Biomarkers for Early Detection of Cesarean Scar Ectopic Pregnancy

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BACKGROUND

- Cesarean scar ectopic pregnancy (CSEP) occurs in 1 in 2000 pregnancies and is associated with **significant maternal morbidity and mortality**
- Delayed and misdiagnosis occurs in ~15% of cases.[1,2]
- CSEP is thought to be part of the placenta accreta spectrum (PAS).[3]
- Several biomarkers for PAS show promise as a diagnostic tool.[4,5]

HYPOTHESIS

- Patients with CSEP will have a distinct biomarker signature compared to patients with an intrauterine pregnancy.
- Patients with CSEP will have a similar biomarker signature to previously published findings in patients with PAS

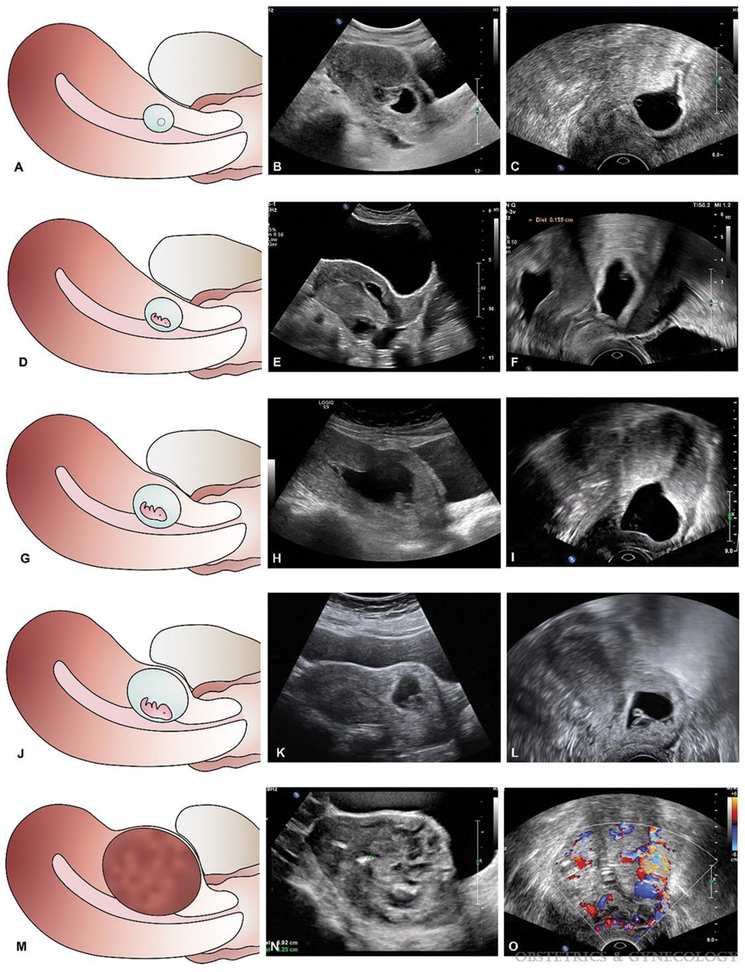
SPECIFIC AIMS

- Establish a biobank repository of blood (plasma), urine, and placental tissue of patients at risk for and with CSEP
- Validate that patients with CSEP have a distinct biomarker profile compared with control cases

OBJECTIVE

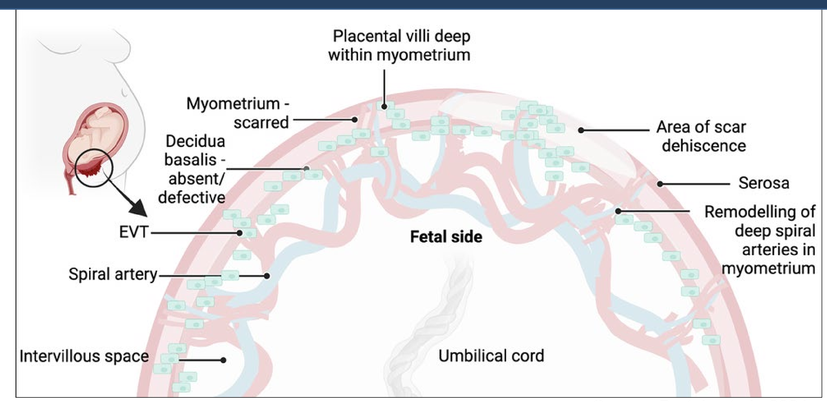
- Our long-term goal is to improve access to early and accurate early diagnosis of CSEP through non-invasive testing paired with imaging

METHODS



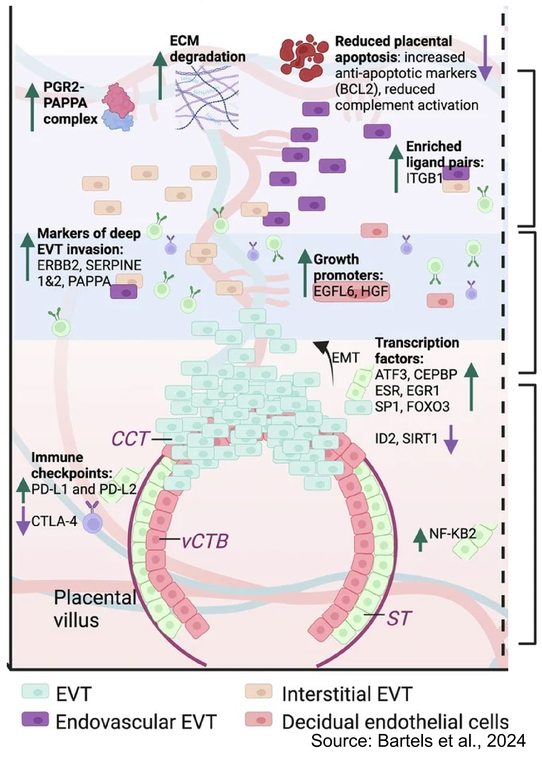
Source: Ban et al., 2023

Figure 1: Classification of cesarean scar ectopic pregnancies. A-C:Type I. D-F: Type IIA. G-I: Type IIB. J-L: Type IIIA. M-O: Type IIIB.



Source: Bartels et al., 2024

Figure 2: Current understanding of etiology of PAS



Source: Bartels et al., 2024

Figure 3: Biomarkers signaling changes related to PAS

	Controls	Samples
Inclusion	• Age >18 • > 5 weeks GA • Intrauterine pregnancy and risk factor for CSEP • Undergoing termination of pregnancy	• Age >18 • > 5 weeks GA • Radiologic diagnosis of CSEP
Exclusion	• Active malignancy • Current diagnosis of DM or HTN • Known fetal anomalies	

Biomarkers of interest:

- PAPP-A
- Antithrombin III
- Plasminogen activator inhibitor
- Soluble Tie2
- Soluble VEGF receptor 2

REFERENCES

1. Miller R, Timor-Tritsch IE, Gyamfi-Bannerman C. Society for Maternal-Fetal Medicine (SMFM) Consult Series #49: Cesarean scar pregnancy. *Am J Obstet Gynecol*. 2020;222(5):B2-B14. doi:10.1016/J.AJOG.2020.01.030
2. Timor-Tritsch IE, Monteagudo A. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. *Am J Obstet Gynecol*. 2012;207(1):14-29.
3. Timor-Tritsch IE, Monteagudo A, Cali G, et al. Cesarean scar pregnancy and early placenta accreta share common histology. *Ultrasound Obstet Gynecol*. 2014;43(4):383-395. doi:10.1002/UOG.13282doi:10.1016/J.AJOG.2012.03.007
4. Shainker SA, Silver RM, Modest AM, et al. Placenta accreta spectrum: biomarker discovery using plasma proteomics. *Am J Obstet Gynecol*. 2020;223(3):433.e1-433.e14. doi:10.1016/J.AJOG.2020.03.019
5. Lyell, D., Faucett, A., Baer, R. et al. Maternal serum markers, characteristics and morbidly adherent placenta in women with previa. J Perinatol 35, 570–574 (2015). https://doi.org/10.1038/jp.2015.40
6. Ban, Yanli , Shen, Jia, Wang, Xia, et al. Cesarean Scar Ectopic Pregnancy Clinical Classification System With Recommended Surgical Strategy. *Obstetrics & Gynecology. 2023;* 141(5): 927-936, DOI: 10.1097/AOG.0000000000005113
7. Bartels, H.C., Hameed, S., Young, C. et al. Biological comparisons between pre-eclampsia and placenta accreta spectrum. npj Womens Health 2, 30 (2024). https://doi.org/10.1038/s44294-024-00034-y