Intraamniotic infection/inflammation in threatened midtrimester miscarriage, cervical insufficiency, and preterm labor without cervical changes

Bo Hyun Yoon, MD, PhD, Roberto Romero, MD DMedSci, Kyung Joon Oh, MD, PhD, Hyeon Ji Kim, MD, Eunjung Jung, MD, Francesca Gotsch, MD, Manaphat Suksai, MD

PII: S0002-9378(22)02590-X
DOI: https://doi.org/10.1016/j.ajog.2022.12.312
Reference: YMOB 14901


Received Date: 19 December 2022
Accepted Date: 19 December 2022


This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2022 Published by Elsevier Inc.
Reply to Letter to the Editor

Intraamniotic infection/inflammation in threatened midtrimester miscarriage, cervical insufficiency, and preterm labor without cervical changes

We thank Drs Jiang and Li for their interest in our work and are glad to provide responses to the questions. The gold standard for the diagnosis of intra-amniotic infection or intra-amniotic inflammation is analysis of amniotic fluid. An extensive body of literature shows that neither analysis of maternal blood nor that of cervicovaginal fluid has sufficient accuracy to replace amniotic fluid analysis for the diagnosis of intra-amniotic infection/inflammation. Therefore, amniocentesis is offered at the Seoul National University to patients admitted with the diagnosis of preterm labor, cervical insufficiency, and increased uterine contractility even in the absence of cervical changes.\textsuperscript{1,2} The rationale is two-fold: that intra-amniotic infection/inflammation is present in a fraction of patients diagnosed with each obstetrical syndrome and that infection/inflammation can be successfully treated after accurate diagnosis, as reported by our group.\textsuperscript{3,4} The practice at Seoul National University was described in the Study Design section of our paper.\textsuperscript{4} Patients could consent or decline a diagnostic procedure and also consent or decline to participate in an observational study, which asked patients to donate a sample for research purposes. Genetic studies of amniotic fluid are not part of the standard work-up in cases of threatened miscarriage. Regarding cervical length follow-up, we did not have a standardized protocol for this procedure, and clinical management was left to the discretion of the treating clinicians. The third question was about the performance of cervical cerclage after the exclusion of intra-amniotic infection/inflammation in patients with cervical dilatation. We agree with Drs Jiang and Li that cerclage is indicated in patients with cervical insufficiency. We note that the criterion for enrollment in our study was
patients with threatened second-trimester miscarriage, and the inclusion required regular uterine contractility. ⁴ The diagnosis of cervical insufficiency is made when there is painless cervical dilatation in the absence of regular uterine contractions. In reference to the question of amniocentesis and cervical cerclage, our view is that amniocentesis should be performed before the placement of an emergency cerclage, given the high prevalence of intra-amniotic infection/inflammation,¹ ⁵ the poor outcome of patients who undergo cerclage despite intra-amniotic infection/inflammation,⁶ and the encouraging results of our previous studies that demonstrated intra-amniotic infection/inflammation can be eradicated.³ The authors also asked about the long-term follow-up of survivors. Of the 15 patients with intra-amniotic inflammation in this study, 9 delivered before 22 weeks of gestation and 5 delivered after 34 weeks of gestation.⁴ We described that those 5 newborns survived without morbidity in Tables 2 and 3. We also described that one of the limitations of this study was “…lack of follow-up beyond the neonatal period…”⁴

Bo Hyun Yoon, MD, PhD
Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Republic of Korea
Biomedical Research Institute, Seoul National University Hospital, Seoul, Republic of Korea
yoonbh@snu.ac.kr

Roberto Romero, MD, DMedSci
Perinatology Research Branch, Division of Obstetrics and Maternal-Fetal Medicine, Division of Intramural Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, US Department of Health and Human Services, Bethesda, MD, and Detroit, MI, USA
prbchiefstaff@med.wayne.edu

Kyung Joon Oh, MD, PhD
Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Republic of Korea
Department of Obstetrics and Gynecology, Seoul National University Bundang Hospital, Seongnam-si, Republic of Korea
Hyeon Ji Kim, MD  
Department of Obstetrics and Gynecology, Seoul National University, Bundang Hospital, Seongnam-si, Republic of Korea

Eunjung Jung, MD  
Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, Michigan

Francesca Gotsch, MD  
Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, Michigan

Manaphat Suksai, MD  
Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, Michigan

**Funding:** This correspondence was supported, in part, by the Perinatology Research Branch, Division of Obstetrics and Maternal-Fetal Medicine, Division of Intramural Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, U.S. Department of Health and Human Services (NICHD/NIH/DHHS); and, in part, with Federal funds from NICHD/NIH/DHHS under Contract No. HHSN275201300006C. Dr. Romero has contributed to this work as part of his official duties as an employee of the United States Federal Government.

**Disclosure:** The authors declare no conflicts of interest.
References


