Researchers find clues to mystery of preterm delivery

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Researchers at Yale School of Medicine have found that excessive formation of calcium crystal deposits in the amniotic fluid may be a reason why some pregnant women suffer preterm premature rupture of the membranes (PPROM) leading to preterm delivery.

This is a key breakthrough in solving the mystery of preterm birth, a leading cause of death and permanent disability in newborns. The findings will be presented in an abstract at the Society for Maternal-Fetal Medicine Scientific Sessions on February 10 in San Francisco, California.

Researchers know that infection, maternal stress and placental bleeding can trigger some preterm deliveries, but the cause of many other preterm deliveries remains unknown. In these cases, women experience early contractions, cervical dilation and a torn amniotic sac.

A team of researchers in the Department of Obstetrics, Gynecology & Reproductive Sciences at Yale, including first author Lydia Shook and her mentor Irina Buhimschi, M.D., investigated the idea that calcification—excessive buildup of calcium—of the fetal membranes may lead to PPROM and preterm birth. "We noticed that in many women, analysis of the proteins in their amniotic fluid did not show signs of inflammation, and we could not find any cause for their preterm birth," said Shook, a Yale medical student. "We took a fresh look for what was causing breakdown of the membranes, which can lead to lost elasticity, integrity and eventually rupture."

Scientists know that calcifying nanoparticles are involved in many degenerative conditions including arthritis and atherosclerosis. "These mineral-protein complexes can disrupt normal cellular processes and cause cell death," Shook said. "We wondered whether they could also be responsible for damage to the fetal membranes in pregnant women."

Shook and her co-authors used a stain to look for calcium deposits in placental and fetal membrane tissue from patients with PPROM and preterm birth, as well as full-term deliveries. They used a sterile culture technique to determine whether amniotic fluid can form nanoparticles. They then exposed fetal membranes to the cultured nanoparticles to determine their ability to induce cell dysfunction, damage and cell death.

The team found evidence of calcification of fetal membranes collected from preterm deliveries. Fetuin, one of the major proteins involved in nanoparticle formation, was found in these deposits. Levels of fetuin in amniotic fluid were lower in women who delivered with PPROM compared to those who delivered early with intact membranes.

"This preliminary evidence suggests that amniotic fluid has the potential to form nanoparticles and deposit them in the fetal membranes," said Shook. "Low fetuin may be a biomarker for women at risk of PPROM. The goal of this research is to identify women at risk of developing this condition early in their pregnancy and to intervene with targeted therapy."

Provided by Yale University