Maternal insulin resistance changes pancreas, increases metabolic disorders risk in offspring

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A growing proportion of women of childbearing age are among the estimated one in three Americans who have insulin resistance—a metabolic disorder that can be a precursor to a number of health problems, including diabetes, heart disease and cancer. Metabolic changes in the mother during pregnancy have been linked to impaired fetal development and an increased risk of obesity, diabetes and cardiovascular problems as children reach adulthood, but the physiological origins of these changes in children are unknown.

According to researchers from the Joslin Diabetes Center and the Department of Medicine at Harvard Medical School, "Since insulin resistance alters the metabolic status in the affected individuals, its presence in women during pregnancy has the potential to be detrimental to growth and metabolism in the offspring. Thus, insulin resistance directly impacts pregnant women and also their offspring." The research team—which included Sevim Kahraman, Ercument Dirice, Dario DeJesus, Jiang Hu and Rohit Kulkarni—used a mouse model of insulin resistance to find out how it affects metabolism and endocrine pancreas development in the offspring.

Insulin is a hormone created in the beta cells (?-cells) of the pancreas. It is released into the bloodstream following the ingestion of food to help the body's cells absorb sugars and starches (in the form of glucose) from digested food. With insulin resistance, the body becomes desensitized to insulin and doesn't use it effectively to absorb glucose. Glucose builds up in the blood and the body produces more insulin to cope, which leads to an excess of both glucose and insulin in the blood. Over time, insulin resistance can set the scene for other metabolic disorders, such as diabetes, and increased risk of cardiovascular disease.

During pregnancy, the mother's body makes changes to support the developing fetus. Among these are increased levels of insulin and reduced blood glucose. But in mothers with insulin resistance, these changes do not occur. The research team found that the insulin-resistant mice started pregnancy with elevated levels of insulin and comparable blood glucose, which increased even further late in pregnancy when compared with control mice whose blood glucose levels decreased normally. Pups born to insulin-resistant mothers showed changes in pancreatic development, including a reduction in the number of islets. These pups were born smaller but experienced an "overgrowth," quickly catching up in weight and surpassing control offspring by rapidly adding fat mass. They also displayed higher plasma glucose and insulin levels shortly after birth, showing early development of insulin resistance.

"The most profound differences in metabolic parameters between control offspring born to control and insulin-resistant mothers were evident during the early postnatal days, a stage that is approximately equivalent to postnatal human infancy or human childhood in mice," the research team wrote. "These results have potential implications for humans if maternal insulin resistance increases the risk of insulin resistance and obesity in children."

More information: "Maternal insulin resistance and transient hyperglycemia impact the metabolic and endocrine phenotypes of offspring." *American Journal of Physiology - Endocrinology and Metabolism* Published 15 November 2014Vol. 307no. 10, E906-E918DOI: 10.1152/ajpendo.00210.2014