

SUPPLEMENTARY APPENDIX

Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2

mRNA COVID-19 vaccine

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Supplementary Figures

Supplementary Figure S1

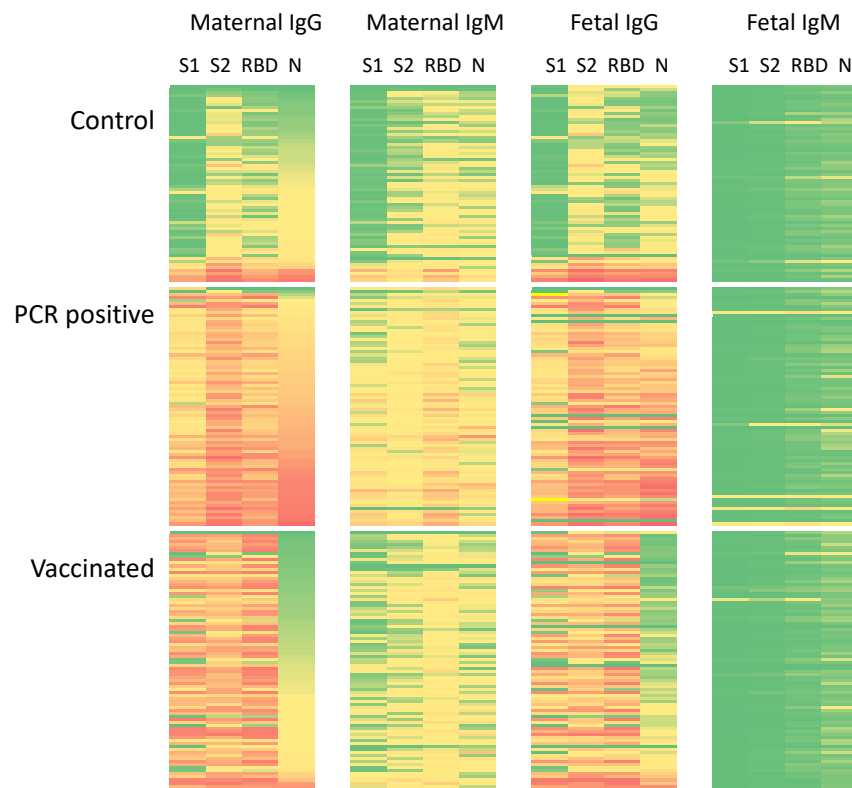


Figure S1 Serological heat map

The heat map was generated from the acquired IgG and IgM serological data segregated by the main recruitment groups (Control, PCR-positive, and Vaccinated patients). From left to right Maternal IgG (S1, S2, RBD, N), Maternal IgM (S1, S2, RBD, N), Fetal IgG (S1, S2, RBD, N) and Fetal IgM (S1, S2, RBD, N). Each row represents matched maternal-fetal data, ranked by the maternal IgG reactivity to N antigen within each group (Low, green; high, red). Note the small number of serologically N⁺ mothers (high N in red) within the control and the vaccinated groups.

Supplementary Figure S2

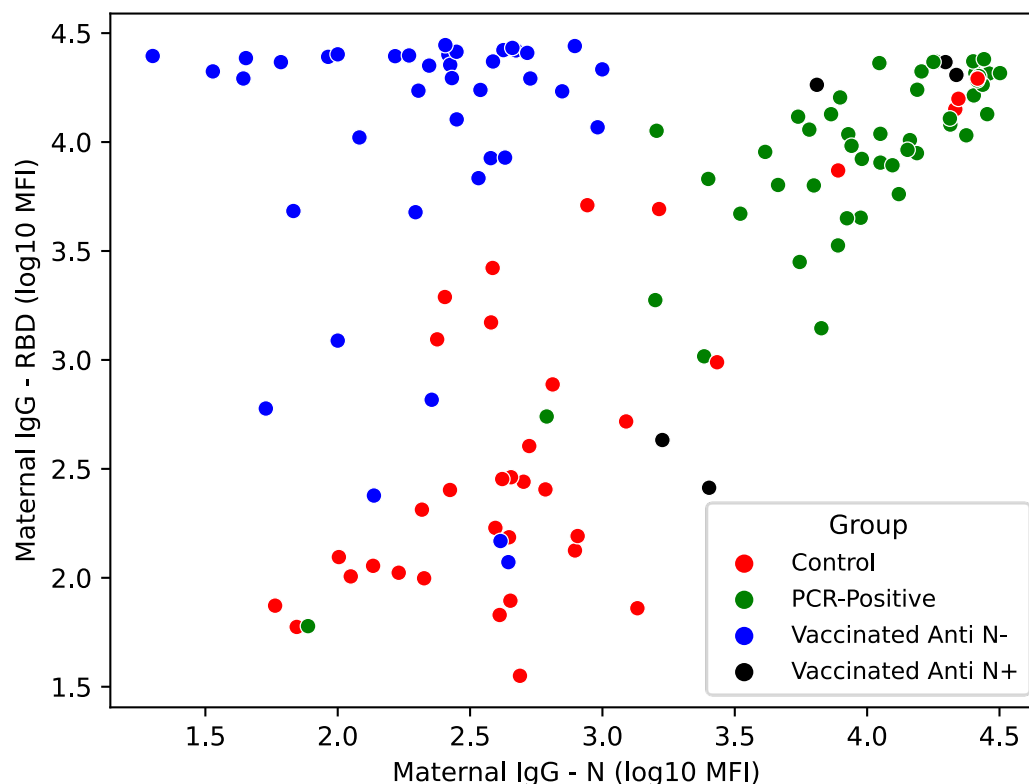


Figure S2 Cluster analysis of all study participants by maternal response to N and RBD. Since Nucleocapsid antigen (N) is present in the intact virus but is not included in the BNT162b2 mRNA COVID-19 vaccine, high IgG titer for N reveals patients exposed to the virus. On the other hand, RBD is present in the vaccine as well as the virus. Thus, high IgG for both RBD and N reveal a small number of patients exposed to the virus within the control group (red) as well as vaccinated (black), which cluster with the PCR-positive group (green; upper right cluster). Low IgG for N and high IgG for RBD was found for the majority of the vaccinated patients (blue; upper left corner). The unvaccinated control group which showed no humoral response indicative of prior infection cluster in the bottom lower corner (red).

Supplementary Figure S3

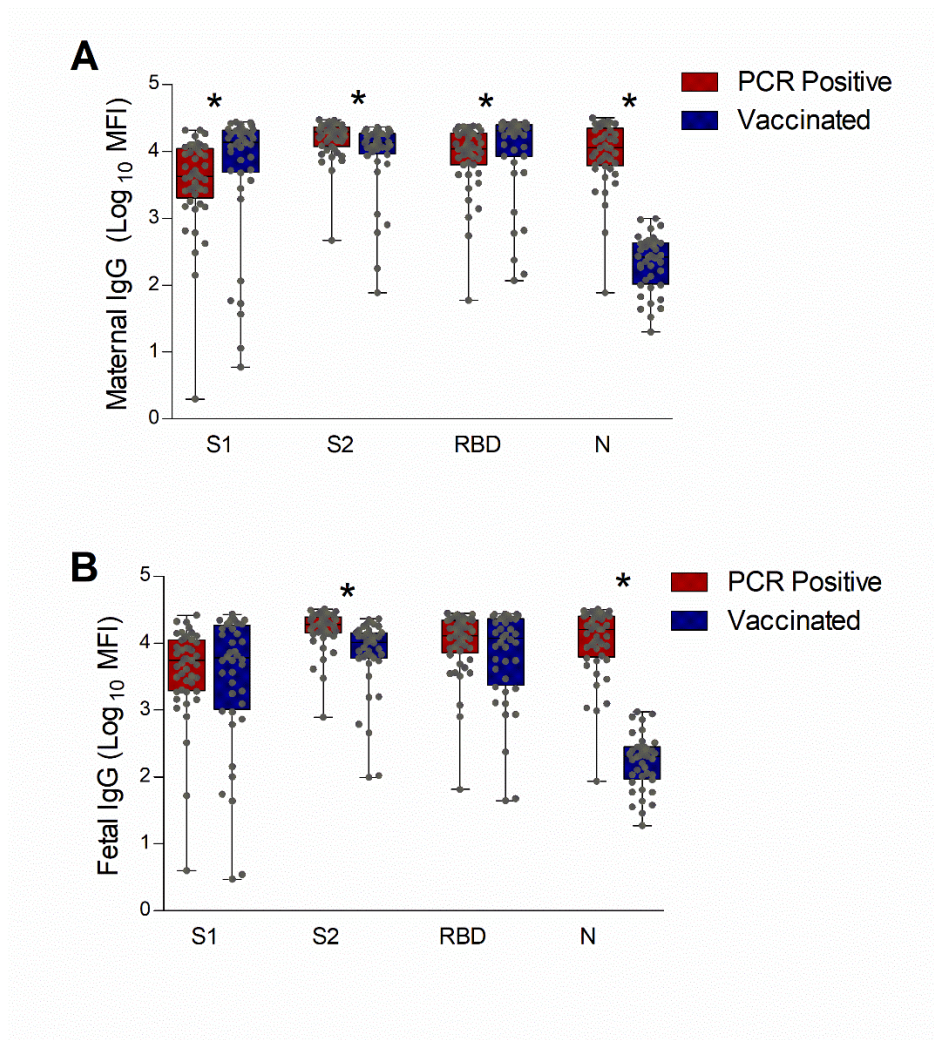
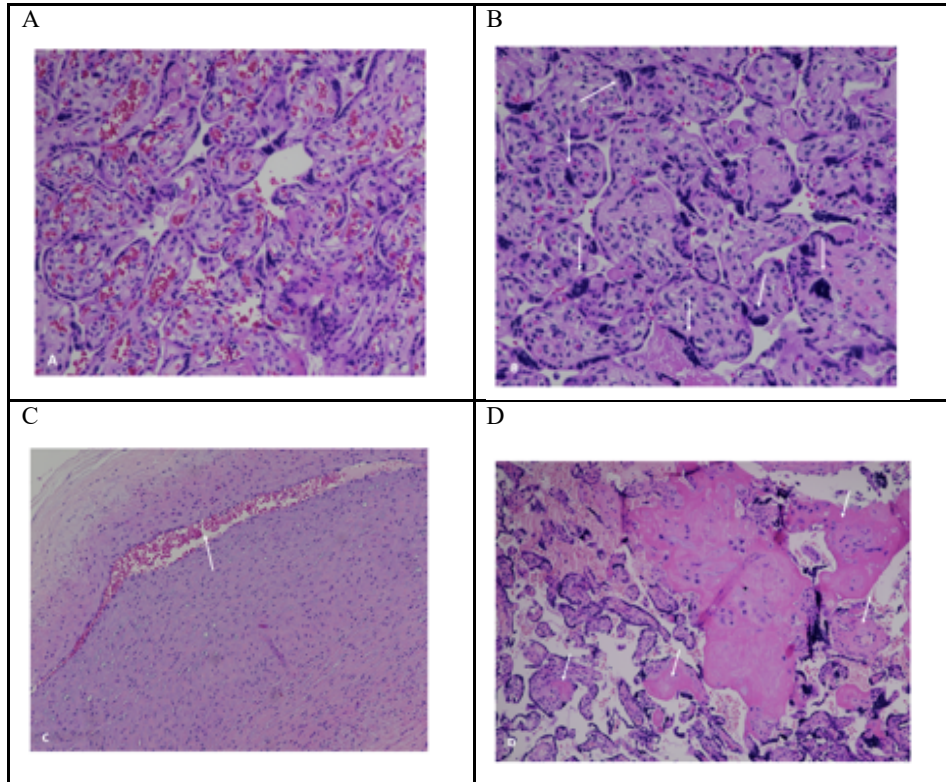


Figure S3. Maternal and fetal IgG for S1, S2 RBD and N following SARS-Co2 infection vs. vaccination. *indicate a significant difference in antibody levels between PCR positive vs. vaccinated patients (Wilcoxon Rank Sum Test).

Supplementary Figure S4 Placental Samples Examination



Supplementary Figure S4. Placental Samples Examination. hematoxylin-eosin, original magnification X10

- A- Normal histologic appearance of placental villi (from a vaccinated patient)
- B- Maternal vascular malperfusion lesion- increased syncytial knots (arrows) (from past covid 19 infected parturient)
- C- Fetal vascular malperfusion lesion- chorionic vessel with intramural fibrin deposition. Arrow towards vessel lumen (from a vaccinated patient)
- D- Maternal vascular malperfusion lesion- increased intervillous fibrin deposition (arrows) (from past covid 19 infected parturient)

Supplementary Tables

Supplementary Table S1. Statistical analysis of maternal and fetal serological response to vaccination. Analysis of the data presented in Figure 3D

Ab type	Comparison	Statistical test	P value
IgG S1	Maternal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	< 0.0001
	Fetal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	< 0.0001
	Maternal vs. fetal Ab concentrations within the Control group	Paired t-test	0.0034
	Maternal vs. fetal Ab concentrations within the 1 st Dose group	Paired t-test	0.0050
	Maternal vs. fetal Ab concentrations within the 2nd Dose group	Paired t-test	0.0071
	Maternal vs. fetal Ab concentrations within the Fully-vaccinated group	Paired t-test	0.0085
IgG S2	Maternal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	< 0.0001
	Fetal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	< 0.0001
	Maternal vs. fetal Ab concentrations within the Control group	Paired t-test	0.4190
	Maternal vs. fetal Ab concentrations within the 1 st Dose group	Paired t-test	0.0203

	Maternal vs. fetal Ab concentrations within the 2nd Dose group	Paired t-test	0.0930
	Maternal vs. fetal Ab concentrations within the Fully-vaccinated group	Paired t-test	0.0197
IgG RBD	Maternal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	< 0.0001
	Fetal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	< 0.0001
	Maternal vs. fetal Ab concentrations within the Control group	Paired t-test	0.0084
	Maternal vs. fetal Ab concentrations within the 1 st Dose group	Paired t-test	0.0052
	Maternal vs. fetal Ab concentrations within the 2nd Dose group	Paired t-test	0.0069
	Maternal vs. fetal Ab concentrations within the Fully-vaccinated group	Paired t-test	0.0339
IgG N	Maternal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	0.3016
	Fetal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	0.3869
	Maternal vs. fetal Ab concentrations within the Control group	Paired t-test	0.0142
	Maternal vs. fetal Ab concentrations within the 1 st Dose group	Paired t-test	0.0562
	Maternal vs. fetal Ab concentrations within the 2nd Dose group	Paired t-test	0.2313
	Maternal vs. fetal Ab concentrations within the Fully-vaccinated group	Paired t-test	0.08903

Ab type	Comparison	Statistical test	P value
IgM S1	Maternal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	< 0.0001
	Fetal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	0.1176
	Maternal vs. fetal Ab concentrations within the Control group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the 1 st Dose group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the 2nd Dose group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the Fully-vaccinated group	Paired t-test	< 0.0001
IgM S2	Maternal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	0.0417
	Fetal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	0.7675
	Maternal vs. fetal Ab concentrations within the Control group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the 1 st Dose group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the 2nd Dose group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the Fully-vaccinated group	Paired t-test	< 0.0001
IgM RBD	Maternal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	0.0067
	Fetal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	0.0560

	Maternal vs. fetal Ab concentrations within the Control group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the 1 st Dose group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the 2nd Dose group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the Fully-vaccinated group	Paired t-test	< 0.0001
IgM N	Maternal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	0.9558
	Fetal Ab concentrations among groups	Kruskall–Wallis one-way ANOVA, followed by Dunn's All-Pairwise Comparisons Test.	0.1804
	Maternal vs. fetal Ab concentrations within the Control group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the 1 st Dose group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the 2nd Dose group	Paired t-test	< 0.0001
	Maternal vs. fetal Ab concentrations within the Fully-vaccinated group	Paired t-test	< 0.0001

Supplementary Table S2

Placental Samples Examination

Placental pathology examinations were performed on randomly taken placental tissue samples of 1X1 cm³ thickness, that were fixed in formalin and embedded in paraffin blocks for microscopic assessment. All examinations were done by a single pathologist (author L.S.), who

was blinded to the study groups the samples were taken from. Placental lesions were divided into 3 main groups: 1. Maternal vascular malperfusion (MVM) lesions that included: decidual vasculopathy, increased syncytial knots, villous agglutination, increased intervillous fibrin deposition, and villous infarcts; 2. Fetal vascular malperfusion (FVM) lesions that included large vessel thrombosis or fetal thrombotic vasculopathy, hypovascular, fibrotic and avascular villi; 3. Chronic villitis that was defined as villitis of unknown etiology, plasma cell deciduitis, or chronic intervillitis;

Fourteen placental tissue samples were microscopically examined. The rate of malperfusion lesions was similar in the examined placental tissue

Placental lesions	Control n=5	Past Covid -19 n=3	Vaccinated n=6
MVM	1	2	2
FVM	2	0	2
Chronic villitis	0	0	1