GESTATIONAL COVID19: MORPHOLOGICAL ALTERATIONS AND DECREASED HLA-G EXPRESSION CAUSED BY SARS-COV-2 INFECTION

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Abstract

The evaluation of the effect of SARS-CoV-2 infection during pregnancy has raised interest. Even if virus vertical transmission is still controversial. we previously showed that SARS-CoV-2 infection caused molecular perturbation in placental tissues and fetal organs present SARS-CoV-2 positivity[1,2].

Aim of the Study

Evaluate the morphological effects of SARS-CoV-2 infection in maternal and fetal tissues in correlation to pregnancy biomarkers (e.g. HLA-G).

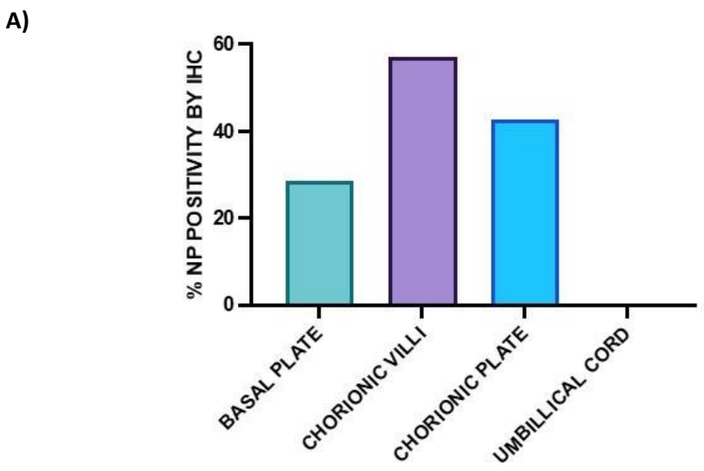
Materials and Methods

Subjects: 7 pregnant women with symptomatic respiratory SARS-CoV-2 infection and compared with 7 non-COVID control subjects.
Samples: placental / chorionic villi, chorionic plate, basal plate, and umbilical cord tissues
Immunohistochemistry: for SARS-CoV-2 Nucleoprotein (NP) and Human Leukocyte Antigen-G (HLA-G)
Morphology evaluation: by H/E staining

Results

Evaluation of SARS-CoV.2 in situ infection

The 57%, 42,8%, and 28,6% of placental / chorionic villi, chorionic plate, and basal plate, respectively, were found positive for NP antigen (**Fig.1 A**; $p<0.01$, Fisher exact test), while none of the umbilical cords stained for NP. Placental / chorionic villi samples showed the highest positivity for NP.(**Fig.1 B**).



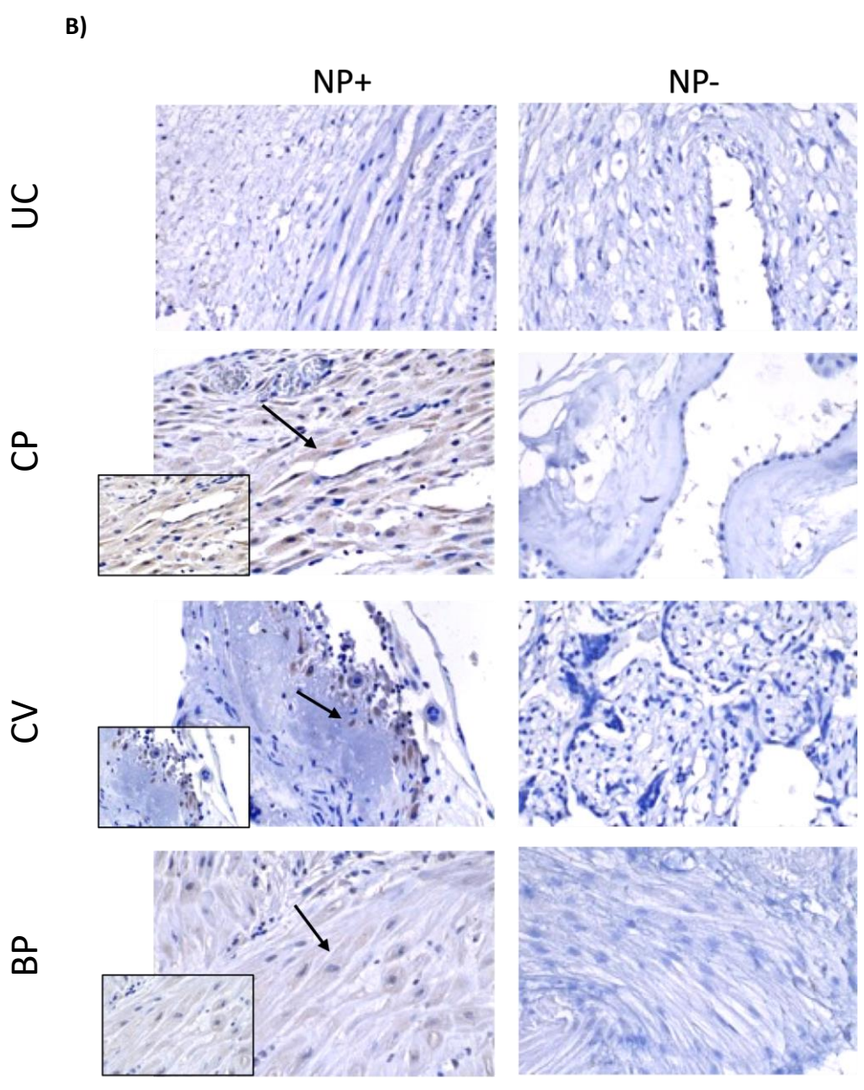


Figure 1. Frequencies of positive samples for the presence of SARS- CoV-2 NP protein **A**) and IHC analysis for SARS-CoV-2 NP in basal plate (BP), chorionic villi (CV), chorionic plate (CP) and umbillical cord (UC) tissues **B**). 40x and 60x magnification.

Morphology and inflammatory status evaluation

The presence of NP positivity correlated with high levels of the fibrinoid component in placental / chorionic villi, altered epithelial layer in chorionic plate and leukocyte infiltration in basal plate. (**Figure 2**)

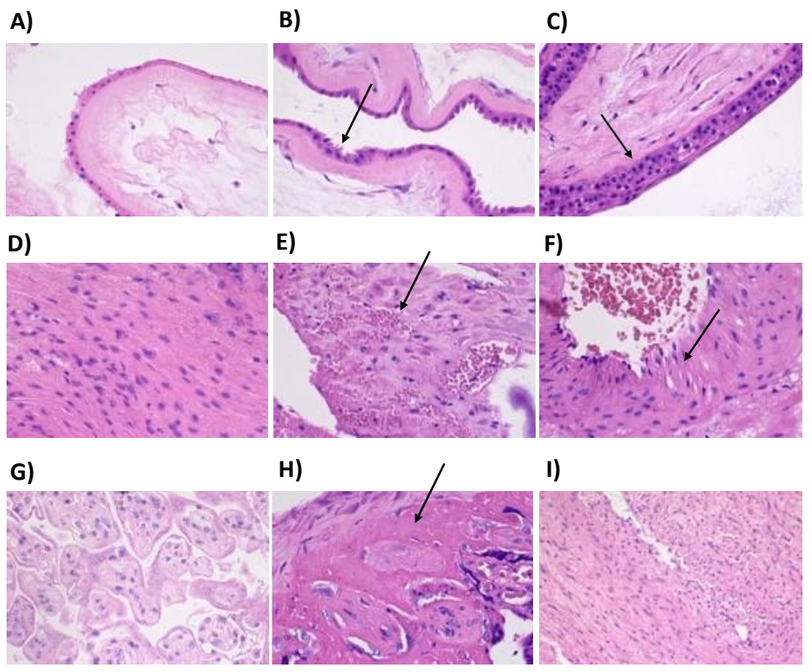


Figure 2. H/E analysis for chorionic plate (**A-C)**, basal plate (**D-F**), chorionic villi (**G-H**) and umbillical cord (**I**) NP+ tissues. Morfological alteration (**B, C, H** and **F**) and inflamatory infiltrates (**E**) are indicated by arrows. 60x magnification.

Evaluation of HLA-G expression

All placental / chorionic villi samples were found positive for HLA-G, independently from NP staining. All the NP positive chorionic plate and half of the NP positive basal plate samples expressed HLA-G. On the contrary, the placental / chorionic villi, chorionic plate, and basal plate of all non-COVID subjects were positive for HLA-G, with a higher H-score in comparison to pathological samples (**Fig.3**; $p<0.05$, Student t test).

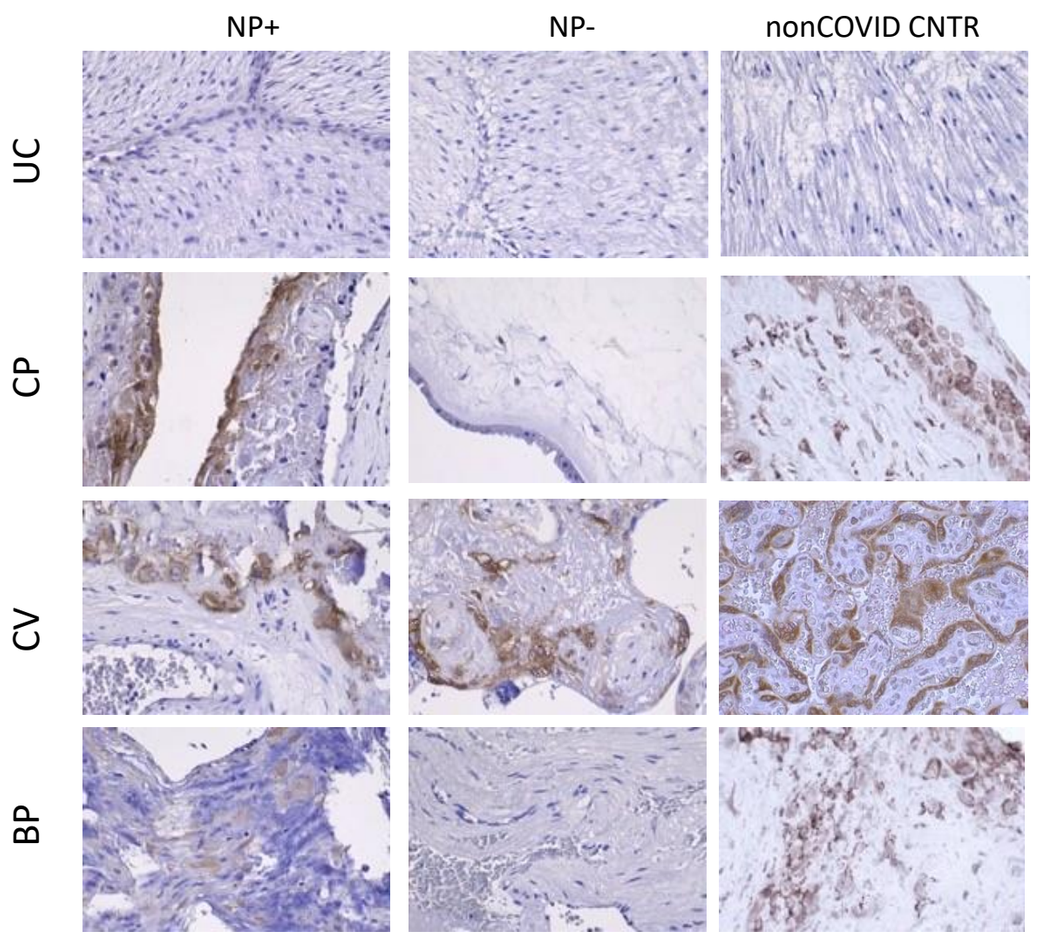


Figure 3. IHC analysis for HLA-G expression in basal plate (BP), chorionic villi (CV), chorionic plate (CP) and umbillical cord (UC) tissues in NP+ and NP- COVID samples, compared to nonCOVID controls (CNTR) . 60x magnification..

Conclusions

The presence of SARS-CoV-2 NP expression in gestational tissues correlates with morphological alterations and a decreased HLA-G expression compared to the control group. These data suggest a possible implication of SARS-CoV-2 infection in morphological and protein expression modification during pregnancy, which might impact on infection susceptibility, pregnancy complications, and vertical transmission.

References

1. Schiuma G, Beltrami S. et al Effect of SARS-CoV-2 infection in pregnancy on CD147, ACE2 and HLA-G expression; Placenta, 2023
2. Greco S., et al. Case report: Tissue positivity for SARS-CoV-2 in a preterm born infant death of thrombosis: possible intrauterine transmission, Frot. Med., 2023