Study finds low anti-Ro titers are not associated with fetal heart block

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New research from an ongoing study that will be presented at ACR Convergence 2023, the American College of Rheumatology's (ACR) annual meeting, shows that pregnant women with very low titers of anti-

Ro antibodies are at minimal to no risk of fetal atrioventricular (AV) block, a serious disorder affecting the heart's electrical system.

After birth, fetal AV block requires lifelong pacemaker treatment or cardiac transplantation and may be fatal. However, pregnant patients with higher titer antibodies seem to be at greatest risk at risk for fetal AV block and may benefit from ambulatory fetal heart rhythm monitoring, which can detect AV block when treatment may be most effective.

Anti-Ro antibodies are autoantibodies that react with two proteins, Ro52 and Ro60, inside cells. The antibodies are associated with many autoimmune diseases, including lupus, Sjögren's, and rheumatoid arthritis although they also are present in many people without any rheumatic disease symptoms. Fetal AV block can occur as a result of anti-Ro antibodies.

Types of AV block

- Early damage (first-degree AV block): The signals that control the heartbeat are delayed, but fetal heart rate and rhythm are normal.
- Evolving damage (second-degree AV block): Electrical signals are partially blocked, and the fetal heart rhythm is irregular.
- Complete damage (third-degree AV block): Electrical signals within the heart are completely blocked and the fetal heart rate is slow.

Complete AV block is usually irreversible and leads to perinatal death in about 17% of cases. AV block can occur within hours of a normal heart rhythm and progress from partial to complete AV block within 12 hours. Because this progression occurs so rapidly, weekly or biweekly fetal echocardiograms, the current standard of care for anti-Ro positive

pregnancy surveillance, will only detect this fleeting transition period serendipitously. This presents a dilemma for clinicians, who must weigh the rarity and seriousness of the condition against the burden of ongoing surveillance during the second trimester, when anti-Ro antibodies first begin passing into the fetal circulation through the placenta to the fetus.

Given these challenges of costly surveillance and a brief window of time for detection of evolving AV block, Jill Buyon, MD, director of the division of rheumatology at the NYU School of Medicine in New York City and director of the NYU Lupus Center, and Bettina Cuneo, MD, professor of research at the University of Arizona (Tucson) College of Medicine, drew on prospective data from a national, multi-race study of pregnant women for their own study called STOP BLOQ (Surveillance and Treatment to Prevent Fetal Atrioventricular Block Likely to Occur Quickly).

The study assesses whether anti-Ro levels could classify risk for fetal AV block, and whether ambulatory fetal heart rhythm monitoring performed by the pregnant patient could detect evolving AV block before it became irreversible.

The STOP BLOQ study began three years ago and is ongoing. To date, 483 pregnant patients from 22 sites across the U.S. have completed 17–26 gestational weeks of the monitoring period. The subjects were risk-stratified into high and low anti-Ro60 and anti-Ro52 titers, based on previous data from Buyon and Cuneo, showing that patients with titers less than 1,000 units per mL were at very low risk for fetal AV block. Pregnant women also monitored their fetus' heart rhythm and rate three times a day. The monitor recordings were reviewed by a pediatric cardiologist who sent the subject for a fetal echocardiogram if the monitoring was abnormal.

Of pregnant subjects enrolled, 37% had low anti-Ro52 and anti-Ro60

titers and none developed fetal AV block. Overall, 45 high-titer pregnant subjects presented with abnormal fetal heart rate monitoring and urgent echocardiograms revealed AV block in 10 fetuses. In contrast, fetal AV block was not initially detected by any of the weekly or biweekly surveillance echocardiograms.

Buyon and Cuneo were satisfied to learn that the antibody titer thresholds were accurate and that women with low antibody titers presumably do not need monitoring. At the same time, in women with high-titer antibodies, home monitoring accurately detected all abnormal fetal heart rhythms.

The investigators acknowledge that ultrasound home monitoring three times a day for two months can be challenging, but hope in the future to have devices that differentiate abnormal from normal heart rhythms. They anticipate that the study's results will reduce detecting only potentially reversible fetal AV block, the need for costly and ineffective echocardiograms, and empower women to take a role in their own care.

Other challenges are harder to resolve. Buyon notes that "many women were tested by highly used commercial laboratories, which do not titer the anti-Ro antibodies, so risk is harder to stratify." The interpretation of the home monitoring was best done by a pediatric cardiologist, which is difficult in the real world setting, and the numbers of cases with heart block were small "because this is a rare disease."

Still, Buyon and Cuneo believe the study will set a precedent for universal screenings for anti-Ro antibodies and lead to the generation of evidence-based management guidelines for these high-risk pregnancies.

More information: Abstract #1682: Bettina Cuneo et al, Prospective Evaluation of Anti-SSA/Ro Pregnancies Supports the Utility of High Titer Antibodies and Fetal Home Monitoring for the Detection of Fetal

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