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Evaluation of levels of circulating mitochondrial DNA in maternal blood as markers of Intrauterine Growth Disorders

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According to the CDC, obesity is defined as having a BMI of 30kg/ m^2 or more. This condition leads to complications during pregnancy, like babies being born small or large for their gestational age (SGA and LGA pregnancies, respectively). Intrauterine growth restriction (IUGR) also known as fetal growth restriction is the inability of a fetus to reach its capacity for growth. According to the American College of Obstetricians and Gynecologists, it is "the most common and complex problem in modern obstetrics." Fetal Growth Disorders (FGD) are linked with several other events like congenital anomalies, cerebral palsy, neonatal death, metabolic disorders and more. FGDs are currently detected by ultrasonographic monitoring and clinical evaluation. The precision of such approaches is limited by fetal size, usually requiring mid to late gestational age for detecting FGD. Hence, the development of high precision methods enabling early detection is needed. Circulating fetal DNA holds a high potential value for monitoring fetal health. Cell-free fetal DNA is abundantly released into the bloodstream of the mother, thus providing a noninvasive opportunity for collection of fetal DNA through the mother's plasma. This study was designed to evaluate a method for FGD detection based on the ratio of DNA between mitochondrial and nuclear circulating in the plasma fraction of maternal blood. By targeting specific DNA sequences through qPCR, it is possible to quantify the DNA that is released mitochondria and the nucleus from the total amount of isolated nuclei acids. Blood samples will be collected from pregnant women at different gestational age and the plasma fraction will be separated by centrifugation. The DNA present in the plasma will be isolated using the Circulating Nucleic Acids kit (Qiagen). The mitochondrial-nuclear DNA ratio (MNR) in maternal plasma will be quantified using qPCR. In this approach mitochondrial and nuclear DNA are quantified using assays specific for mitochondrial and nuclear DNA sequences, respectively. We hypothesize that the MNR will be significantly different in patients with FGD compared with normal growing pregnancies. Circulating mitochondrial levels will be compared with normal, LGA and SGA pregnancies at each trimester and will be evaluated using statistical methods (i.e. ANOVA, Kruskal-Wallis test). The variable information collected for the study (e.g. age, BMI, etc.) will be assessed by multivariate analysis. This study will be the first to evaluate the utility of MNR as a marker for monitoring fetal growth. We anticipate that MNR that indicate FGDs in pregnancies will enable an individual approach to manage these pregnancies. These disorders will be predicted and identified earlier than by standard methods, and plans can be created for each patient to treat them according to their individual disorders.

Life Sciences