Maternal-fetal immunologic response to SARS-CoV-2 infection in a symptomatic vulnerable population: A prospective cohort

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Summary: In this prospective study of pregnant women and their newborn, days between symptom onset and childbirth and gestational age affect maternal and neonatal SARS-CoV-2 specific IgG as well as placental antibody transfer. Maternal milk RBD-specific IgA correlated with maternal IgG.

Footnote Page

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Abstract:

Background:

COVID-19 disproportionally affects pregnant women and their newborn, yet little is known about the variables that modulate the maternal-fetal immune response to infection.

Methods:

We prospectively studied socioeconomic, biologic and clinical factors affecting humoral immunity in 87 unvaccinated pregnant women admitted to hospital in the Buenos Aires metropolitan area for symptoms consistent with COVID-19 disease.

Results:

The number of days between symptom onset and childbirth predicted maternal and newborn virus Spike protein Receptor Binding Domain (RBD)-specific IgG. These findings suggest newborns may benefit less when mothers deliver soon after COVID-19 infection. Similarly, a longer time between symptom onset and birth predicted higher in utero transfer of maternal IgG and its concentration in cord blood. Older gestational ages at birth were associated with lower maternal IgG: cord blood IgG ratios. Eighty seven percent of women with confirmed SARS-CoV-2 infection developed RBD-specific IgA responses in breast milk within 96 h of childbirth. IgA was not significantly associated with time from infection but correlated with maternal serum IgG and placental transfer.

Conclusions

These results demonstrate the combined role of biologic, clinical and socioeconomic variables associated with maternal SARS-CoV-2 RBD-specific antibodies and supports early vaccination strategies for COVID-19 in socioeconomically vulnerable pregnant women.

Keywords: COVID-19, SARS-CoV-2, Pregnancy, Newborn, Antibody

1. Introduction:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread globally since early 2020, infecting an immunologically naive population and causing significant morbidity and mortality. SARS-CoV-2 infection in pregnant women can result in severe complications, including an increased chance of hospitalization and ICU admission [1] and a requirement for mechanical ventilation to alleviate respiratory distress [2]. There is also a greater likelihood of fetal intrapartum distress [3] and preterm delivery [4].

The immune response to the virus in unvaccinated individuals includes both innate and adaptive immunity [5]. One immunological signature in recovered individuals is production of virus-specific antibodies including those directed at the Spike protein Receptor Binding Domain (RBD) [6]. Seropositive recovered individuals have an estimated 89% protection from reinfection for at least 6 months[7]. Circulating resting memory B cells directed against SARS-CoV-2 have been detected in unvaccinated non-pregnant convalescent individuals, indicating establishment of a robust antigen-specific, long-lived humoral immune memory compartment [8]. The antibody response to the virus has a high degree of heterogeneity and correlates with disease severity [9]. Patterns of IgG production over time, by age, and according to sex vary in different populations (8). IgA production is also significant during the early SARS-CoV-2–specific humoral immune response [10].

The neonatal immune defense against infection by several pathogens is mainly dependent on innate immune effectors, IgA-containing maternal milk, and IgG delivered by transplacental transport mechanisms [11]. Understanding the humoral response to SARS-CoV-2 infection in pregnant women, and the degree to which that response is transferred via the placenta and breast milk is essential for understanding protection from COVID-19 in utero and in neonates. Recent studies have demonstrated that biologic and clinical factors encountered during pregnancy can affect the antibody delivery to the fetus [12,13]. In human milk, studies have suggested the presence of virus-

specific IgA in mothers previously infected with SARS-COV-2 [14], but little is known about the variables that modulate IgA concentrations in human milk.

Environmental factors and socioeconomic vulnerabilities are variables are known to modulate disease severity and death by COVID-19 [15]. Recently, in Peru, socioeconomic status and overcrowding have been associated with SARS-CoV-2 seroprevalence and severity[16–18]. Therefore, there is an urgent need to understand the biologic and socio-economic variables that modulate humoral maternal-fetal immunity. Such information may inform the implementation of appropriate maternal vaccination strategies and strengthen the understanding between public health and COVID-19.

2. Methods:

A prospective multicenter cohort study was performed on pregnant women admitted due to symptomatic COVID-19 disease in a network of 9 maternity hospitals in the metropolitan area of Buenos Aires, Argentina, from July 10, 2020, to October 1, 2020. Institutional review board (IRB) approval was obtained from each institution (ClinicalTrials.gov Identifier: NCT04362956).

Study Population

Consent was obtained from women upon admission the hospital. Inclusion criteria included female sex, pregnancy at 24 or more weeks of gestation, and admission to the obstetric ward presenting with fever and one or more respiratory symptoms (cough, sore throat, respiratory difficulty). Further criteria included a diagnosis of pneumonia with no other explainable cause. A SARS-CoV-2 infection diagnosis was achieved by polymerase chain reaction (NP-PCR) of nasopharyngeal swab samples. At the time of the study there were no clear guidelines of neonatal diagnostic protocols for infants born to women with COVID-19. For study purposes, nasopharyngeal swabs were obtained from newborns only once within 48 hours of life. The reported SARS-CoV-2 variants in Argentina during this time

period were mostly Gamma and Lambda [19]. Recruited women who continued with their pregnancy but did not give birth by the end of the study and samples were not collected were not analyzed in the study.

Study Definitions and Data and Sample Collection

Upon inclusion, demographic, socioeconomic and clinical data were collected for 14 days for both the mother and the newborn or newborns in the case of multiple births. Maternal illness was classified as mild, moderate, severe, or critical based on the USA National Institutes of Health guidelines for severity of clinical presentation [20]. Preterm delivery was defined as less than 37 weeks' gestation, and term was defined as 37 or more weeks' gestation.

Women had blood drawn (5 ml) and umbilical cord blood (3 ml) was obtained at the time of birth. After centrifugation serum was frozen at -80°C until antibody titer determination. Human milk (1-5 ml) was obtained within 96 hours after childbirth using a standardized cleaning procedure in conjunction with pump or hand expression. Briefly, before Ab testing, milk samples were thawed, centrifuged at 800g for 15 min at room temperature, fat was removed, and supernatant transferred to a new tube following best practices for human milk study for COVID-19 research [21]. Skimmed acellular milk was aliquoted and frozen at -80°C until testing. Maternal serum samples and admission information were used as controls if women met the inclusion criteria but tested negative for SARS-CoV-2.

Antibody Measurements

To quantify SARS-CoV-2-specific IgG antibody concentrations in maternal serum and cord blood, 96-well ELISA plates (Nunc, Thermo Scientific, Rochester, NY) were coated with recombinant SARS-CoV-2-Spike protein RBD (Rankin Laboratory, Oklahoma Medical Research Foundation, Oklahoma City, OK) at a final concentration of 10 µg/ml in carbonate coating buffer and incubated overnight at 4°C.

Wells were washed with PBS-0.5% v/v Tween (PBST) then blocked with 0.1% w/v Bovine Serum Albumin (BSA) in PBS for 2 hours at room temperature. Wells were washed with PBST before adding sera diluted in PBS with 0.1% Tween at 4°C overnight. Wells were washed with PBST and then incubated for 1h with a 1,000-fold dilution of Horse-Radish Peroxidase (HRP) labeled goat anti-human IgG (Jackson Immunoresearch, West Grove, PA) in PBS. Wells were washed and developed for 2 min at room temperature with ABTS substrate (KPL, Gaithersburg, MD). A 10% w/v SDS solution was used to stop the reaction. IgG concentrations were determined by measuring the optical density (OD) at 405nm and values were extrapolated from a standard curve. To generate the standard curve, a positive control SARS-CoV-2 spike-specific IgG (Active Motif, Carlsbad, CA) was serially diluted against a constant RBD coating concentration. This was done for each ELISA plate. Data were analyzed using Graphpad Prism 8.0 software (La Jolla, CA.)

SARS-CoV-2 RBD-specific IgA antibodies were detected in milk samples in a similar manner to serum IgG except that HRP-labeled goat anti-human serum IgA (Jackson Immunoresearch, West Grove, PA) was used as the detection Ab. A positive control RBD-specific IgA was not available for the study. Data were expressed as Absorbance at 405 nm (A_{405}) for a 1/16 dilution of serum. Extensive titrations of selected samples were used to show that A_{405} at a 1/16 dilution correlated with endpoint titer.

Statistical Analysis

Outcome variables were examined for outliers and skewness, and descriptive statistics were computed. Data transformations in the Box-Cox family were applied to outcomes found to depart severely from normality. To identify predictors for use in multiple regression, bivariate analyses were conducted using the following procedures: (a) for categorical predictors' effects on skewed outcome variables, we used nonparametric methods (Mann-Whitney and Kruskal-Wallis tests); (b) for

continuous variables' relationships with the transformed variables, we used Pearson's correlation coefficient; and (c) for relationships between binary predictors and continuous outcomes unaffected by skewness or outliers, we computed independent t tests for unequal sample sizes. Predictors detected as significantly related to IgG or IgA in bivariate analyses were included in hierarchical multiple regression analyses. More distal, socioeconomic variables were entered as the first block, then more proximal biologic and clinical factors were added to the model as the second block. Thus, the analysis tested the effect of biologic and clinical factors after accounting for socioeconomic variables. All maternal serum samples were used for maternal antibody studies, including those with undetectable IgG values. Matched maternal-newborn samples were used for cord blood antibody response and placental antibody transfer ratio (maternal serum IgG: cord blood IgG). To examine the effect of twins in the data, sensitivity analyses were conducted, randomly omitting data from one twin in each pair to determine whether dependence between the pairs had a notable effect on results. Analyses were performed in SAS®, version 9.4, and R, version 4.1.1.

3. Results:

We recruited 112 women **(Figure 1).** Eighty-seven women tested positive for COVID-19, with 57 mothers' results being matched with cord blood sera from their 59 infants. Milk was obtained from 58 mothers, with 51 mothers (87.9%) also having blood test results. A total of 32 mothers with tested milk and blood sera were matched with their infants' data.

Sample Characteristics

Demographic results are presented in **Table 1**. Mothers ranged from 15 to 49 years (median age 30.8 years; 25th and 75th percentiles: 26.1-34.9). Sixteen mothers (18.4%) had obesity, and 8 mothers (9.2%) smoked during pregnancy. Regarding the socioeconomic vulnerabilities, 14 women (17.5%) lived in crowded conditions, 12 (15.8%) lived far from the hospital, 13 (16.3%) had no sewage system at home, 27 (33.8%) were unemployed and more than half (n = 42, 52.5%) had no medical insurance,

reflecting the degree of vulnerability of this population. Median gestational age at maternal hospitalization was 36 6/7 weeks (25th and 75th percentiles: 32 4/7 -39 0/7) with almost half (n = 38, 43.7%) presenting before term gestation. Preterm birth was unrelated to these socioeconomic variables.

Of the 59 infants, 35.6% (n = 21) were female, and the incidence of cesarean delivery was 71.2% (n = 42), exceeding the national average rate (28.4%-57.7%) [22] , with almost half of these due to emergent C-section (n = 26). Twenty-three babies (38.9%) were born preterm compared to a local preterm rate of 8% [23].

Clinical outcomes

The clinical outcomes are shown in **Table 2.** At the time of the study, all symptomatic women were hospitalized for observation. Eighty of the 87 women had disease severity ratings; 50 (62.5%) had mild disease, 14 (17.5%) had moderate, 12 (15%) had severe and 4 (5%) had critical disease. One mother who was admitted 8 days after symptom onset was hospitalized in the ICU for 8-14 days and died of COVID-19; her late preterm baby survived. Forty-seven percent of women remained admitted for more than a week; the rest had less than 7 days of hospitalization. The median days since symptoms onset to childbirth was 14 days (25th and 75th percentiles: 5.5-45.5).

Seventeen babies (28.8%) were admitted to the NICU. Among infants born from SARS-CoV-2 positive mothers only 1 infant tested positive, a full-term baby who stayed in the mother's hospital room. Fourteen infants required respiratory support. By the end of the study period most babies (n = 52, 91.2%) were discharged to their home, 4 (7%) remained hospitalized and 1 died of complications from preterm birth. The reasons for hospitalization of 2 babies after discharge were jaundice and a brief resolved unexplained event (BRUE).

Maternal antibody concentration

Figure 2 shows the distributions of antibody responses, with $\log_{10}$ transformations on the maternal IgG, cord blood IgG and maternal-cord blood IgG ratio to adjust for skewness. Time from symptoms onset was positively correlated with maternal serum IgG concentration (r = 0.48, p = 0.0002); days of gestation at hospitalization trended toward a negative correlation with maternal antibody response (r = -0.26, p = 0.0544); and mothers having a college education was associated with maternal IgG (Mann-Whitney test = 1.99, p = 0.0464). However, multiple regression analysis found that only time since symptom onset significantly predicted maternal IgG (p = 0.0004), with the model explaining 22.7% of the variance in IgG (Model 1, Table 3). A greater numbers of days between symptom onset and delivery was associated with higher maternal IgG concentrations.

Cord blood antibody concentration

Figure 2 shows the distribution of cord blood IgG concentration. Unlike the maternal IgG, gestational age had no relationship with IgG concentration in umbilical cord blood (r = 0.06, p = 0.6404). No socioeconomic variables were detected as significantly related to the log-transformed cord blood IgG concentrations, so only clinical variables were included in a one-block regression analysis. Cord blood IgG was positively related to time from symptoms onset to birth (p = 0.0002) and unrelated to mother's days of gestation at hospitalization (p = 0.8485) (Model 2, Table 3). The model explained 23.9% of the variance in umbilical cord blood concentration. The positive regression coefficient suggests that newborns born after a recent maternal infection may carry low protection against SARS-CoV-2 infection.

Maternal-fetal antibody transfer

The efficiency of the placenta in regulating maternal IgG transfer to the fetus is a fundamental biologic variable in neonatal immune protection. Thus, we investigated the ratio of maternal serum IgG levels at childbirth to IgG umbilical cord blood levels as an indication of maternal-fetal antibody transfer ability (Figure 2). Having maternal IgG levels similar to cord blood IgG (a lower mother: baby ratio), is interpreted as better antibody transfer ability. Model 3, Table 3 shows the results of the hierarchical regression analysis. The first block had crowded conditions as the only socioeconomic predictor that was significant in bivariate analysis (Mann-Whitney test = -1.99, p = 0.0471), with the second block consisting of time since symptoms onset and gestational age at birth. Longer times since symptoms onset trended toward predicting higher ratios of maternal serum IgG: cord blood IgG (p = 0.0524). Older gestational ages were associated with lower ratios (p = 0.0307). Although only 7 mothers reported living in crowded conditions, they had lower ratios (p = 0.0259). These three variables explained 20.4% of the variance in the ratios.

Overall, these results suggest that placental transfer becomes less efficient with time since infection and may be more efficient close to term gestation.

Maternal milk SARS-CoV-2 specific IgA

RBD-specific IgA was measured in milk samples (Figure 3). Of the 58 samples obtained within 96 h of childbirth, 51 (87%) had detectable RBD-specific IgA. The distribution of human milk RBD-specific IgA was symmetric without outliers and did not require transformation. SARS-CoV-2 in the milk samples was undetectable by RT-PCR.

Pearson's correlation was used to analyze the relationships between milk IgA and (a) maternal serum IgG, (b) cord blood IgG, (c) the ratio of maternal IgG to cord blood IgG, (d) gestational age at birth, (e) time since symptoms onset, and (f) maternal age (Figure 4). Maternal IgG serum production and IgA maternal milk presence were positively related (r = 0.41, p = 0.0016) (Figure 4a).

Figure 4b illustrates the non-significant relationship between cord blood IgG serum production and IgA maternal milk (r = 0.16, p = .3961). Human milk IgA was directly correlated with the maternal IgG: cord blood IgG ratio (r = 0.53, p = 0.0018) (Fig. 4c).IgA concentration was unrelated to days since maternal symptoms to childbirth (r = 0.04, p = 0.7871) (Figure 4e) and maternal age (r = -0.02, p = 0.8871) (Figure 4f). The sample size was deemed to be too small to support a multiple regression analysis.

All analyses were repeated after randomly excluding data from one twin within each of the two sets. Results were consistent with the complete data set, so we have reported the original results.

4. Discussion:

In this study 87 pregnant women admitted with COVID-19 were evaluated for variables associated with differential production of virus-specific IgA and IgG. Our study population presented with more severe disease than other cohorts of symptomatic pregnant women [24–26], with 20% having severe or critical disease. Our cohort had higher proportions of preterm birth (38.9%) and C-section (65.1%) than the national values (35,7%) [27], consistent with reports on COVID-19 disease during pregnancy [22]. None of the 14 neonates admitted to the NICU needing respiratory support were diagnosed with SARS-CoV-2 infection or pneumonia and all of them were born preterm. This suggests that the reason for respiratory distress was attributable to prematurity-associated lung disease or respiratory distress syndrome.

Although we did not evaluate the SARS-CoV-2 neutralizing capacity of IgG and IgA, several studies have documented a strong correlation between neutralizing antibody titers and RBD-specific antibody titers [28–30]. Like other reports, maternal and fetal antibody concentration was related to time elapsed from infection to delivery.

Maternal IgG is transported across the placenta by an active, neonatal Fc receptor (FcRn)-mediated process during pregnancy. This transport confers short-term passive immunity [31] and protect

infants against infections during their first months of life. To design appropriate vaccination strategies, it is important to consider concentrations of IgG transferred from mother to infant during pregnancy and determine the biologic and environmental variables that affect it. We evaluated the efficiency of transfer according to gestational age at the time of birth at a single point in time. In our study, placental IgG antibody transfer was more efficient later in gestation (lower ratio of maternal serum IgG: cord blood IgG) and less efficient earlier in gestation (higher ratio). Our results at first appear to be contrary to results shown by Edlow et al. [32]. In that study there was reduced IgG transport in maternal–fetal dyads during the third trimester in pregnant women with COVID-19 disease. The Edlow study analyzed samples from 64 SARS-CoV-2 positive mothers in the USA of which a third were asymptomatic and only 18% delivered a preterm baby. Although the sample size of both studies is small, it is possible the apparently divergent findings may be reconciled by consideration of the socioeconomic background in both countries and the clinical severity of the disease. As indicated by our study, these factors may explain the differences in placental IgG transfer during gestation. The placental FcRn receptors are known to have differential affinity for the IgG subclasses [33] and IgG subclass levels can differ between two populations with specific genetic and socioeconomic backgrounds[34]. We speculate that this may explain, in part, the contrasting findings. Our findings reinforce the notion that pregnant women should be immunized as early as possible to allow sufficient time for development of a protective IgG response that can be transferred in utero. In addition, it is key to investigate further into immunologic details of not only the quantity of antibody placental transfer but the function and the influence of vaccination in IgG subclass and the protective consequences to the offspring.

Multiple small studies have demonstrated that human milk from mothers who had previously been infected contained SARS-CoV-2 specific antibodies and that these antibodies were capable of neutralizing the virus [35–37]. Recently, a large prospective study from the Netherlands showed that 524 of 2312 lactating mothers (23.1%) had SARS-CoV-2 specific IgA, with the median age of infants being 34 weeks [38]. Little is known about content and factors that modulate IgA in human milk

early after childbirth when neonates are most vulnerable to infections. In our study, 87% of women had presence of IgA within the first 96hs after childbirth, with higher levels of IgA in milk if children were delivered preterm. Studies on the IgA profile in breast milk from mothers delivering preterm infants have shown inconsistent results, with some showing no difference in total IgA [39] and other showing an elevated concentration [40]. In addition, SARS-CoV-2 specific IgA in milk was not strongly associated with time from infection, suggesting that breastfeeding may be even more important to protect the newborn in women who become infected or vaccinated closer to childbirth and lack the necessary timing to achieve maternal-fetal antibody transfer.

Lastly, there is limited data reporting on socioeconomic variables that affect maternal-fetal SARS-COV-2 antibody response on pregnant women. Melamed et al. showed that SARS-CoV-2 transmission among pregnant women in New York City was associated with neighborhood- and building-level markers of large household membership, household crowding, and low socioeconomic status [17]. In our study, women who did not finish college had a higher IgG concentration than women who had a complete college education, but this relationship did not persist when entered in a multiple regression analysis with days since symptoms onset and days of gestation at hospitalization predicting maternal IgG. Although crowded living conditions were associated with a lower ratio of maternal serum IgG: cord blood IgG or a more efficient placental antibody transfer, we had only 7 mothers from crowded living conditions in this multivariable analysis. Taking all of this into account, it appears that a vulnerable environmental background may result in higher viral exposure that results in a higher antibody response and in addition improved placental antibody transfer that may benefit the newborn immunity.

A larger sample size and multiple postpartum observations would have allowed greater flexibility in assessing more complex models. In addition, longitudinal observations of antibody kinetics in single individuals should enhance the understanding of humoral response in this population. A portion of maternal sera could not be matched with umbilical cord serum due to limited research staff at the

height of the pandemic and the ability to be present at childbirth. Ultimately, despite the limitations inherent in small studies this work has demonstrated the potential effects of socioeconomic factors to explore in large-scale follow-up studies.

The results of this study help us understand the risk of infantile vulnerability and may inform maternal SARS CoV-2 vaccination strategies. In addition, our results confirm the potential for maternally derived SARS-CoV-2 specific antibodies to provide early neonatal protection from Covid-19 disease.

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Figure 1. Study Flow Diagram

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

Table 1: Demographic Characteristics for Mothers (N = 87) and Infants (N = 59)

Maternal Characteristic	**n/N (%) [a] or *M (25th – 75th percentiles)***
Age	*30.4 (26.1-34.9)*
Ethnicity	
European-Latin	50 (50.0)
European-Other	3 (2.8)
Native	38 (35.9)
Other	12 (11.3)
Highest education	
Some primary school	7 (8.5)
Completed primary school	22 (26.8)
High school	31 (37.8)
College	22 (26.8)
Obesity	16 (18.4)
Smoked during pregnancy	10 (8.9)
Crowded living conditions	14 (17.5)
Far from hospital	12 (15.8)
No sewage system	13 (16.3)
No running water	13 (16.5)
Unemployed	27 (33.8)
Uninsured	42 (52.5)
Infant Characteristic	
Female sex	21 (35.6)
Preterm birth	23 (38.9)
Delivery type	
Vaginal	17 (28.8)
Scheduled C-section	16 (27.1)
Emergency C-section	26 (44.1)

[a] Percentages were calculated on available data, with number of missing observations ranging from 5 (highest education) to 11 (far from hospital). Percentages may not sum to 100% due to rounding.

Table 2: Clinical Outcomes

Maternal Outcomes (n = 87)	**n (%) [a] or *Median (25th-75th percentiles)***
Number of weeks gestation at hospitalization	*36 6/7 weeks (32 4/7 – 39 0/7)*
Admitted in active labor	8 (6.8)
Disease severity	
Mild	50 (62.5)
Moderate	14 (17.5)
Severe	12 (15.0)
Critical	4 (5.0)
Disposition	
< 1 week of hospitalization	40 (52.6)
Hospitalization lasting 1+ weeks	35 (46.1)
Death	1 (1.3)
Days between symptom onset and delivery	*14 (5-45)*
ICU days	
0	65 (82.3)
1-7	5 (6.3)
8-14 days	6 (7.6)
15+ days	3 (3.8)
Infant Outcomes (n = 59)	
NICU admission	17 (28.8)
Supplemental O2	6 (35.3) [b]
Mechanical ventilation	5 (29.4) [b]
Non-invasive ventilation	3 (17.7) [b]
Disposition	
Home	52 (91.2)
Continued hospitalization	4 (7.0)
Death	1 (1.8)
Delayed cord clamping	49 (86.0)
Feeding, 15 days post-discharge (n = 36)	
Exclusive breast feeding	20 (46.5)
Formula	4 (9.3)
Combination of breast and formula feeding	10 (23.3)
Continued hospitalization	2 (4.7)
Feeding, 30 days post-discharge (n = 29)	
Exclusive breast feeding	14 (48.3)
Formula	3 (10.3)
Combination of breast and formula feeding	11 (37.9)
Continued hospitalization	1 (3.4)
Rehospitalization	2 (3.4)

[a] Percentages were calculated on available data; 11 observations were missing from maternal disposition, 2 from infant disposition, 8 from maternal ICU days, 16 observations were missing for feeding 15 days post-discharge, and 30 observations were missing for feeding 30 days post-discharge. Percentages may not sum to 100% due to rounding. [b] Percentage of the 17 babies admitted to NICU.

Figure 2. Distributions of Antibody Responses

Figure 2

Mother's serum SARS-CoV-2 specific IgG (n=87), cord blood SARS-CoV-2 specific IgG (n= 59), and mother's and cord blood ratio (n=59). Means are shown with diamond shapes.

Figure 3. Distributions of RBD-specific IgA response in human milk

Figure 3

Distribution of RBD-specific IgA from milk samples (n = 51). The diamond shape represents the mean.

Table 3: Multiple Regression Coefficients

Model 1: Maternal IgG [1]	*Unstandardized Coefficients*		*t*	*p*
	B	*Std. Error*		
Block 1				
(Constant)	-0.963	0.394	-2.44	0.0168
College education	-0.982	0.760	-1.29	0.2001
Block 2				
(Constant)	-0.146	2.716	-0.05	0.9574
College education	-0.435	0.705	-0.62	0.5393
Days since symptom onset	0.043	0.012	3.69	0.0004*
Days gestation at hospitalization	-0.008	0.010	-0.79	0.4303
Model 1: Cord blood IgG [1]				
(Constant)	-2.303	1.833	-1.26	0.2144
Days since symptom onset	0.030	0.007	4.00	0.0002*
Days gestation at hospitalization	0.001	0.007	0.19	0.8485
Model 3: Transfer ratio [1]				
Block 1				
(Constant)	-0.023	0.376	-0.06	0.9524
Crowding	-1.782	0.994	-1.79	0.0793
Block 2				
(Constant)	6.519	3.170	2.06	0.0456
Crowding	-2.189	0.950	-2.30	0.0259*
Days since symptom onset	0.022	0.011	1.99	0.0524
Gestational age at birth	-0.027	0.012	-2.23	0.0307*

[1] *Log_{10} transformation applied*

Figure 4. Human Milk IgA's Relationship with IgG, Gestational Age, Days Since Infection and Maternal Age

Figure 4

Correlation between human milk SARS-CoV-2 specific IgA and (a) maternal IgG (log_{10}), (b) baby's IgG (log_{10}), (c) transfer ratio (log_{10}), (d) gestational age at birth (square root transformation), (e) number of days from infection to delivery, and (f) maternal age. Human milk IgA was significantly related to (a) log_{10} maternal IgG and (c) log_{10} transfer ratio, but not (b) log_{10} baby IgG, (d) gestational age, (e) days since infection, or (f) maternal age.

Figure 1

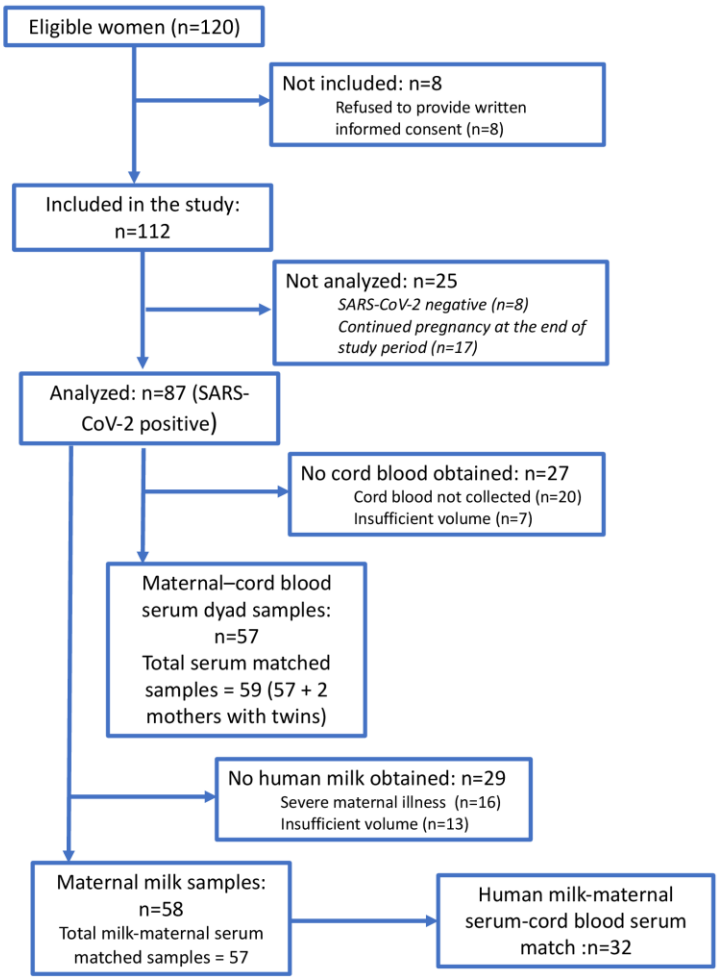

Figure 2

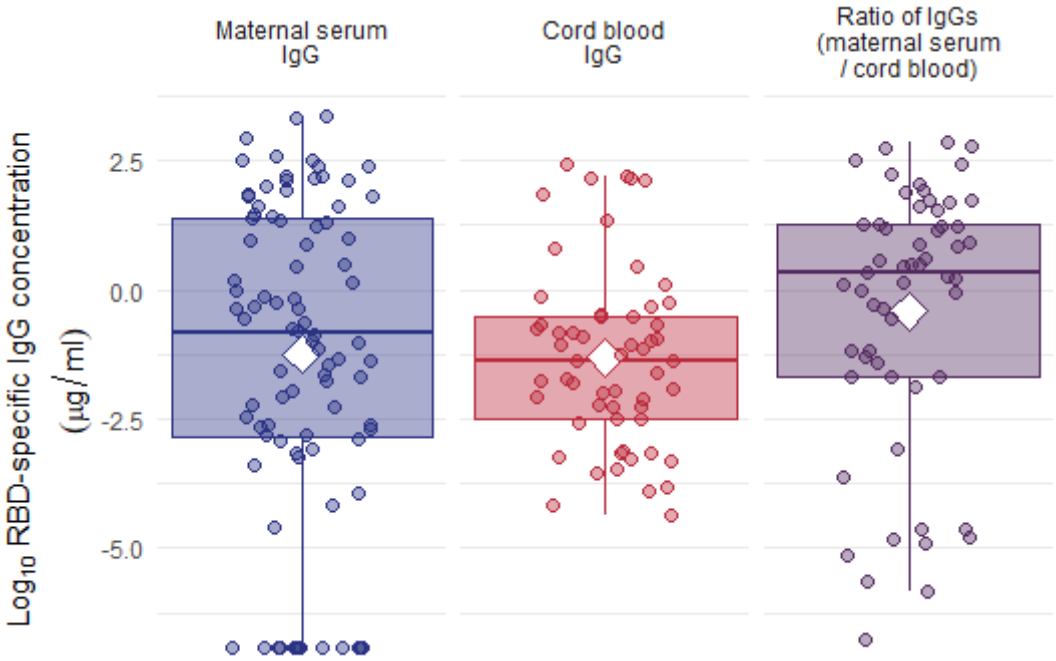

Figure 3

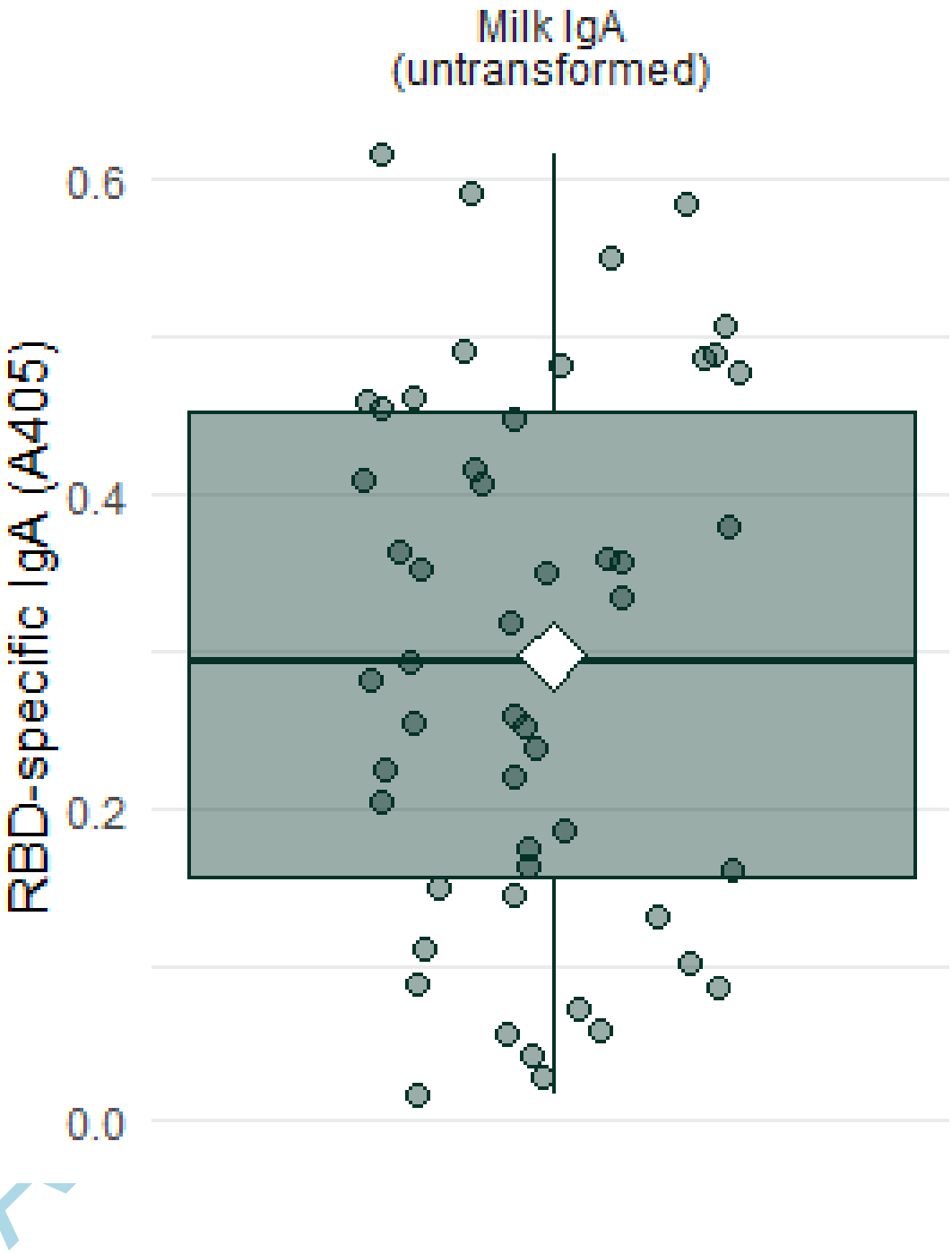

Figure 4