How maternal fat metabolism very early in pregnancy and fetal abdominal growth influence child weight and adiposity

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A new study, led by researchers at the University of Oxford, UK, in collaboration with the University of California, Berkeley, U.S.,

published today in *Lancet Diabetes & Endocrinology* identifies, as early as the fifth month of pregnancy, patterns of fetal abdominal growth associated with maternal lipid metabolites that track newborn growth, adiposity and development into childhood. These fetal growth patterns are also associated with blood flow and nutrient transfer by the placenta, demonstrating a complex interaction between maternal and fetal nutrition early in pregnancy that influences postnatal weight and eventually adult health.

The researchers monitored the growth inside the womb of over 3,500 babies in six countries (Brazil, Kenya, Pakistan, South Africa, Thailand, and the United Kingdom) using serial fetal ultrasound scans throughout pregnancy, and analyzed blood samples taken from the women early in pregnancy and from the umbilical cord at birth. They then monitored the growth and development of the infants until 2 years of age.

José Villar, Professor of Perinatal Medicine at the University of Oxford, who co-led the study says that "this is the first comprehensive evidence, across geographic populations, of the complex interaction between maternal and fetal metabolism that regulates, early in pregnancy, unique fetal trajectories linked specifically to weight, adiposity and development during childhood. The study complements our previous work that identified fetal head growth trajectories associated with different developmental, behavioral, visual and growth outcomes at 2 years of age. In simple terms: the growth of babies' bodies and brain track separately and early—while still within the womb."

Aris Papageorghiou, Professor of Fetal Medicine at the University of Oxford, who co-led the study, says that "the study is unique for many reasons. Each pregnancy was accurately dated by ultrasound at less than 14 weeks' gestation; all fetuses were scanned with the same type of ultrasound machine every 5 weeks; and ultrasound and pediatric specialists around the world were trained to measure fetal and child

growth in a standardized manner using identical equipment."

"Much has been said about the importance of the first 1000 days of life in determining future health outcomes. This study provides evidence of distinct patterns of fetal abdominal growth and placental transfer and how they relate to longer term health. The finding of an association with maternal lipid metabolism early in pregnancy also provides unique insights into how the mother's health and diet influence her child's adiposity."

Stephen Kennedy, Professor of Reproductive Medicine at the University of Oxford, who co-led the study, says that "this landmark study has provided valuable new insights into the biological origins of childhood obesity, which is one of the most pressing public health issues facing governments around the world. The findings could contribute to earlier identification of infants at risk of obesity. Policymakers must take notice of these findings in their efforts to prevent the oncoming epidemic of obesity with all its likely adverse social and economic consequences."

The paper complements work published by the same groups in 2021 that identified fetal head growth trajectories that are associated with different developmental, behavioral, visual and growth outcomes at 2 years of age. Very importantly, in both studies, the same critical time period close to the fifth month of pregnancy is the starting point for accelerated or decelerated fetal growth that is sustained into early childhood.

More information: José Villar et al, Association between fetal abdominal growth trajectories, maternal metabolite signatures early in pregnancy, and childhood growth and adiposity: prospective observational multinational INTERBIO-21st fetal study, *Lancet Diabetes & Endocrinology* (2022). DOI: 10.1016/S2213-8587(22)00215-7