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Placental transfer of SARS-CoV-2 antibodies in mother-neonate pairs: a prospective nested cohort study

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Abstract

Background Newborns depend on the transfer of IgG across the placenta to acquire protection against pathogens. We assessed the placental transfer of SARS-CoV-2 antibodies, primarily derived from infection, from seropositive pregnant women enrolled in a pregnancy cohort in Kilifi, Kenya.

Methods The study was nested within a prospective observational multi-country cohort study. All available paired maternal delivery and cord blood samples were selected. Maternal sera were tested for SARS-CoV-2 receptor binding domain (RBD) IgM/IgG total antibodies using the Wantai assay. For positive samples, maternal and corresponding cord blood samples were tested for SARS-CoV-2 IgG antibodies against the spike (anti-spike) and nucleocapsid proteins (anti-NCP) using ELISA kits from Euroimmun.

Results A total of 492 (56.1%) out of 877 maternal delivery samples were positive for RBD IgM/IgG total antibodies. Of these, 416 (84.6%) were seropositive for either anti-NCP IgG, anti-spike IgG antibodies or both. A total of 412 out of 496 (83%) cord blood samples tested positive for either anti-NCP or anti-spike antibodies. The geometric mean ratio was 1.04 (95% CI: 0.90, 1.21), indicating no significant difference between the anti-spike IgG concentration in cord and maternal blood samples. The log-transformed maternal and cord blood anti-spike IgG concentrations showed a weak positive correlation ($r = 0.364$, $n = 496$, $p < 0.001$). No maternal or neonatal factors were associated with the anti-spike IgG placental transfer ratio.

Conclusion Placental transfer of SARS-CoV-2 antibodies was evident in a population of pregnant women whose immunity was primarily derived from infection given the low SARS-CoV-2 vaccine coverage in the study area. The positive correlation between maternal and cord blood anti-spike concentrations suggests that interventions that increase maternal antibody concentrations such as vaccination may increase passive immunity and protection against severe COVID-19 disease in neonates.

Keywords COVID-19, SARS-CoV-2 antibodies, Seropositivity, Placental transfer, Efficiency

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Introduction

Neonates rely on innate immune responses and maternally derived antibodies, specifically IgG, for protection against infections [1]. Transplacental transfer of IgG SARS-CoV-2 antibodies is thought to confer protection to the foetus and newborn against SARS-CoV-2 infection [2]. Whereas transplacental SARS-CoV-2 infection has been documented [3], this is a rare occurrence despite evidence of in-vivo replication of SARS-CoV-2 in placental tissue where increased intensity of placental infection correlated with severity of maternal COVID-19 symptoms and adverse pregnancy outcomes like stillbirth [4–6]. This is similar to other viral infections such as hepatitis B where intrauterine infection does occur and higher maternal viral loads being an independent risk factor for vertical transmission [7]. IgG is the only class of antibodies transferred across the placenta, facilitated by the neonatal Fc receptor (FcRn) on placental syncytiotrophoblast [8, 9]. The efficiency of maternal antibody transfer depends on factors such as gestational age, birth weight, maternal infectious diseases and inflammation, maternal IgG titres, and placental pathologies [8, 10–12].

The global COVID-19 pandemic prompted studies to elucidate its scope and consequences within communities [13]. In Kilifi County where the current study was carried out, there was a marked increase in SARS-CoV-2 seroprevalence over time, from a low of 0% in March 2020 to a high of 89.4% in February 2022, reflecting the growing exposure within the population [14]. Pregnant women are susceptible to SARS-CoV-2 infection and progression to COVID-19 can increase risk of poor obstetric and neonatal outcomes [15]. Globally, the number of children exposed to maternal SARS-CoV-2 infection in utero has been, and remains, substantial especially in regions with low vaccination rates for pregnant women [16–18]. In the absence of approved vaccines for neonates, passive transfer of maternal antibodies across the placenta plays a critical role in providing early protection against SARS-CoV-2. Understanding the extent and efficiency of this transfer is essential for evaluating neonatal vulnerability and informing maternal immunization strategies.

Studies from Uganda, Malawi, South Africa, and Ghana have consistently demonstrated efficient placental transfer of SARS-CoV-2 antibodies [19–21]. These findings emphasize the robust immune response and the potential benefits of maternal immunization in enhancing neonatal health, particularly in regions with high infectious disease burdens [21]. However, total IgG concentration in adults has been shown to vary across populations, with higher concentrations found in sub-Saharan Africa (SSA), possibly due to a higher infectious disease burden [22, 23]. Region specific variation in IgG concentration could influence the efficiency of placental transfer of pathogen-specific IgG. In addition, maternal conditions such as HIV infection and placental malaria, which have variable prevalence across countries in SSA, have been shown in some studies to impair the efficiency of transplacental antibody transfer to newborns, with these studies reporting marked reductions in antibody levels in affected women [12, 24].

Understanding antibody transfer efficiency and its impact on perinatal health following a natural SARS-CoV-2 infection or vaccination could inform vaccination strategies to better protect newborns [25, 26]. Assessing the prevalence of SARS-CoV-2 antibodies in cord blood can provide valuable insights regarding passive transfer and potential protection for neonates [27]. In this study, we assessed placental transfer of SARS-CoV-2 antibodies by testing paired maternal and cord blood samples from SARS-CoV-2 seropositive pregnant women enrolled in a pregnancy cohort in Kilifi, Kenya, a malaria endemic area with a HIV prevalence of 4.4% [28].

Methodology

Study design and population

This study was nested within a prospective observational multi-country cohort study, the PREgnancy Care Integrating Translational Science Everywhere (PRECISE) study [29]. The PRECISE network established a biorepository with matching clinical and non-clinical data to evaluate placental disorders (hypertension, foetal growth restriction, preterm birth, and stillbirth) in sub-Saharan Africa [30]. For this study, we used data and samples collected from pregnant women receiving care and at delivery from Rabai and Mariakani hospitals in Kilifi County, Kenya, from March 2020 to March 2022 [14, 31, 32]. Notably, most participants were not vaccinated against SARS-CoV-2 as the study was conducted before widespread vaccination programmes at the population level, and during the period of uncertainty regarding vaccine safety in pregnancy [14]. SARS-CoV-2 vaccination in Kenya was only recommended in August 2021, a few months to the end of participant recruitment [33]. By December 2021, vaccine coverage in Kilifi County was only 7.2% among adults [34]. Participant level data on SARS-CoV-2 vaccination status was not collected as the approved study protocol and questionnaire used at the time of participant recruitment did not provide for this.

Study procedures

Sample collection, pre-processing, and storage

Cord blood was collected within 30 min of placental delivery and using aseptic techniques to minimize the risk of contamination from maternal blood or other body fluids [29]. Maternal blood was collected within 48 h of delivery. Serum aliquots were stored in −80℃ freezers at

the study sites and later shipped to the main biorepository at Aga Khan University, Nairobi, for long-term storage at −80℃.

Sample selection process

All available paired maternal delivery and cord blood samples were selected. Maternal sera were tested for SARS-CoV-2 receptor binding domain (RBD) (IgM/IgG) total antibodies. For mothers, whose delivery samples tested positive, maternal and corresponding cord blood samples were tested for SARS-CoV-2 antibodies against the spike (S) and nucleocapsid proteins (NCP).

Laboratory analysis

Testing for SARS-CoV-2 antibodies was conducted via ELISA assays at the Aga Khan University laboratory, using the ETI-MAX 3000 from Diasorin, Italy, a fully automated microtiter plate analyser. SARS-CoV-2 serology was assessed by three different assays targeting the RBD (total antibodies), anti-spike, and anti-NCP. We tested the maternal blood for RBD IgM/IgG total antibodies using the Wantai kit (Beijing Wantai Biological Pharmacy Enterprise Co., Ltd, Beijing, China) as a screening test. The manufacturer reported assay sensitivity is 94.36%, with a specificity of 100%.

Maternal serum and cord blood were analysed using two ELISA kits from Euroimmun, Germany. The QuantiVac assay (anti-spike) is a quantitative assay whose values correspond to the level of SARS-CoV-2 neutralizing antibodies, a surrogate for immunity, with a reported sensitivity of 80% and a specificity of 98.5%. The assay had a measurement range of 1 to 120 RU/ml. Euroimmun anti-NCP ELISA (IgG) is a semi-quantitative immunoassay with a reported sensitivity of 94.6% and specificity of 99.8% in samples collected at least 10 days after confirmed SARS-COV-2 infection. Anti-SARS-CoV-2 NCP ELISA was positive with an optical density ratio ≥ 1.1, indeterminate between 0.8 and 1.1, and negative <0.8. All assays were conducted following the manufacturer's instructions which include a 1:101 dilution step of the serum.

To ensure the reliability and accuracy of the assays, all three SARS-CoV-2 ELISA kits were verified using 20 known negative serum samples collected prior to the COVID-19 pandemic, as well as 22 serum samples positive for antibodies against both spike and nucleocapsid proteins obtained from individuals who had a positive SARS-CoV-2 PCR. All three kits exhibited sensitivities and specificities of 100%.

The use of assays targeting antibodies against the spike protein is particularly relevant in population-based seroprevalence studies, especially in settings with low SARS-CoV-2 vaccine uptake [35], as these antibodies may serve as a surrogate for neutralizing activity. Testing for antibodies against NCP helps in distinguishing SARS-CoV-2 infection from vaccination.

Ethical approval

All participants provided written informed consent to participate in the PRECISE study which included biological sample collection, storage, and use of the data and samples to answer the study objectives including identifying drivers of adverse pregnancy outcomes in SSA. The PRECISE study obtained ethical approval from the Aga Khan University Ethics Review Committee (2018/REC-74) and King's College London BDM Research Ethics Subcommittee (Ref HR-17/18–7855). The study was conducted in accordance with the local legislation and institutional requirements.

Data analysis

Patient clinical characteristics and demographics were summarized with the median and inter-quartile range (IQR) calculated for continuous variables and percentages calculated for categorical variables.

A true positive for the maternal blood was a positive result on both the Wantai and any of the Euroimmun tests. Seropositivity in cord blood was defined as any positive result from either the Euroimmun anti-spike IgG or the anti-NCP IgG assays. Univariable binary logistic regression models were used to calculate the odds ratio of a cord blood sample being seropositive overall and for anti-NCP IgG and anti-spike IgG separately for selected maternal and neonatal factors such as maternal age, body mass index (BMI), mid-upper arm circumference (MUAC), gravidity, gestational age, birth weight and mode of delivery.

Antibody concentrations in maternal and cord blood were reported as geometric mean concentrations (GMC) with 95% confidence intervals (CI), where the GMC was calculated as the antilog of the mean of the log-transformed antibody concentrations.

To assess placental antibody transfer, the transfer ratio was calculated for each infant by dividing the cord blood anti-spike IgG concentration by the maternal anti-spike IgG concentration. Transfer ratios were reported as geometric mean ratios (GMR) with 95% confidence intervals.

Anti-spike IgG concentrations below the lower or above upper limit of detection for the QuantiVac assay were imputed with a value equal to the corresponding threshold values. Specifically, concentrations <1 were assigned as 1, and values >120 were assigned as 120. Relative units (RU/mL) <8 was scored negative, ≥ 8 and <11 was scored borderline, and ≥ 11 was scored positive.

Data were analysed using IBM SPSS Statistics, Version 25 (Chicago, IL, USA), and R Version 4.3.0 (R Foundation, Indianapolis, IN, USA).

Results

Between March 2020 and March 2022, there were 1,394 births at the study sites. Paired maternal delivery and cord blood samples were available for 877 women. Of these samples, 492 (56.1%) tested positive for RBD IgM/IgG total antibodies on the Wantai assay and had corresponding cord blood samples tested. The sample selection and testing process is shown in Fig. 1. The median (IQR) maternal age was 27 (24 to 32) years with the majority of mothers aged between 19–29 years (311/492, 63.2%). The median gestational age was 39.2 (37.4 to 40.5) weeks at delivery and a median birth weight of 3002.5 (2700 to 3267.5) grams, with 87.8% (431/491) having normal birth weight (≥ 2500 g) as shown in Table 1.

SARS-CoV-2 seropositivity

A total of 492 (56.1%) out of 877 tested maternal delivery samples were positive for IgM/IgG total antibodies. Of these, 416 [84.6%, (95% CI: 81.4–87.7)] were seropositive for either anti-NCP IgG or anti-spike IgG antibodies and 231 [55.5%, (95% CI: 50.8–60.3)] were positive for both antibodies (Fig. 2).

For cord blood samples, 412 [83.1%, (95% CI: 79.8–86.4)] tested positive for either anti-NCP IgG or anti-spike IgG antibodies and 258 [62.6%, (95% CI: 57.9–67.3)] were positive for both antibodies (Fig. 2). A total of 296 samples (71.8%, 95% CI: 67.5–76.2%) tested positive for anti-NCP antibodies, 374 (91.0%, 95% CI: 88.2–93.8%) tested positive for anti-spike antibodies.

Table 2 shows concordance in seropositivity between maternal and cord blood for anti-NCP and anti-spike IgG.

Placental transfer of antibodies from mother to neonate

The maternal and cord blood anti-spike GMC were 20.7 (95% CI: 18.6, 23.1) and 21.3 (95% CI: 18.4, 24.7)

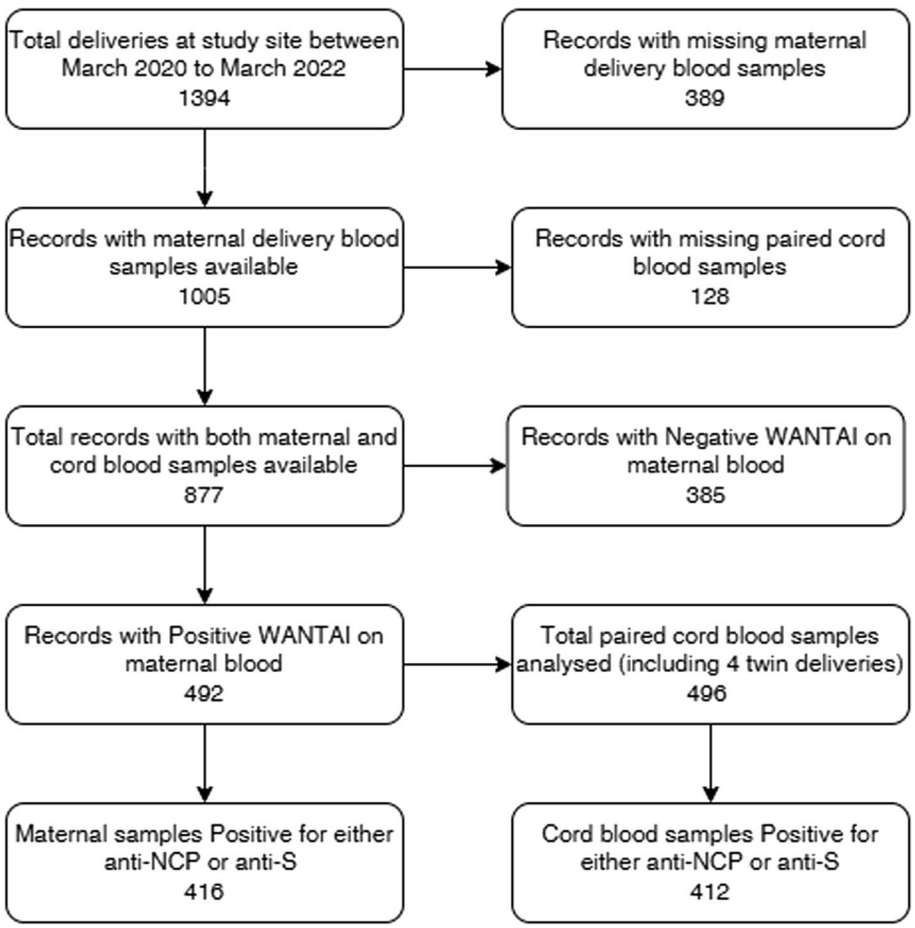

Fig. 1 Study flow diagram showing sample selection for analysis

Table 1 Maternal and newborn characteristics

Maternal characteristics	Seropositive ($n = 416$)	Seronegative ($n = 76$)
Maternal age (years), Median (IQR)	27.0 (23.0, 32.0)	28.0 (24.0, 32.0)
Maternal age group (years), n (%)		
< 30	267 (64.2%)	49 (64.5%)
> = 30	149 (35.8%)	27 (35.5%)
BMI (kg/m^2), Median (IQR)	24.8 (21.9, 28.6)	23.0 (20.7, 25.5)
Missing	5	1
BMI category, n (%)		
Underweight (< 18.5)	11 (2.7%)	4 (4.7%)
Normal (18.5–24.9)	201 (48.9%)	50 (58.8%)
Overweight (25–29.9)	123 (29.9%)	23 (27.1%)
Obese (> 30)	76 (18.5%)	8 (9.4%)
Missing	5	1
Mid-upper arm circumference (cm), n (%)		
Malnourished (MUAC < 21 cm)	9 (2.2%)	3 (3.9%)
Underweight (21 ≤ MUAC < 23 cm)	37 (9.0%)	12 (15.8%)
Normal weight (23 ≤ MUAC < 27 cm)	156 (37.8%)	39 (51.3%)
Overweight (27 ≤ MUAC < 31 cm)	120 (29.1%)	15 (19.7%)
Obese (MUAC ≥ 31 cm)	91 (22.0%)	7 (9.2%)
Missing	3	0
Health facility, n (%)		
Mariakani (urban)	203 (48.8%)	41 (53.9%)
Rabai (rural)	213 (51.2%)	35 (46.1%)
Infant characteristics	$n = 412$	$n = 84$
Gestational age (weeks), Median (IQR)	39.2 (37.4, 40.5)	39.0 (37.4, 40.7)
Missing	25	6
Gestation at birth (weeks + days), n (%)		
Preterm 20 + 0—36 + 6 weeks	73 (18.8%)	14 (18.0%)
Term 37—41 + 6 weeks	291 (75.0%)	58 (74.4%)
Post-term ≥ 42 + 0 weeks	24 (6.2%)	6 (7.7%)
Missing	24	6
Birth weight (grams), Median (IQR)	3013.8 (2708.8, 3306.3)	2925 (2632.5, 3240)
Missing	2	1
Birth weight (grams), n (%)		
1000–1499	1 (0.2%)	0 (0.0%)
1500–2499	45 (11.0%)	14 (16.9%)
> = 2500	362 (88.7%)	69 (83.1%)
Missing	4	1
Mode of delivery, n (%)		
Cesarean section	43 (10.4%)	15 (18.3%)
Vaginal	369 (89.6%)	67 (81.7%)
Missing	0	2
Number of infants, n (%)		
Singleton	408 (99.0%)	80 (95.2%)
Twins	4 (1.0%)	4 (4.8%)

respectively. The GMR for the placental transfer of anti-spike IgG was 1.04 (95% CI: 0.90, 1.21) which indicated no significant difference between the anti-spike IgG concentration in the cord and maternal blood samples. Figure 3 shows the placental transfer ratio for each mother-infant pair, while Fig. 4 shows the individual

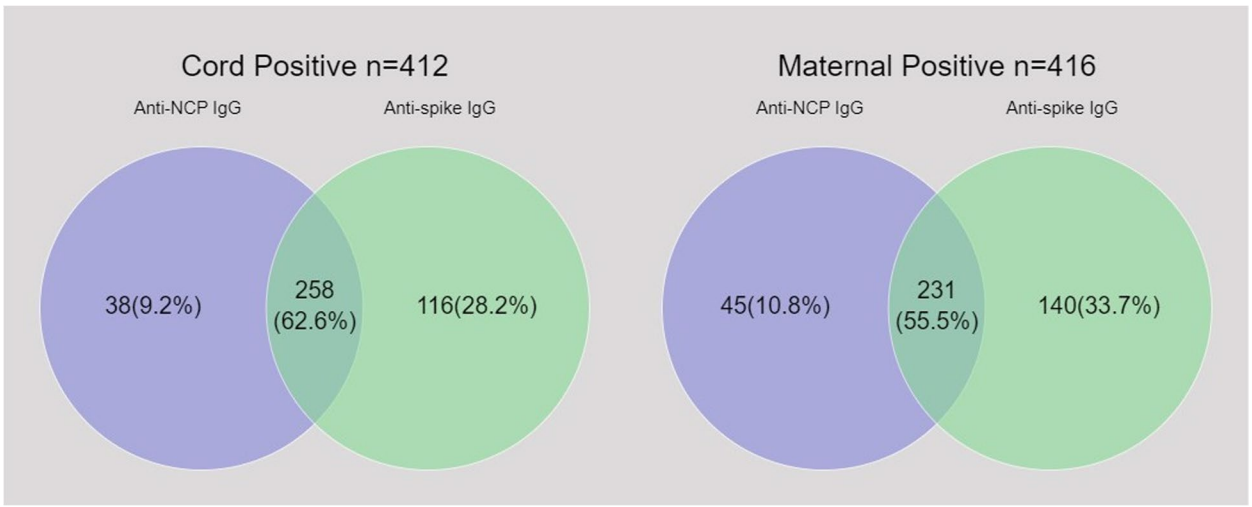

Fig. 2 Maternal and cord blood seropositivity for anti-NCP IgG and anti-spike (anti-S) IgG. Key: Seropositivity of maternal (left) and cord (right) samples for either anti-NCP IgG or anti-spike IgG or both. Seropositivity against anti-NCP IgG alone (light blue), anti-spike IgG alone (green), and both antigens (aqua green)

Table 2 Maternal and cord blood seropositivity for anti-NCP & anti-spike IgG

Overall	**Cord n (%)**	
Maternal	Negative, $n = 84$	Positive, $n = 412$
Negative	29 (35%)	48 (12%)
Positive	55 (65%)	364 (88%)
Anti-NCP IgG	Cord n (%)	
Maternal	Negative, $n = 200$	Positive, $n = 296$
Negative	141 (70%)	76 (26%)
Positive	59 (30%)	220 (74%)
Anti-S IgG	Cord n (%)	
Maternal	Negative, $n = 122$	Positive, $n = 374$
Negative	56 (46%)	67 (18%)
Positive	66 (54%)	307 (82%)

maternal and cord blood anti-spike IgG concentrations, with each mother-infant pair connected by a line.

The log-transformed maternal and cord anti-spike IgG concentrations showed a weak positive correlation ($r = 0.364$, $n = 496$, $p < 0.001$).

Association between maternal and neonatal factors and placental transfer of SARS-CoV-2 antibodies

Of the maternal and neonatal factors tested, only MUAC had an association with cord blood seropositivity where a MUAC ≥ 31 cm increased the odds of anti-spike IgG seropositivity with an OR of 1.88 (1.02, 3.66) (Table 3).

Maternal and neonatal factors were not associated with the anti-spike IgG placental transfer ratio (e.g., maternal age and gravidity with GMRs of 0.99 (0.97, 1.02) and 0.99 (0.92, 1.07), respectively) (Table 4).

Discussion

We determined placental transfer of SARS-CoV-2 antibodies in pregnant women positive for RBD antibodies secondary to infection evidenced by a high prevalence of anti-NCP antibodies and the low SARS-CoV-2 vaccine coverage in the study area [14]. Whereas similar studies have been carried out in East Africa, this is the first study from Kenya that has addressed placental transfer and its determinants.

The overall cord blood SARS-CoV-2 seropositivity was 83.1% with a GMR of 1.04, indicating no significant difference between the anti-spike IgG concentration in the cord and maternal blood samples. This suggests efficient transplacental transfer of maternal antibodies to the infant, with antibody levels in the cord blood mirroring those in maternal blood. A study from Uganda and Malawi had similar findings although GMRs for anti-spike antibodies varied from 0.7 to 1.7 with a general increase noted with each subsequent wave of the COVID-19 pandemic [19]. In this study, possible explanations for such variations include heterogeneity in the immune response to prior infection or SARS-CoV-2 vaccination, the emergence of different variants of SARS-CoV-2 at different phases of the pandemic, the gestation at which infection took place, and variations in the sensitivity and specificity of assays [36–39]. SARS-CoV-2 infections earlier in the second and third trimesters, severity of COVID-19 and a higher concentration of maternal SARS-CoV-2 IgG antibodies have been associated with a

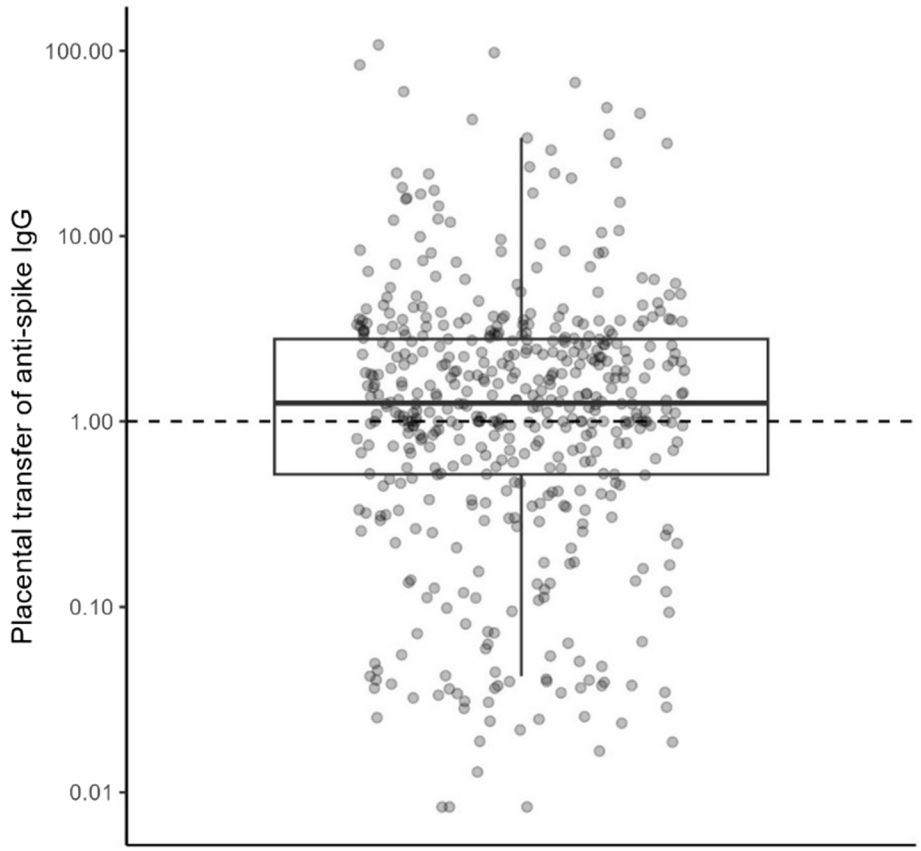

Fig. 3 Placental transfer of anti-spike IgG for each mother-infant pair. Each point represents the placental transfer for one mother-infant pair. The boxplot shows the median and inter-quartile range

greater likelihood of transplacental transfer of IgG [40]. This study did find a weak positive correlation between the concentration of maternal and cord blood anti-spike IgG concentrations.

Studies have shown variations in placental transfer efficiency of SARS-CoV-2 antibodies, particularly during specific waves of the pandemic [19, 39]. Acute SARS-CoV-2 infection in the third trimester has also been shown to result in reduced placental transfer efficiency linked to glycosylation of the Fc portion of SARS-CoV-2 antibodies [38]. While some studies have indicated a robust maternal immune response after SARS-CoV-2 infection in pregnancy, others demonstrate that the ratio of SARS-CoV-2 antibodies in cord blood to maternal levels is low [41]. Our study was conducted prior to the widespread implementation of SARS-CoV-2 vaccination hence the findings largely reflect immunity acquired from infection. Kilifi County had previously been reported to have had one of the highest SARS-CoV-2 seropositivity rates in Kenya [14, 42]. With the absence of antibody transfer in several cases in this study, further investigation is needed to understand the factors contributing to this variability. This has a potential policy implication, as neonates rely on passive immunity from mothers for protection in the absence of vaccination.

The current study found no association between maternal age, BMI, gestational age, birth weight, or mode of delivery and the placental transfer efficiency of SARS-CoV-2 IgG antibodies to newborns. This contrasts with previous findings, including a study in Iran, which showed that low neonatal birth weight and maternal obesity were associated with reduced transplacental antibody transfer ratio [43]. Tallarel et. al. reported that higher maternal BMI negatively influences the efficiency of transplacental antibody transfer [44], potentially due to disruption in placental function, particularly syncytiotrophoblasts involved in transplacental IgG transport [10]. Furthermore, Wilcox et al. noted that the transfer of IgG from mother to foetus depends on gestational age particularly after the 36th week of gestation, IgG subclass and glycosylation, maternal IgG concentration, maternal disease and birthweight with conflicting evidence regarding the complexities of these relationships [45]. In the analysis

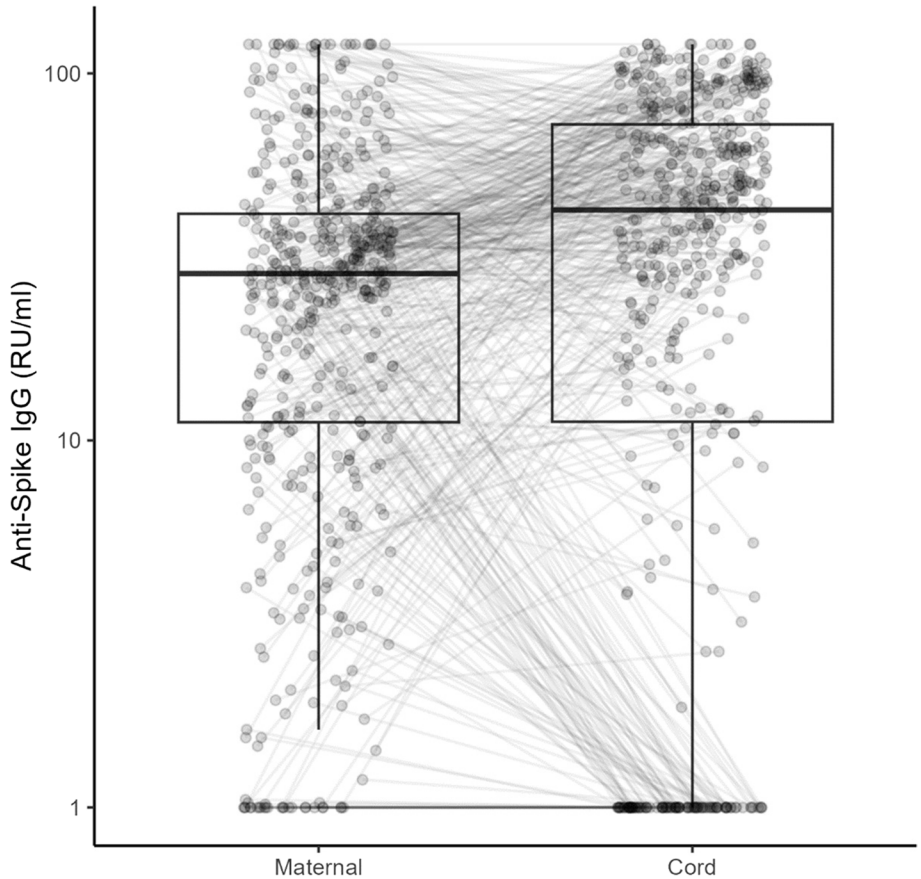

Fig. 4 Paired maternal and cord blood anti-spike IgG concentrations. Points show the anti-spike IgG concentration in each maternal and cord blood sample, and the lines connect the anti-spike IgG concentration for each mother-infant pair. The boxplots show the median and inter-quartile range

of factors associated with cord seropositivity, MUAC > 31 cm was the only factor with a confidence interval which did not overlap the null value. Given the number of comparisons included in this paper this is likely to be a chance finding.

We hypothesize that the differences in our findings could be attributed to population-specific factors such as genetic or immunological response variations including pregnancy-induced changes in immunity which could influence placental function or antibody transfer [8, 12, 22]. For example, serum IgG levels in adults, a known determinant of placental transfer of antibodies, has been found to be higher in SSA compared to the US [23]. Hypergammaglobulinemia and placental malaria have been associated with reduced placental transfer of measles antibodies possibly due to saturation of the placental FcRn receptor used in IgG transfer and subsequent lysosomal destruction of unbound IgG in the placenta [12]. In the setting of immunosuppressed states like HIV or infections like placental malaria, the efficiency of placental transfer can be affected [24, 46].

Study strengths

The study's strengths included a large number of maternal and cord blood samples, and directly addressing the clinically relevant question of maternal-foetal antibody transfer to newborns. As it is likely that most women enrolled during the study period had not received the SARS-CoV-2 vaccine, the study offers unique insight into transplacental transfer in the setting of naturally acquired immunity [14]. The use of a validated quantitative assay that has been shown to correlate well with the level of SARS-CoV-2 neutralizing antibodies enabled the calculation of a GMR and determination of correlation between the level of antibodies in maternal and cord blood samples.

Study limitations

This study has several limitations. First, majority of the mothers were asymptomatic and we did not perform SARS-CoV-2 PCR which would have provided a more accurate estimate of the time of infection relative to sample collection. Estimating the time of infection

Table 3 Maternal and neonatal factors associated with cord positivity for anti-NCP IgG, anti-spike IgG, and overall

	Overall				Anti-NCP				Anti-Spike			
Characteristic	**N**	**Event N**	**OR[1]**	**95% CI[1]**	**N**	**Event N**	**OR[1]**	**95% CI[1]**	**N**	**Event N**	**OR[1]**	**95% CI[1]**
Maternal age (years)	496	412	0.99	0.95, 1.03	496	296	1.01	0.98, 1.04	496	374	0.99	0.96, 1.03
Maternal age												
< 30	319	263	—	—	319	184	—	—	319	238	—	—
> = 30	177	149	1.13	0.70, 1.88	177	112	1.26	0.87, 1.85	177	136	1.13	0.74, 1.75
BMI category												
Normal	253	209	—	—	253	149	—	—	253	185	—	—
Underweight	15	10	0.42	0.14, 1.41	15	6	0.47	0.15, 1.33	15	9	0.55	0.19, 1.70
Overweight	136	116	1.22	0.70, 2.21	136	86	1.20	0.78, 1.85	136	105	1.24	0.77, 2.05
Obese	86	71	1.00	0.53, 1.95	86	51	1.02	0.62, 1.68	86	70	1.61	0.89, 3.04
Gravidity	496	412	1.03	0.92, 1.16	496	296	1.07	0.98, 1.18	496	374	1.01	0.91, 1.12
Gravidity												
1	122	100	—	—	122	69	—	—	122	89	—	—
2	115	92	0.88	0.46, 1.69	115	65	1.00	0.60, 1.67	115	86	1.10	0.62, 1.97
3	106	94	1.72	0.82, 3.78	106	65	1.22	0.72, 2.07	106	87	1.70	0.91, 3.26
> = 4	153	126	1.03	0.55, 1.91	153	97	1.33	0.82, 2.17	153	112	1.01	0.59, 1.73
Term												
Term 37–41 + 6 weeks	349	291	—	—	349	202	—	—	349	260	—	—
Preterm 20–36 + 6 weeks	87	73	1.04	0.56, 2.03	87	59	1.53	0.94, 2.55	87	69	1.31	0.75, 2.38
Post-term > = 42 weeks	30	24	0.80	0.33, 2.23	30	18	1.09	0.51, 2.39	30	22	0.94	0.42, 2.32
Birth weight (grams)	493	410	1.00	1.00, 1.00	493	294	1.00	1.00, 1.00	493	372	1.00	1.00, 1.00
Mode of delivery												
Cesarean section	58	43	—	—	58	33	—	—	58	40	—	—
Vaginal	436	369	1.92	0.98, 3.59	436	263	1.15	0.66, 2.00	436	334	1.47	0.79, 2.65
MUAC category												
Normal weight (23 ≤ MUAC < 27 cm)	197	165	—	—	197	116	—	—	197	147	—	—
Malnourished (MUAC < 21 cm)	12	10	0.97	0.24, 6.50	12	8	1.40	0.42, 5.38	12	8	0.68	0.20, 2.64
Underweight (21 ≤ MUAC < 23 cm)	49	35	0.48	0.24, 1.02	49	24	0.67	0.36, 1.26	49	30	0.54	0.28, 1.05
Overweight (27 ≤ MUAC < 31 cm)	137	113	0.91	0.51, 1.64	137	80	0.98	0.63, 1.53	137	104	1.07	0.65, 1.79
Obese (MUAC ≥ 31 cm)	98	86	1.39	0.70, 2.93	98	66	1.44	0.87, 2.41	98	83	1.88	1.02, 3.66

[1]*OR* Odds Ratio, *CI* Confidence Interval

would be essential in assessing maternal antibody kinetics and subsequent transplacental transfer given that the half-life of anti-spike antibodies has been shown to be as long as 198.8 days [47]. Secondly, differences in assay sensitivity and specificity between testing methods could lead to false-negative results [48]. In the current study, we tested cord blood samples for anti-spike and anti-NCP antibodies using Euroimmun tests that have been found to be less sensitive than the Wantai test used to screen the maternal blood samples [14, 39]. Testing the cord blood samples with the Wantai RBD IgM/IgG total antibodies kit may have resulted in a higher seroprevalence. Thirdly, we performed multiple comparisons evaluating several covariates and their association with placental transfer of antibodies without carrying out any power analysis. It is possible that the lack of association seen for some of the covariates could be due to insufficient power.

Conclusion

The findings of this study demonstrate the transfer of SARS-CoV-2-specific antibodies from mothers potentially conferring immunity to their newborns. Importantly, no specific maternal or neonatal characteristics were associated with impaired antibody transfer. Overall, this study contributes to our understanding of antibody transplacental transfer from natural immunity to SARS-CoV-2 infection in a region with a high infectious disease burden. The positive correlation between maternal and cord blood anti-spike concentrations suggests that interventions that increase maternal antibody concentrations such as vaccination may increase passive immunity and protection against severe COVID-19 disease in neonates.

Table 4 Factors associated with the anti-spike IgG placental transfer ratio

Characteristic	N	GMR	95% CI
Maternal age	496	0.99	0.97, 1.02
Maternal age (years)	496		
< 30		Ref	
≥ 30		1.12	0.82, 1.52
BMI category	490		
Normal		Ref	
Underweight		0.61	0.25, 1.46
Overweight		0.98	0.69, 1.39
Obese		0.99	0.66, 1.50
Gravidity	496	0.99	0.92, 1.07
Gravidity	496		
1		Ref	
2		0.95	0.62, 1.45
3		1.41	0.91, 2.17
≥ 4		0.95	0.64, 1.42
Gestational age at delivery (weeks + days)	466		
Term 37 + 0—41 + 6 weeks		Ref	
Preterm 20_0—36 + 6 weeks		1.07	0.72, 1.59
Post term ≥ 42 + 0 weeks		0.97	0.52, 1.81
Birth weight (grams)	493	1.00	1.00, 1.00
Mode of delivery	494		
Caesarean section		Ref	
Vaginal		1.2	0.76, 1.89
MUAC category	493		
Normal weight (23 ≤ MUAC < 27 cm)		Ref	
Malnourished (MUAC < 21 cm)		0.88	0.33, 2.35
Underweight (21 ≤ MUAC < 23 cm)		0.62	0.37, 1.05
Overweight (27 ≤ MUAC < 31 cm)		0.95	0.66, 1.38
Obese (MUAC ≥ 31 cm)		0.87	0.58, 1.31
Malaria	496		
Negative		Ref	
Positive		1.08	0.33, 3.48
Unknown		0.93	0.62, 1.39
HIV	496		
Negative		Ref	
Positive		0.6	0.19, 1.93
Unknown		0.93	0.66, 1.31

This aligns with global efforts to enhance maternal and neonatal health, particularly through optimizing maternal immunization strategies and addressing the determinants of effective passive immunity. Future research should explore the long-term persistence and functional efficacy of these maternally derived antibodies in neonates and potential factors that might influence the efficiency and durability of antibody transfer.

Abbreviations

BMI	Body Mass Index
CI	Confidence intervals (CIs)
COVID-19	Coronavirus Disease 2019
ELISA	Enzyme linked immunosorbent assay
IgG	Immunoglobulin G
IgM	Immunoglobulin M
NCP	The Euroimmun anti-SARS-CoV-2 NCP ELISA test (NCP- Nucleocapsid)
PCR	Polymerase Chain Reaction
PRECISE	PREgnancy Care Integrating translational Science Everywhere

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Group members of the PRECISE Network
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Authors' contributions
AM: Formal Analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. AK: Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Writing – review & editing. MM: Preparation of the dataset, cleaning and troubleshooting. IM: Preparation of the dataset, cleaning and troubleshooting, sample processing & shipping. JM: Preparation of the dataset, cleaning and troubleshooting, sample processing & shipping. LC: Writing – review & editing, Data analysis, Visualization. MV: Writing – review & editing. RC: Writing – review & editing. PvD: Funding acquisition, Methodology, Writing – review & editing. KLD: Funding acquisition, Methodology, Writing – review & editing. MT: Funding acquisition, Writing – review & editing. GO: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing.

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Data availability

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Declarations

Ethics approval and consent to participate

All participants provided written informed consent to participate in the PRECISE study including biological sample collection and storage and use of the data and samples for future research. The study was approved by the Aga Khan University Ethics Review Committee (2018/REC-74) and King's College London BDM Research Ethics Subcommittee (Ref HR-17/18–7855. This study adhered to the ethical principles outlined in the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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