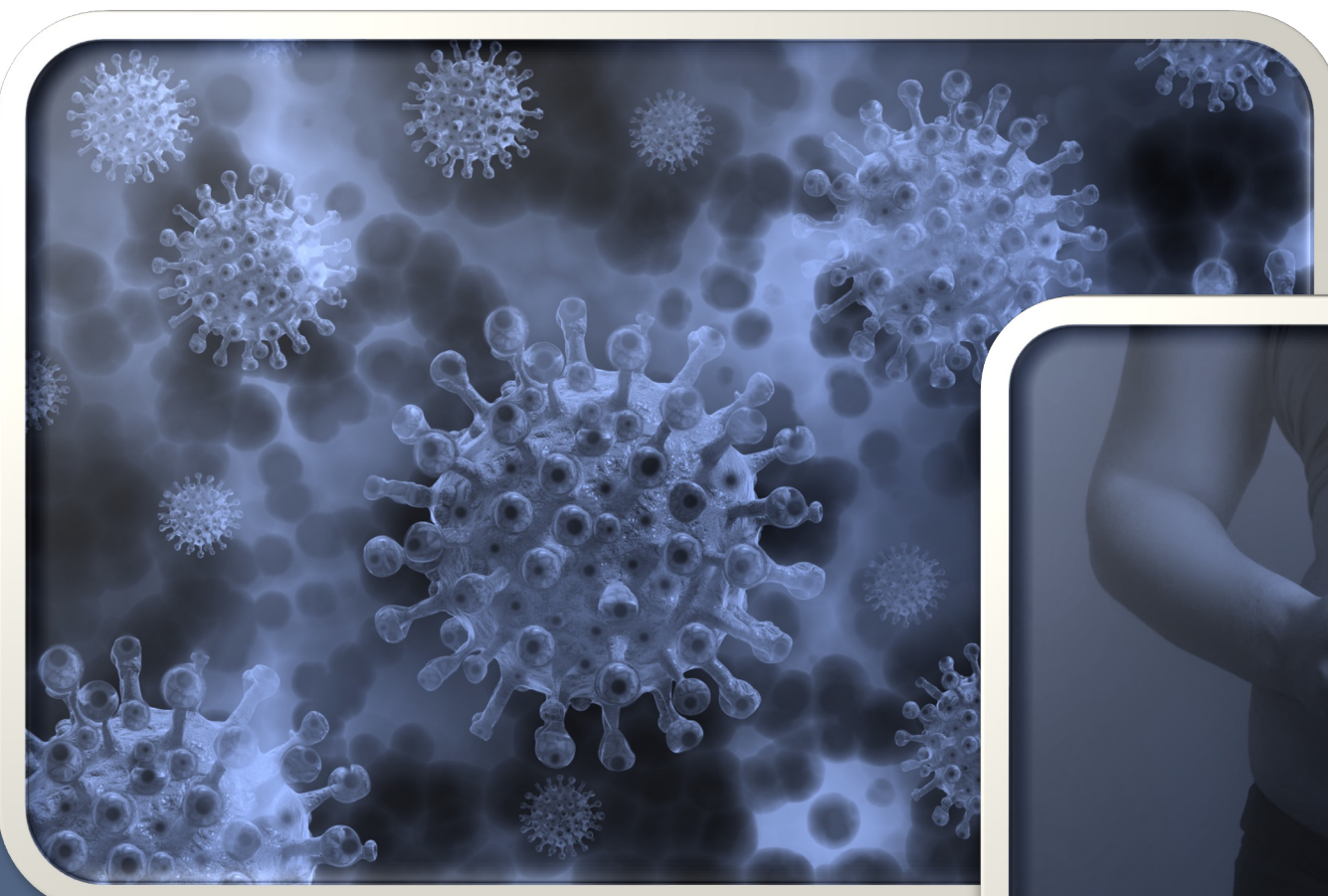


Second Trimester Miscarriage and Retained Placenta Associated With SARS-CoV-2 Placentitis: A Case Report

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Background

- The disease course of COVID-19 appears to be similar in the pregnant and non-pregnant populations, with most infections being mild. There is emerging evidence of the **SARS-CoV-2 infection** leading to pregnancy complications, with reports linking it to **miscarriage, preterm delivery, growth restriction and stillbirth**. Rates of stillbirth and preterm birth have previously been shown to be three times higher in women who are SARS-CoV-2 positive¹, and this rate appears to be rising further.
- Like many other viruses including rubella, varicella-zoster, parvovirus B19, cytomegalovirus, and zika virus, SARS-CoV-2 has been shown to replicate in the placenta. Studies have confirmed **SARS-CoV-2 placentitis as a distinct pathological entity**, with massive perivillous fibrin deposition +/- chronic histiocytic intervillitis², but it should be noted that **not all women who are COVID-19 positive will demonstrate changes in their placenta**. It has also been shown that the **extent of histological changes of placentitis does not correlate with severity of clinical symptoms**^{2,3}.
- We present a case of **second trimester miscarriage and retained placenta, with confirmed SARS-CoV-2 placentitis**, in an asymptomatic patient with a negative lateral flow test and with no known history of COVID-19 infection. To our knowledge this is the first published case of retained placenta associated with SARS-CoV-2 placentitis.

Case Report

- A 19 year old Eastern European patient presented with a **two day history of pain and vaginal bleeding at 15+2 weeks** into her first pregnancy. She spoke no English so was seen with an interpreter. She was **unvaccinated against COVID-19, and had no current or previous symptoms**, normal observations, and a **negative lateral flow test**. She had no co-morbidities, no previous smear tests, she was a non-smoker, and had a normal body mass index of 21.4.
- After delivery of the foetus, the placenta could not be delivered by controlled cord traction, so she was **taken to theatre for manual removal of placenta**. It was noted to be a challenging procedure due to an **extremely adherent placenta**. It was removed piecemeal using both suction and polyp forceps, under ultrasound guidance, and the tissue was found to have an **unusually gritty texture**. Estimated blood loss was 150ml, and she was discharged the following day with no subsequent complications.

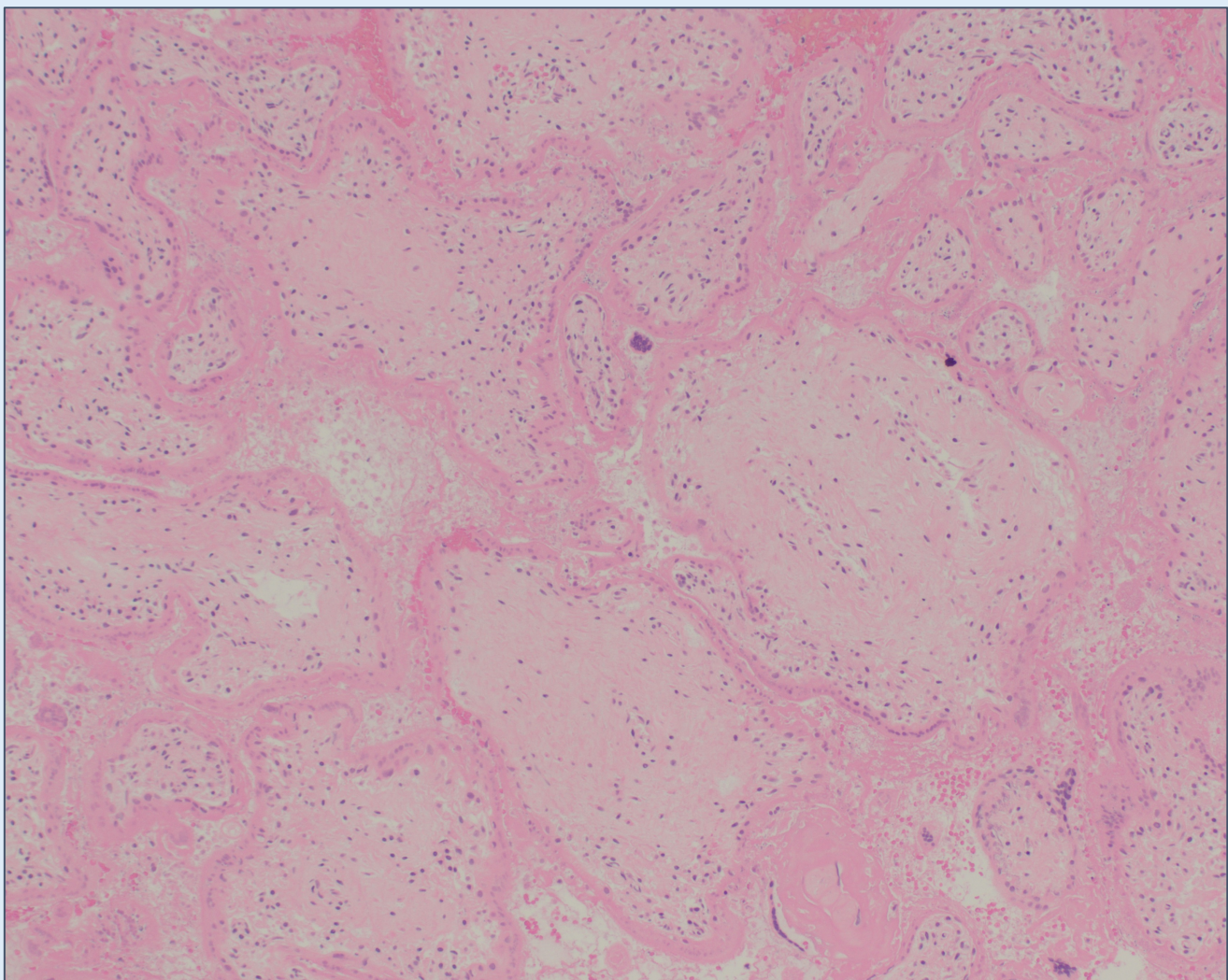


Figure 1: Massive perivillous fibrin deposition with mixed inflammatory cells and necrosis

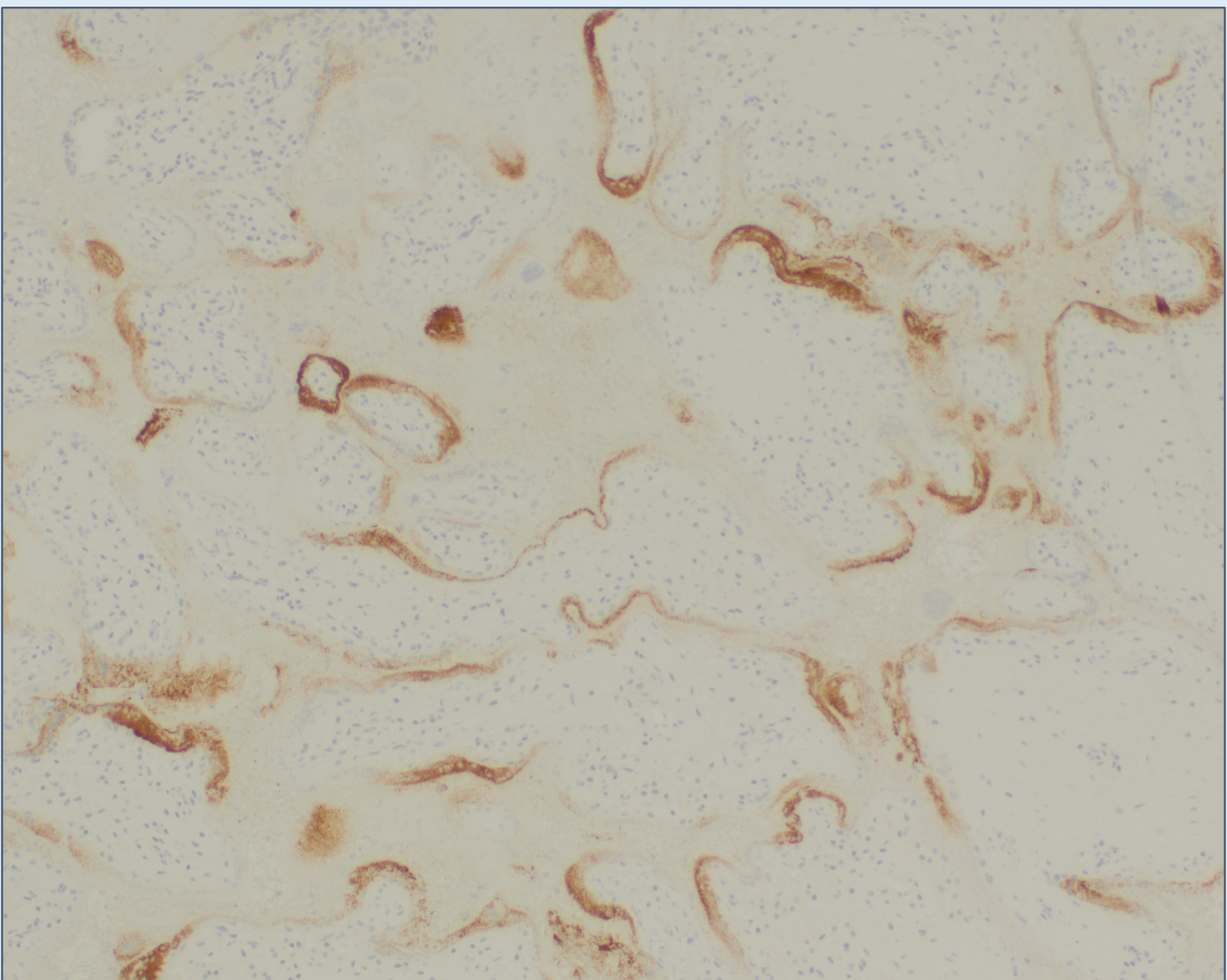


Figure 2: SARS-CoV-2 immunostaining demonstrating trophoblast outlines of the entrapped chorionic villi

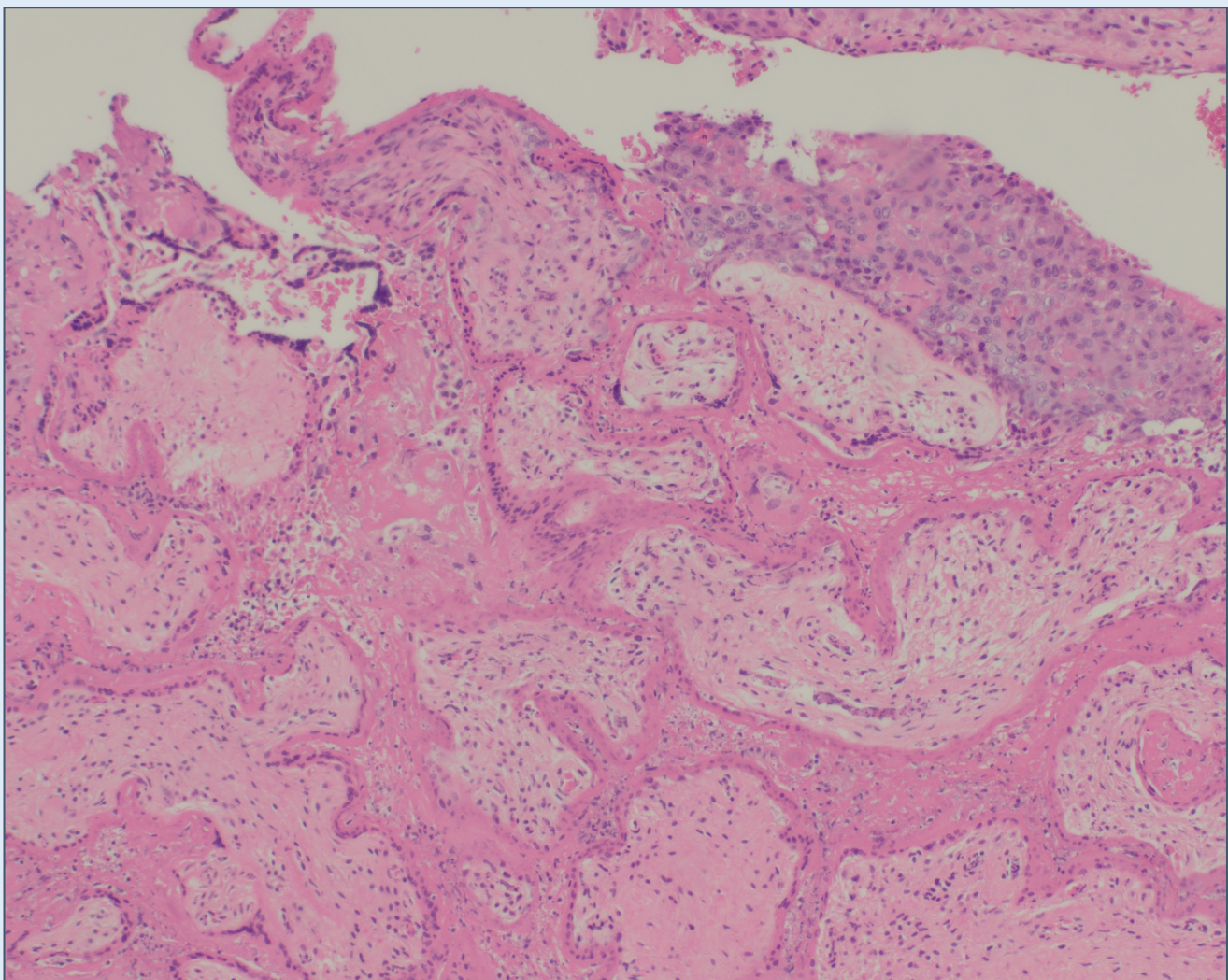


Figure 3: Patchy acute inflammation in the basal decidua

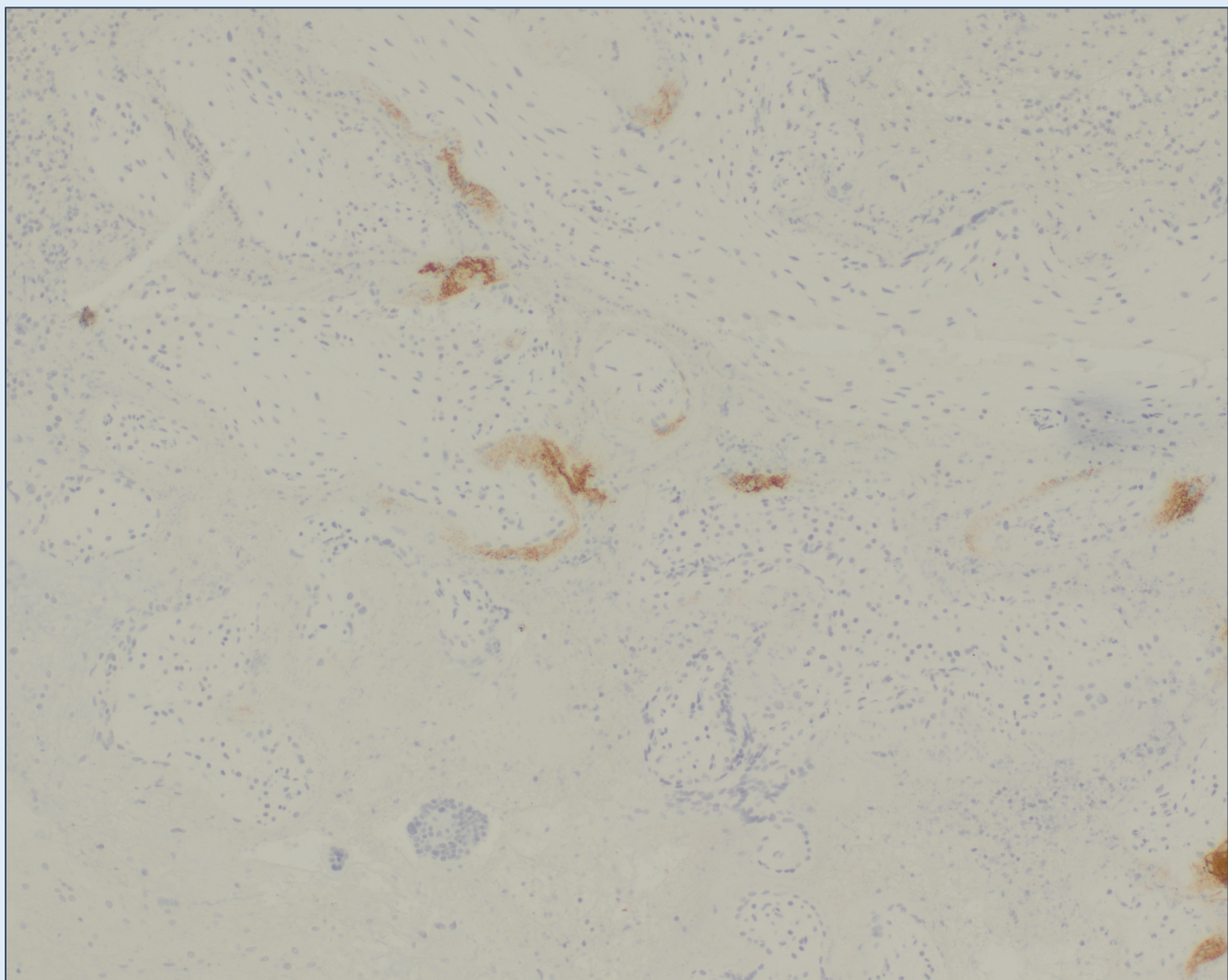


Figure 4: SARS-CoV-2 immunostaining in the basal decidua

- Placental histopathology revealed a 77 gram placenta of approximately 110 x 100 x 20mm size. There was **massive perivillous fibrin deposition with patchy necrosis of the trophoblast outlines of the chorionic villi** (Figure 1), and fragmented inflammatory debris in the intervillous space. Acute inflammation, haemorrhage and congestion was noted in the basal decidua (Figure 3). **SARS-CoV-2 immunostaining carried out was diffusely positive** (Figures 2 and 4), and highlighted the trophoblast outlines of many of the entrapped villi. Features were consistent with **SARS-CoV-2 placentitis**.
- Patient serology confirmed the **presence of SARS-CoV-2 IgG**, indicating previous exposure to COVID-19. The parents declined post mortem examination.

Discussion

- SARS-CoV-2 placentitis has been found to be a distinct pathological entity**, with massive perivillous fibrin deposition (MPFD) +/- chronic histiocytic intervillitis (CHI), which is different to the histological changes seen with other vertically transmitted viral infections. In this case MPFD was seen, without CHI. Both of these changes have been seen in placentas before the SARS-CoV-2 pandemic, but with a low incidence, and thought to have an immunological basis². To the best of our knowledge, SARS-CoV-2 placentitis has not previously been linked to an adherent placenta requiring manual removal.
- The mechanism of why some mothers with SARS-CoV-2 infection develop these histological changes is not yet understood**, and the proportion is largely unknown. Stenton *et al* have hypothesised that it may be a synergistic effect of the immunological dysregulation induced by the virus, and an underlying thrombophilia in either mother or fetus, that triggers the CHI-MPFD pathway².
- As demonstrated by this case where the patient had never been symptomatic, **there appears to be no correlation between the severity of illness in mothers with COVID-19, and pregnancy outcomes**^{2,3}. **Placentitis should be considered even in asymptomatic patients and those without a known history of COVID-19 infection**. In this case, where there are no other risk factors for late miscarriage, it is highly possible that the placental histological changes contributed to the second trimester loss, and potentially also the abnormally adherent placenta.
- UK Obstetric surveillance data has shown that COVID-19 vaccination uptake in pregnant women remains lower than that of the general population**, particularly in the non-English speaking population. This could potentially be due to poor understanding or explanation; in this case the patient confirmed she had no objection to the vaccination. Although it is uncertain if prior vaccination would have prevented maternal SARS-CoV-2 infection, it is possible that it may have prevented this outcome.

Conclusion

- This case demonstrates that **SARS-CoV-2 placentitis is a complication that may occur even in an asymptomatic mother, and the extent of the histological changes does not correlate with clinical symptoms or severity of maternal disease**.
- In this case it is possible that the placental histological changes contributed to both the second trimester loss, and the adherent placenta requiring manual removal.
- As it has the potential to cause fetal compromise at any gestation, **pregnant women should be strongly advised to be vaccinated against SARS-CoV-2 infection**.