

Tulane Researchers Find Association Between Low Birthweight and Type 2 Diabetes

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Dee Boling dboling@tulane.edu

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New research published in *Diabetologia* (the journal of the European Association for the Study of Diabetes) shows that a genetically lowered birthweight increases the risk of developing type 2 diabetes. The study was led by Dr. Tiange Wang, postdoctoral research fellow, and Dr. Lu Qi, professor of epidemiology, with the Tulane University School of Public Health and Tropical Medicine.

While low birthweight has been associated with a high risk of type 2 diabetes in observational studies, it remains unclear whether this relation is causal. Factors due to socioeconomic status and lifestyle are difficult to fully eliminate in observational studies. However, genetic association analysis is less likely affected by these confounding factors and has been increasingly employed to establish causality.

This new study included 3,627 type 2 diabetes cases and 12,974 controls of European ancestry from the Nurses' Health Study (a large study of nurses in the U.S.) and the Health Professionals Follow-up Study (a large study of male health professionals in the U.S.). The authors created a genetic risk score (GRS) based on five low birth weight-related genetic variations known as single nucleotide polymorphisms (SNPs).

The analysis showed that for each one point increase in GRS (with the score ranging from 1-10), the risk of developing type 2 diabetes increased by 6%. Using a statistical technique called Mendelian randomisation, the authors further found evidence that the low birthweight was actually causing the excess risk in type 2 diabetes. This type of analysis is, say the authors, a new approach for establishing

causal relationships in studies of this nature.

The authors say: "Evidence from both population and experimental studies has suggested that restricted early life development has long-term structural and functional influence on individuals' predisposition to an increased risk of metabolic diseases such as type 2 diabetes...however, to our knowledge, this study is the first to investigate the potential causal relation between low birthweight and risk of type 2 diabetes."

Since low birthweight represents restricted intrauterine growth (fetal growth), it cannot be ruled out that it is in fact the risk factors for this restricted growth that are causing the low birthweight and in turn causing type 2 diabetes to develop. Risk factors for restricted intrauterine growth include malnutrition, anaemia, infections, and placental insufficiency.

The authors conclude: "A genetically lowered birth weight was associated with increased susceptibility to type 2 diabetes. Our findings support a potential causal relation between birth weight and risk of type 2 diabetes, providing novel evidence to support the role of intrauterine exposures in the pathogenesis of type 2 diabetes."