maternal IgG concentration by the neonatal IgG concentration. For statistical analysis, log2-transformed antibody concentrations and transfer ratios were reported as geometric mean concentrations with 95% CIs. To evaluate the relationships between the transfer ratio and time between the first dose of the vaccine and delivery, or between the first positive PCR test result among those with symptomatic infection, we employed scatter diagrams and Spearman rank correlation coefficients. The length of time between the onset of symptoms, the first positive PCR test result, or the first dose of the vaccine and delivery was compared using the Mann–Whitney test, seropositivity was compared using the 2 test, and antibody concentrations and transfer ratios were compared using an unpaired, 2-tailed t-test between the analytic groups. To investigate the relationships between the log2-transformed transfer ratio and the interval between an infection or vaccination and delivery, the gestational age at delivery, and maternal factors (hypertensive disorders, diabetes, and obesity) that may alter placental function, we built linear regression models. A two-sided P=0.05 or above was regarded as statistically significant. For the statistical evaluations, SPSS version 22.0 was employed.

RESULTS

A total of 30 women, affected with SARS-COVID during the antenatal period, confirmed with RT-PCR testing were included in this study. Blood samples collected from mothers at the time of delivery and cord blood sample were used for the antibody detection in mothers and neonates respectively.

All 30 mothers who were affected with SARS-COVID-19, developed total and neutralizing antibodies-100% seropositive. No clinical significance was noted on the amount of antibodies developed based on parity, gestational age, severity of illness, infective period, and mode of delivery (Table 1).

The linear association was noted between mother and fetus antibody transfer rates-total antibody (P=0.001) and neutralizing antibody (P=0.00). No statistical significance was noted between the association of maternal and fetal-total and neutralizing antibody titers based on parity, gestational age, severity of illness, duration of maternal infection, presence of comorbidities (GDM, hypertension, preeclampsia, and bronchial asthma), and mode of delivery. Women who tested positive in 3rd trimester (33.3%), showed increased antibody response and transmission compared to those who tested positive in 1st trimester. This is because the antibody levels start to decline after 3 months of infection. Most women who were seropositive had mild to moderate symptoms (83.3%). Severe infection was noted in 5 women (16.6%) who required oxygen supplementations and 2 required heparin therapy. Women with severe illness showed decreased antibody levels-total antibody (≤500–100%), and neutralizing antibody (≤1000–60%), but statistical significance was not proved. Hence, antibody levels did not correlate with the severity of illness (Table 2).

DISCUSSION

SARS-COV-2, the enveloped positive single-stranded RNA virus, poses a great threat to global health due to its emerging and re-emerging nature.[17] The World Health Organization had declared the rapid spreading of SARS-COV-2 as a pandemic on March 11, 2020.[18] SARS-COV-2 raised concern in pregnant women, due to the adverse pregnancy outcomes evidenced with other coronaviruses (SARS, MERS).[19] Vertical transmission causing congenital infection to the fetus was also a major concern, but several studies showed no evidence of vertical transmission noted in the late third trimester. More than 90% develop adaptive immune response-IgG and neutralizing antibodies following COVID-19 infection.[20] Coronavirus uses its receptor binding domain (RBD) of its spike protein to attach to ACE receptors. Neutralizing antibody targets this RBD domain and impairs virus entry, providing the best protection against reinfection.[21]

During the study period, 38 women who delivered in our institute had a history of COVID-19 in the antenatal period. 8 women were excluded from the study as they did not fit into the inclusion criteria. For the remaining 30 mothers, neutralizing antibodies and total antibodies were tested at the time of delivery from mother and fetus and the antibody titers were observed. Factors influencing the antibody production in mothers and factors affecting the antibody transmission from mother to fetus were studied.

The antibodies developed in mothers are of the Delta variant. All 30 mothers who tested positive for SARS-COV-2 developed IgG and neutralizing type of antibodies. All the cord samples collected were also seropositive for antibodies. However, there is a variation in the titer of antibodies level in the neonates. The antibodies titer in mothers ranged from-total antibody (7–470), and neutralizing antibody (56–10.715).

Table 1: Characteristics of seropositive mothers and their antibody concentration

Factors	Parameters	(n=30)	Total antibodies in mothers		P-value	Neutralizing antibodies in mothers		P-value
			≤ 100	> 100		≤ 1000	> 1000	
Parity	Primigravida	14	7	7	1.00	10	4	0.127
	Multipara	16	8	8		7	9	
Gestational age	< 37 weeks	5	1	4	0.142	2	3	0.410
	> 37 weeks	25	14	11		15	10	
Severity of illness	Mild-moderate	25	13	12	0.624	13	12	0.249
	Severe	5	2	3		4	1	
Infective period	< 12 weeks	4	0	4	0.061	3	1	0.387
	12–28 weeks	16	8	8		10	6	
	> 28 weeks	10	7	3		4	6	
Comorbids	Yes	18	9	9	1.000	13	5	0.035
	No	12	6	6		4	8	
Mode of delivery	SVD	16	9	7	0.522	11	5	0.101
	AVD	2	1	1		2	0	
	Elective LSCS	2	0	2		0	2	
	Emergency LSCS	10	5	5		4	6	

Table 2: Characteristics of seropositive mothers and their newborn's antibody concentration

Factors	Parameters	(n=30)	Total antibodies in neonates		P-value	Neutralizing antibodies in neonates		P-value
			≤ 100	> 100		≤ 1000	>1000	
Parity	Primigravida	14	4	10	0.825	7	7	0.491
	Multipara	16	4	12		6	10	
Gestational age	< 37 weeks	5	0	5	0.140	2	3	0.869
	> 37 weeks	25	8	17		11	14	
Severity of illness	Mild-moderate	25	7	18	0.712	10	15	0.410
	Severe	5	1	4		3	2	
Infective period	< 12 weeks	4	0	4	0.431	3	1	0.307
	12–28 weeks	16	5	11		7	9	
	> 28 weeks	10	3	7		3	7	
Comorbidities	Yes	18	5	13	0.866	11	7	0.016
	No	12	3	9		2	10	
Mode of delivery	SVD	16	5	11	0.641	8	8	0.161
	AVD	2	1	1		2	0	
	Elective LSCS	2	0	2		0	2	
	Emergency LSCS	10	2	8		3	7	
Mothers antibody levels	≤ 100	8	8	0	0.001			0.00
	> 100	22	7	15				
	≤ 1000	13				13	0	
	> 1000	17				4	13	

Mothers with higher antibody titers had increased transmission when compared with that of the mothers with lower antibody titers. This indicates that mother's antibody production rate is directly proportional to the transmission rate in neonate.

About 87% transmission of IgG and neutralizing antibodies are seen from COVID-affected mothers to neonates. We measured total antibody and neutralizing antibody levels and found an efficient transfer of antibody from women who were seropositive during pregnancy and a positive correlation between maternal and cord blood antibody levels. A review by Irish Health Information and Quality Authority proposed waning of antibody after 6 months, and T-cell and B-cell responses after 8 months.[22] A recent study conducted by Chia et al., showed the mild disease had rapid waning of neutralizing antibody and severe disease had persistent antibody levels.[23] In our study, patients affected in the first trimester showed less antibody levels when they were tested at the time of delivery. No significance was noted in the antibody levels, based on the severity of infection.

All cord blood samples showed 100% transfer of antibodies if COVID infection was 6 weeks before delivery. Knowing the presence of maternal antibody levels in infants is crucial because of the morbidity associated with pediatric or neonate SARS-COVID infection, adding to the fact that no vaccines are administered to the infants. Based on the fact that immunity wanes off after 6 months, planning of vaccination on the third trimester will benefit neonatal protection.

Limitations of the study

- Study included small group of population
- Small sample size for preterm babies
- Effectiveness of vaccine is not compared
- Lack of information on post-delivery discharge outcomes
- Study was conducted in June 2021, concentrated on Delta strain of virus, other strains should be observed in later studies.

CONCLUSION

In conclusion, the current study has demonstrated that women who were pregnant during the COVID-19 pandemic had good knowledge, attitudes, and practices. It is thought that these positive aspects will be beneficial to expectant mothers who are going through pregnancy while still adhering to health protocols or advice from medical professionals on how to carry a pregnancy safely amid this COVID-19 pandemic. It is also advised that additional education be provided to expectant mothers to lessen their anxiety and that they receive the most recent information on COVID-19 and its prevention.

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RM- Review of literature, acquisition of data, original draft preparation; **NL-** Concept and design of study, preparation of manuscript, interpretation of results, review, and editing; **JV-** Review of literature, statistical analysis, revision of final manuscript.

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