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Neutralizing Antibody Response and Transplacental Transfer in COVID-19 in Pregnancy

Mary C. Cambou[1], Christine M. Liu[1], Thalia Mok[1], Viviana Fajardo-Martinez[1], Sophia G. Paiola[1], Francisco J. Ibarrondo[1], Tara Kerin[1], Trevon Fuller[1,2], Nicole Tobin[1], Gustavo Garcia[1], Debika Bhattacharya[1], Grace M. Aldrovandi[1]
Vaithilingaraja Arumugaswami[1], Patricia Brasil[2], Rashmi Rao[1], Otto Yang[1], Karin Nielsen-Saines[1]
[1]University of California Los Angeles, Los Angeles, CA, United States [2]Fiocruz, Rio de Janeiro, Brazil

BACKGROUND

- There are limited data on how COVID-19 severity and vaccination throughout pregnancy impact maternal neutralizing antibody (NAb) responses and transplacental transfer to the neonate at birth.
- Characterization of the antibody response of *in-utero* SARS-CoV-2 may inform vaccination schedules in pregnancy in order to optimize maternal and neonatal protection.

METHODS

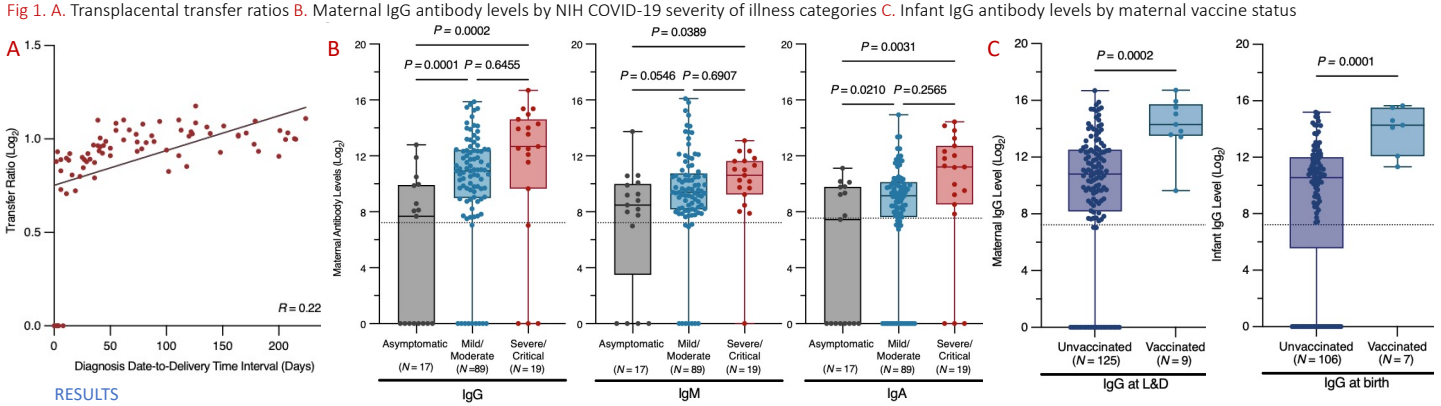
- The COVID-19 Outcomes in Mother-Infant Pairs (COMP) study is a longitudinal cohort of mother-infant dyads diagnosed with SARS-CoV-2 during pregnancy in Los Angeles, and Rio de Janeiro, Brazil.
- Maternal sera collected at enrollment, labor and delivery (L&D), and 6 months post-partum, and infant sera at 24 hours and 6 months, were analyzed by ELISA for IgG, IgM and IgA targeting the receptor binding domain (RBD) of the SARS-CoV-2 spike protein.
- In a subset of unvaccinated mother-infant dyads with evidence of IgG transfer or severe/critical COVID-19 in pregnancy, NAb activity was quantified by plaque reduction neutralization tests (PRNT) using the parental SARS-CoV-2 strain (USA-WA1/2020; Lineage A).

Table 1. Maternal demographics and clinical characteristics (N=238)

Median Maternal Age (IQR)	32 (25-35)
Race/Ethnicity	N (%)
Asian	16 (6.72%)
Black	19 (7.98%)
Mixed/Other	81 (34.03%)
US Latina	85 (35.72%)
White	37 (15.55%)
Enrolled in Brazil	97 (40.76%)
Enrolled in the US	141 (59.24%)
Median Gravida (IQR)	2 (1-4)
Trimester at Diagnosis	N (%)
1st	36 (15.13%)
2nd	97 (40.76%)
3rd	105 (44.12%)
Median Diagnosis Date to Delivery Time in Days (IQR)	74 (31-123)
Medical Comorbidities	N (%)
Pre-Pregnancy BMI>30	20 (8.4%)
Diabetes (Type I or Type II)	5 (2.1%)
Congenital Heart Disease	5 (2.1%)
Asthma	22 (9.24%)
COVID-19 Severity	N (%)
Asymptomatic	27 (11.34%)
Mild/Moderate	160 (67.23%)
Severe/Critical	42 (17.65%)
Vaccinated Prior to Delivery	9 (3.78%)

Transplacental IgG transfer was high following natural in utero SARS-CoV-2 infection & correlated with timing of diagnosis prior to delivery. Maternal vaccination & severe COVID-19 yielded higher Ab levels in mothers and infants at delivery. 50% NAb activity was found in 68% of mothers & 42% of infants tested.

Fig 1. A. Transplacental transfer ratios B. Maternal IgG antibody levels by NIH COVID-19 severity of illness categories C. Infant IgG antibody levels by maternal vaccine status



RESULTS

- A total of 164 maternal specimens were collected at enrollment, 134 at L&D, and 27 at 6 months post-partum, from a total of 238 maternal participants.
- A total of 113 infant specimens were collected at 24 hours of life, and 30 at 6 months of age, from a total of 126 infant participants.
- The majority (72%) of the maternal cohort produced all three anti-SARS-CoV-2 isotypes (IgG, IgM and IgA) at L&D, and 97% had at least one SARS CoV-2 isotype present.
- Transplacental transfer ratios of IgG (Log_2[Infant IgG at birth+1]/[Maternal IgG at L&D+1]) correlate with increasing diagnosis date to delivery time interval (Fig 1A, r=0.22).
- At delivery, maternal IgG, IgM and IgA levels were significantly higher among women with severe/critical disease compared to asymptomatic disease (Fig 1B).
- Maternal and infant IgG levels (ng/mL) at delivery were highest among neonates born to recovered mothers who received the vaccine prior to delivery (Fig 1C), although the transplacental transfer ratios were not significantly different across disease severity classifications. Infant IgG levels significantly decreased at 6 months compared to birth.
- In a subset of 50 unvaccinated mothers and 26 infants, 50% protective neutralization (in vitro NAb titer >1:20) was present in 34 mothers (68%) and 11 infants (42%).

CONCLUSIONS

- Transplacental transfer of anti-SARS-CoV-2 IgG correlates with increasing duration between diagnosis date and delivery.
- While infant IgG levels at birth were the highest among neonates born to recovered mothers who received the vaccine prior to delivery, transplacental transfer ratios were not significantly different across COVID-19 severity classifications.
- Infant IgG levels significantly decreased at 6 months compared to birth, regardless of maternal vaccine status.
- Only one infant was IgM + at birth but PCR negative, suggesting there was no evidence of vertical transmission in the cohort.
- In a subset analysis, less than half of neonates born to unvaccinated mothers had evidence of 50% NAb activity.
- Further research is needed to characterize the functionality and kinetics of maternal and neonatal antibody responses elicited by in utero SARS-CoV-2 natural infection compared with COVID-19 vaccination.

CONTACT INFORMATION

Mary Catherine Cambou, mcambou@mednet.ucla.edu
The details of the COMP study can be found at PMID: 34723226