Elevated blood-sugar levels in pregnancy tied to baby's heart-defect risk

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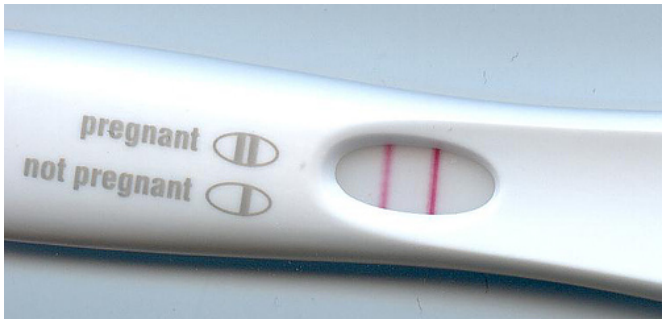

Pregnancy test. Credit: public domain

Pregnant women with elevated blood-sugar levels are more likely to have babies with congenital heart defects, even if their blood sugar is below the cutoff for diabetes, according to a new study from the Stanford University School of Medicine and Stanford Children's Health.

The study, which will be published online Oct. 12 in *JAMA Pediatrics*, extends the scope of prior findings on the connection between maternal diabetes and fetal heart defects. It is the first to show the link in women without a diabetes diagnosis.

"Diabetes is the tail end of a spectrum of metabolic abnormalities," said James Priest, MD, the study's lead author and a postdoctoral scholar in pediatric cardiology. "We already knew that women with diabetes were at significantly increased risk for having children with congenital heart disease. What we now know, thanks to this new research, is that women who have elevated glucose values during pregnancy that don't meet our diagnostic criteria for diabetes also face an increased risk." Priest treats patients with congenital heart defects at the Children's Heart Center at Lucile Packard Children's Hospital Stanford.

Pregnancy normally involves metabolic changes that make blood sugar—glucose—more available to the fetus than to the mother, an important adaptation for ensuring that the fetus gets enough nourishment. However, in some women, especially those who are obese or who have a family history of diabetes, these changes progress too far, to the point that the mother develops gestational diabetes. Although the risks of gestational diabetes have been well-studied, less attention has been paid to smaller metabolic changes in pregnancy.

Two serious heart defects

In the new study, the researchers examined blood samples taken from 277 California women during the second trimester of pregnancy. The control group comprised 180 women carrying infants without congenital heart disease. The others had infants affected by one of two serious heart defects. Fifty-five infants had tetralogy of Fallot, which is characterized by structural problems in the heart and in the blood vessels that connect the heart to the lungs; it is the most common of the heart defects that cause blue baby syndrome, in which a baby is getting too little oxygen. The remaining 42 infants had dextrotransposition of the great arteries, in which the positions of the two main arteries leading from the heart are swapped, preventing oxygenated blood from the lungs from circulating to the body.

The blood samples were collected at different times of the day, and the women were not asked to fast before sample collection. The researchers measured the women's levels of glucose, the main form of blood sugar, and insulin, a hormone that controls blood sugar.

The researchers found that average blood glucose levels were higher in women carrying fetuses with tetralogy of Fallot than in women in the control group, but were not elevated in women whose fetuses had dextrotransposition of the great

arteries. However, women whose fetuses had dextrotransposition of the great arteries had significantly elevated insulin levels.

The scientists used a mathematical model that accounted for both glucose and insulin levels, and was adjusted for the woman's age and ethnicity and whether she had diabetes. In the model, higher glucose levels were correlated with the odds of having a baby with tetralogy of Fallot, but not with dextrotransposition of the great arteries. In the model, however, the relationship with insulin levels was not significant for either birth defect.

Fuel for cells

Glucose is a fundamental fuel for cells, Priest noted, so it is unlikely that it is high glucose itself that damages the fetal heart. "It has to act via some mechanism," he said, adding that the cell's machinery for handling glucose overlaps with important developmental signaling mechanisms, such as the insulin-like growth factor receptors.

"I'm excited by this research because it opens up a lot of questions about how physiologic processes in the mother may be related to congenital heart disease," Priest said. "Most of the time we don't have any idea what causes a baby's heart defect. I aim to change that."

The work is an example of Stanford Medicine's focus on precision health by generating care that is proactive, predictive and personalized.

The study's senior author, Gary Shaw, DrPH, professor of pediatrics in neonatal and developmental medicine, added, "There are several other kinds of structural birth defects, in addition to heart defects, that have been linked with overt diabetes. This new work will motivate us to ask if underlying associations with moderately increased glucose levels may be similarly implicated in risks of some of these other birth defects."

Provided by Stanford University Medical Center