

Being Born into a Pandemic: COVID-19 and Pregnancy

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ABSTRACT

Case #1: 34yo Asian female G2P1001 presents COVID19+ in 1st trimester. PMH insignificant. Meds: prenatal vitamins. Surg Hx: c/s healthy boy (2017). No h/o GHTN, GDM, or eclampsia. D/t COVID19+ infection, frequent fetal u/s monitoring done at 32w5d, 34w5d, 38w0d. Fetal growth over time: 63.4%, 48.8%, 14.3%. Fluid over time: AFI 8.58cm, MVP 4.52cm; AFI 10.86, MVP 3.52; AFI 2.73, MVP <2. Oligohydramnios diagnosed at 38w0d; emergent repeat c/s performed. Mother and baby healthy s/p delivery, d/c home on PPD#2. Pathology of placental tissue shows increases in villous fibrin accumulation and maternal vascular malperfusion.

Case #2: 29yo Caucasian female G1P0 presents to ED at 18w4d with c/o runny nose, cough, and headache; temp. 100.3°F; tests COVID+. PMH insignificant. Meds: prenatal vitamins. No h/o GHTN, GDM, or eclampsia. 21w0d u/s: growth 71.4%, normal anatomy. 30w0d u/s: growth at 82.3%, AFI 15.10cm, MVP 5.38cm. At 39w1d, healthy infant boy (7lb12oz) via VAVD. Mother and baby healthy s/p delivery, d/c home on PPD#2. Placenta not sent for surgical pathology.

Conclusion

Due to the short time course of the COVID19 pandemic, adequate evidence to link maternal-fetal outcomes to infection during pregnancy is just now becoming available. Other coronaviruses, SARS and MERS, are preferentially fatal in pregnant mothers; and, adverse perinatal outcomes in COVID19+ women are appearing. Case reports have associated COVID19 with preterm birth; one study reported 47% preterm deliveries in COVID19+ mothers. Molecular studies have confirmed ACE2 (receptor allowing viral cellular entry) mRNA overexpression in placentas. Placental histopathology has shown maternal-placental interfacing blood vessel anomalies.

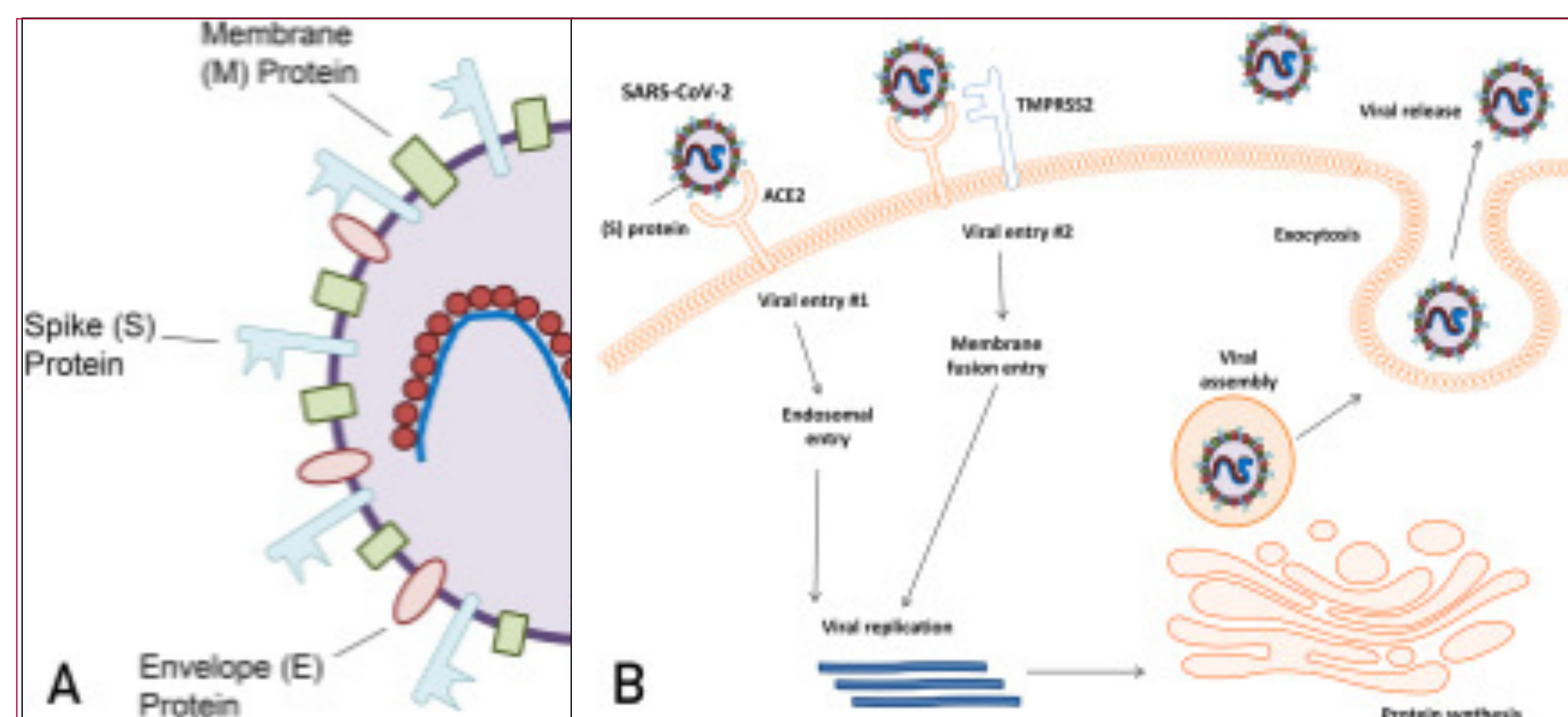
Clinical Significance

COVID19 represents a monumental threat to public health. Pregnant women and fetuses may be at increased risk for complications compared to the general public. As yet, the relationship between COVID19 and pregnancy remains to be clarified and will require further investigations to understand associations and promote evidence-based treatment practices.

BACKGROUND

- The United States saw >26.2 million COVID-19 cases by 2/1/21. Due to the severity of the disease, research and vaccine efforts have been expedited in order to reduce the spread and protect the most vulnerable populations.¹
- Symptoms are highly variable and range from being asymptomatic to having any/all of fever, cough, dyspnea, loss of taste and smell, congestion, sore throat, nausea, vomiting, and diarrhea.
- There are currently three human coronaviruses that can cause a severe respiratory illness, including SARS-CoV-1 (2003) MERS-CoV (2012), and SARS-CoV-2 (2019).
- Several unknowns remain about SARS-CoV-2 due to its novelty. Specifically, inadequate research exists to demonstrate its effects during pregnancy.
- Pregnancy ↑ the risk of respiratory infections and developing complications due to adaptive changes to the cardiopulmonary and immune systems.
- The SARS-CoV and MERS-CoV epidemics were both preferentially fatal in pregnant women.
- Most COVID-19 studies to date have focused on the general population, esp. those with comorbidities, demonstrating the need for research dedicated to the effects of maternal and fetal outcomes for those infected in all stages of pregnancy.

MECHANISM OF COVID-19 CELL ENTRY



Spike protein: COVID-19 antigen attaching to ACE2-R of cells
ACE2-R: receptor on cells that engulfs COVID-19 once bound

- Found on many tissues, e.g. placenta and uterus
- Activity in placenta and uterus ↑ 2x during pregnancy (in mice)
- RAAS activity is ↑ during pregnancy due to ↑ estrogen and progesterone → in turn ↑ ACE2 activity
- Given that ACE2-R exists on pregnancy-associated tissues and ↑ in activity during pregnancy, potential for utero-placental changes and vertical transmission following intrapartum COVID infection requires prompt investigation

PRE-PREGNANCY RISK FACTORS

COVID risk factors: Neither pt had pre-pregnancy risk factors for severe COVID-19 infection

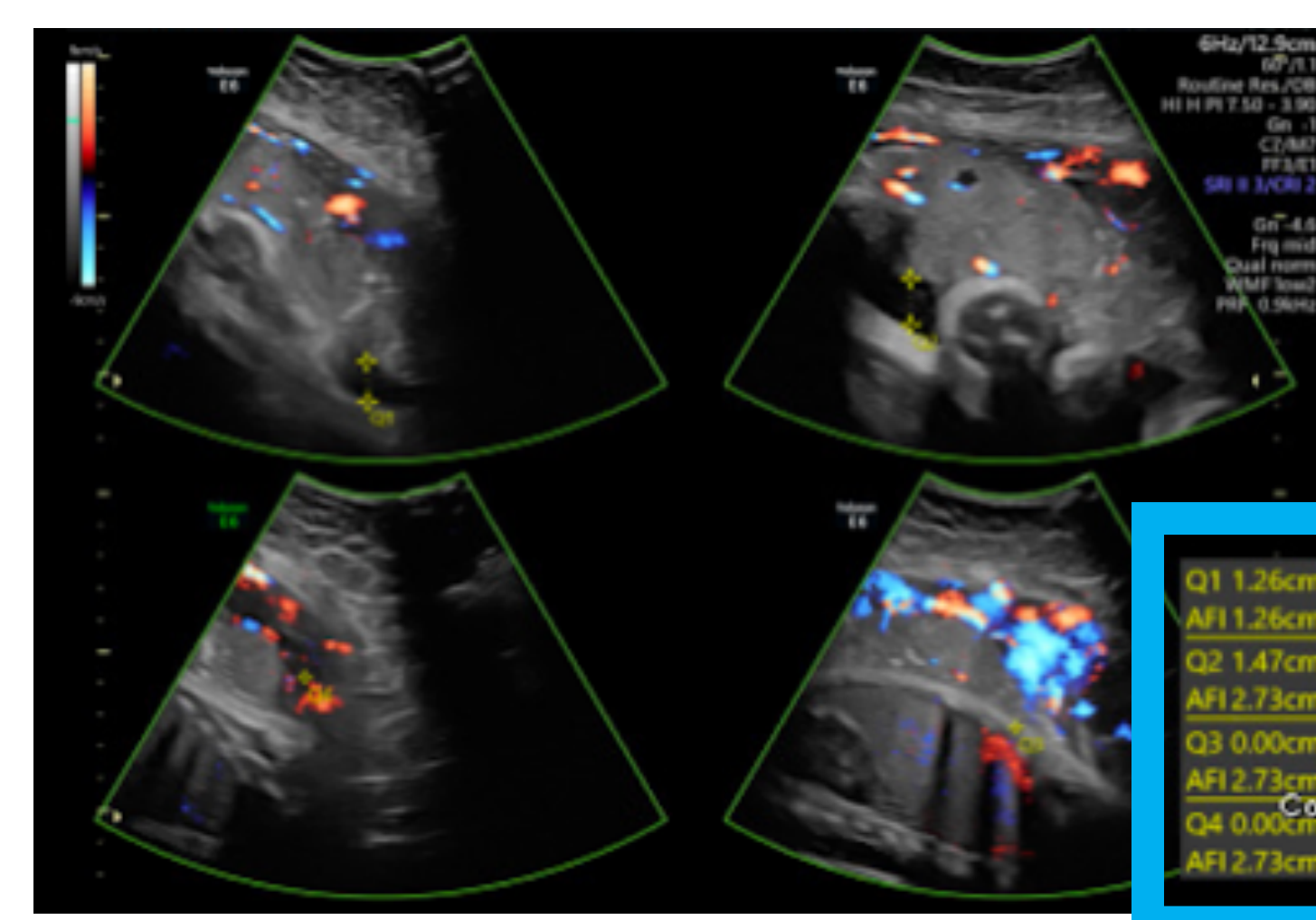
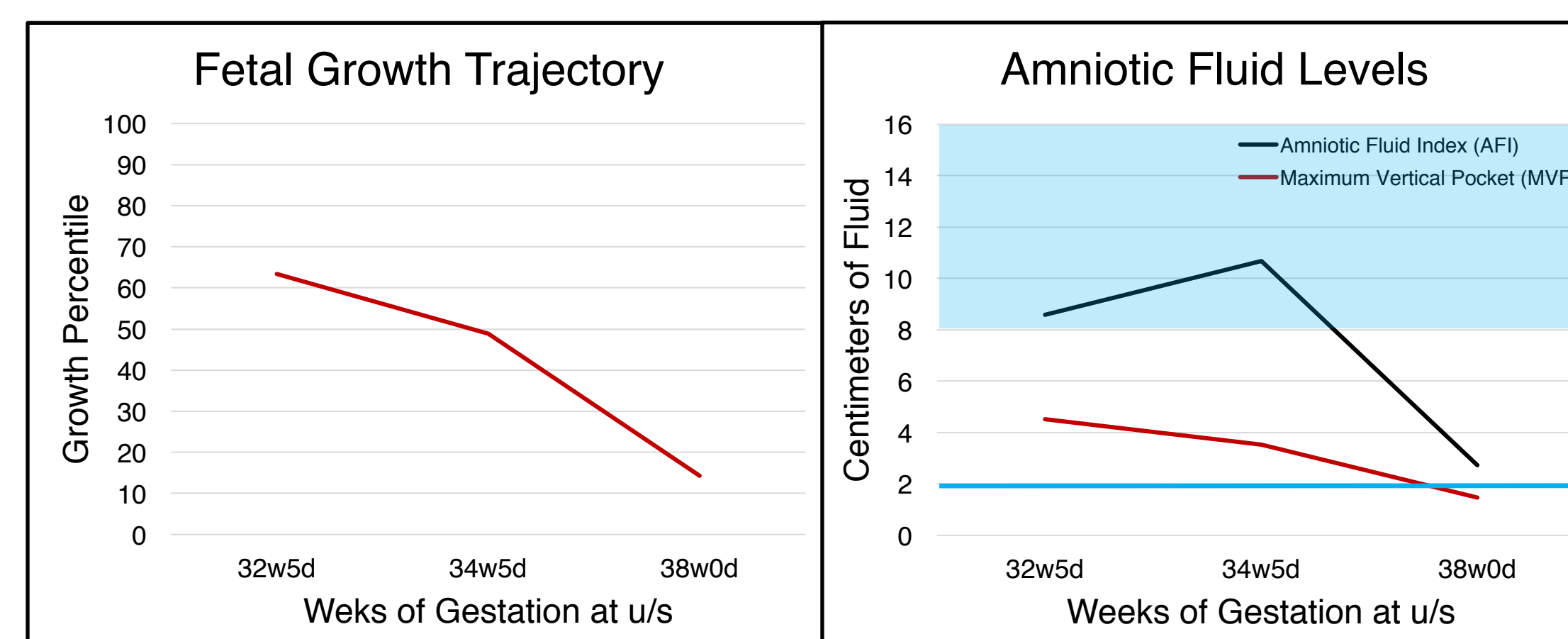
Pregnancy risk factors: Neither pt had pre-COVID risk factors for any pregnancy complications

Maternal COVID symptoms: Although pt #2 had a *slight fever, runny nose, cough, and headache*, neither pt had severe symptoms requiring critical care

Pregnancy complications: Neither pt developed complications despite intrapartum COVID infection

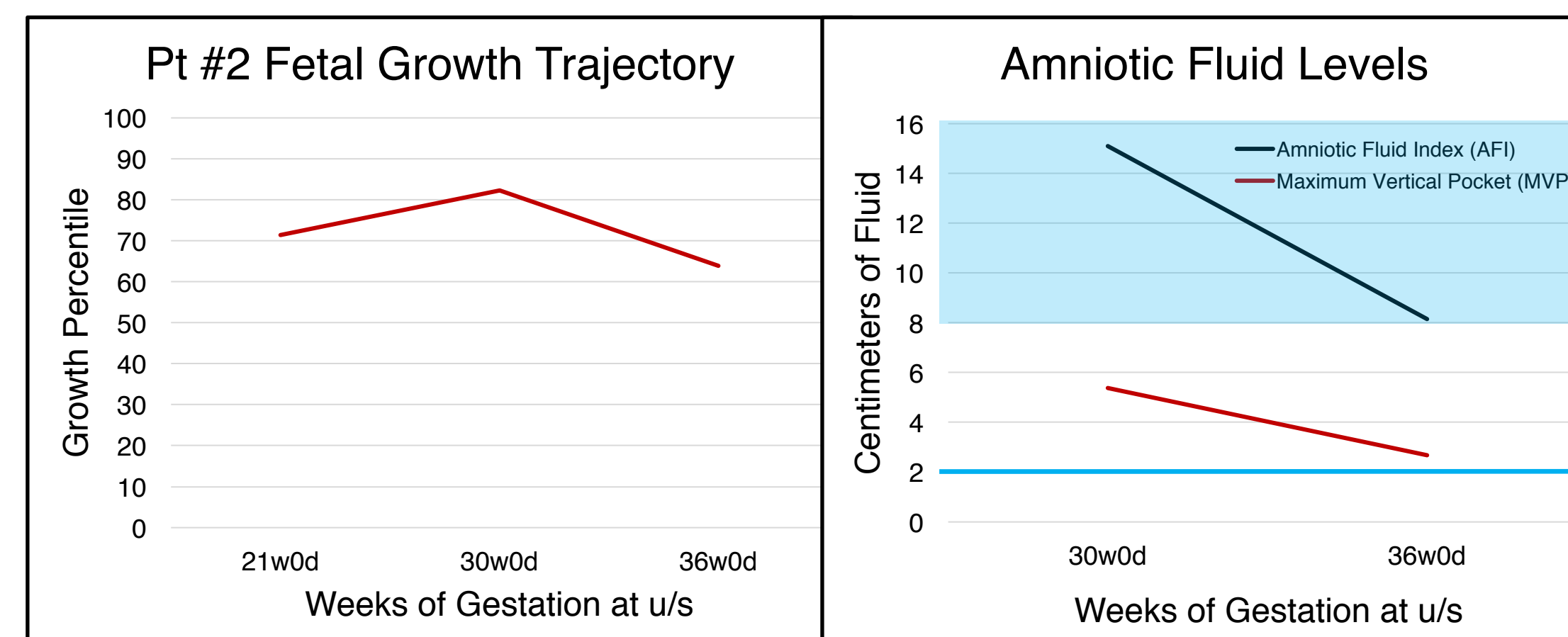
COVID risk factors	Pt#1	Pt#2
Chronic lung dx	<input type="checkbox"/>	<input type="checkbox"/>
HTN	<input type="checkbox"/>	<input type="checkbox"/>
Diabetic/Obesity	<input type="checkbox"/>	<input type="checkbox"/>
Tobacco Use	<input type="checkbox"/>	<input type="checkbox"/>
Pregnancy risk factors		
Prior h/o GHTN, pre-eclampsia, or eclampsia	<input type="checkbox"/>	<input type="checkbox"/>
Prior h/o gestational diabetes	<input type="checkbox"/>	<input type="checkbox"/>
Prior h/o pre-term labor/birth	<input type="checkbox"/>	<input type="checkbox"/>
G, P	G2P1001	G1P0
COVID+ test	1 st trimester	2 nd trimester

PT #1 FETAL U/S DATA



u/s picture to left: pt #1, AFI and MVP measurements (blue box) at 38w0d u/s, meets criteria for oligohydramnios
u/s picture below: pt #2, normal fluid levels and normal fetal anatomy at 30w0d u/s

PT #2 FETAL U/S DATA



Fetus Gender: Both are boys

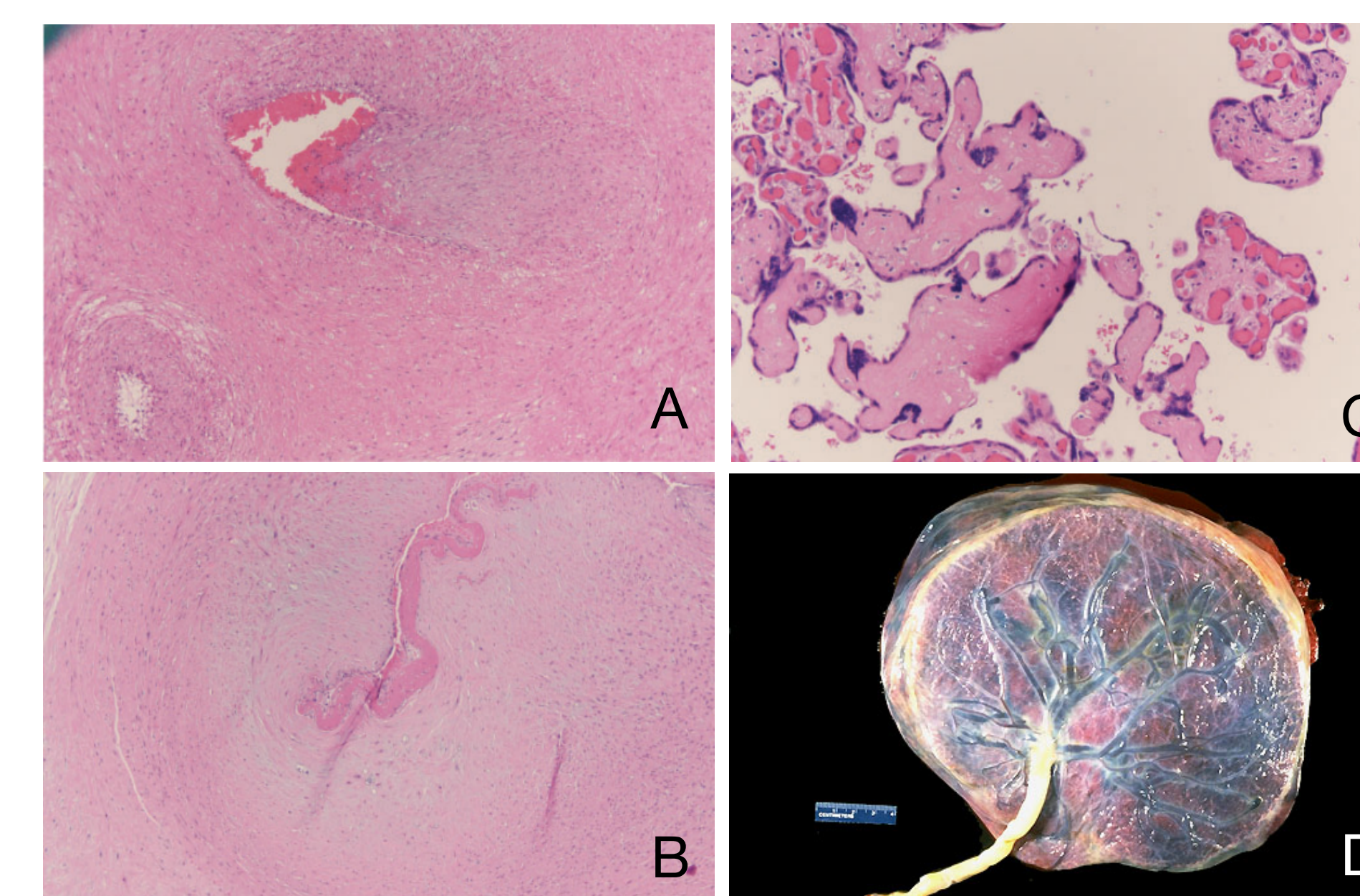
Growth: Fetus #1 growth consistently decreases relative to average during the 3rd trimester; whereas fetus #2 growth stays above 50% throughout

Amniotic Fluid:

- Amniotic Fluid Index (AFI): sum of fluid in all uterine quadrants; *normal is between 8-18* (blue box on graphs); *<5-6 meets criteria for oligohydramnios*
 - it is normal for AFI to decrease during 3rd trimester, but should remain >5-6
- Maximum Vertical Pocket (MVP): max depth of umbilical-cord-and-fetal-part-free fluid in any uterine quadrant; *normal is between 2-8; <2 meets criteria for oligohydramnios* (blue line on graphs)
- Fetus #1 meets criteria for oligohydramnios at 38w0d, possibly d/t COVID-assoc. changes in placental perfusion

PLACENTAL HISTOPATHOLOGY

Fetus #1 placenta was sent for surgical pathology with the following finding reported: "there is minimal evidence of *COVID-19-associated maternal vascular malperfusion, which has been associated with oligohydramnios...*" and there was presence of "*minor focal increases in intervillous/perivillous fibrin accumulation.*" This histopathologic description was similar to that in a study of 20 placentas from mothers with intrapartum COVID infection, pictures below.



A and B) vessels showing intramural, intimal fibrin deposition and representing fetal vascular malperfusion, C) section of avascular chorionic villi; D) is not from the study referenced above, but shows normal gross pathology of a placenta

DISCUSSION

- Patient #1 contracted COVID during her 1st trimester. There was a significant decline in AFI, MVP, and fetal growth trajectory between 34w5d and 38w0d, leading to a diagnosis of oligohydramnios and an emergency c-section. Placental pathology demonstrated changes similar to other reports of COVID+ pregnancies.
- Patient #2 contracted COVID during her 2nd trimester. There was a decrease in her amniotic fluid level, but overall it remained within the normal range until 39w1d when she delivered.
- Our patients tested positive for COVID-19 in different trimesters, which may have influenced the outcomes of the pregnancies.
- Ultimately, these cases help to demonstrate the need for a more comprehensive understanding of women affected by COVID during pregnancy, as this relationship remains unclear.
- Further investigation to understand associations between COVID and pregnancy is needed to promote evidence-based treatment practices.

REFERENCES

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6. Wang J, Yeung Y, Bunick M, Baranishnik C, Scharf F, Yeung C, et al. ACE2 expression and activity are enhanced during pregnancy. Am J Physiol Regul Integr Comp Physiol. 2008 Dec;295(6):R1193-61. doi: 10.1152/ajp-rreg.00590.2008. Epub 2008 Oct 22. PMID: 18945556.
7. Wang J, Yeung Y, Bunick M, Baranishnik C, Scharf F, Yeung C, et al. ACE2 expression and activity are enhanced during pregnancy. Am J Physiol Regul Integr Comp Physiol. 2008 Dec;295(6):R1193-61. doi: 10.1152/ajp-rreg.00590.2008. Epub 2008 Oct 22. PMID: 18945556.