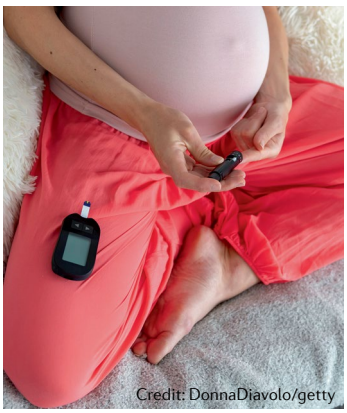
GESTATIONAL DIABETES

Electronic health records to predict GDM


Credit: DonnaDiavolo/getty

The development of gestational diabetes mellitus (GDM), which is defined as high blood glucose levels during pregnancy, is a common complication during pregnancy and can lead to adverse outcomes for both mothers and babies.

GDM is currently diagnosed by performing an oral glucose challenge test. This test is commonly conducted between 24 and 28 weeks of gestation. However, early detection of GDM could help to prevent or minimize the risk of complications. Now, a new study aims at leveraging nationwide electronic health records (EHRs) in order to predict GDM with high accuracy at the start of a pregnancy.

"EHR data are normally challenging to work with because of numerous confounders," explains Eran Segal, co-corresponding author of the study. "In GDM, however, EHR data are powerful, because in several countries (including Israel) all women undergo screening for GDM during pregnancy, which results in 'survey-like' data that are collected across the entire relevant population."

For their study the researchers used comprehensive records of 588,622 pregnancies from 368,351 women. They worked with a subset of these data to develop a model that could predict GDM. Several smaller data subsets, differing from the other records in date and/or geographic location, were then used to validate the model's predictive accuracy. "The model was developed on over 2000 features and performed well," says Segal.

While the majority of features used for developing the model are available at pregnancy initiation, some of the data are gathered throughout the pregnancy. Therefore, the researchers proceeded to derive a questionnaire-based predictor consisting of 9 questions that could be answered at the beginning of a pregnancy. "We found that a model based only on these questions performed nearly as well as the full model," reports Segal.

The team acknowledges that their study has several limitations, including the use or retrospective data. "Going forward, we are planning a prospective clinical trial where we will identify high-risk women and randomize them into either the current standard of care treatment or a lifestyle and dietary treatment change," concludes Segal.

Anna Kriebs, Associate Editor, Nature Communications

ORIGINAL ARTICLE Artzi, N. S. et al. Prediction of gestational diabetes based on nationwide electronic health records. *Nature Medicine* **26**, 71–76 (2020)

AUTOIMMUNITY

IGFs potential biomarkers for type 1 diabetes mellitus

Currently, predicting which individuals at risk of type 1 diabetes mellitus (T1DM) will develop the disease, and how the disease will progress, is challenging. New research published in *Diabetes* suggests that IGF1 and IGF2 could be useful biomarkers for T1DM.

"Prior studies had shown that the IGF axis is dysregulated in established T1DM, however, it remained unclear whether decreased levels or bioavailability of IGFs, as related to IGF binding protein (IGFBP) expression, preceded the clinical diagnosis of T1DM," explain authors Melanie Shapiro and Todd Brusko. The researchers measured serum levels of IGF1, IGF2 and IGFBP in an age-matched, cross-sectional cohort of 305 paediatric and adolescent participants with varying degrees of risk of T1DM.

The analyses revealed that serum levels of IGF1 and IGF2 were statistically significantly lower in participants who were positive for T1DM-predictive autoantibodies (AAb^+) than in AAb^- relatives of participants with T1DM, whereas levels of IGFBP were similar between the groups. Furthermore, levels of IGF1 were shown to decrease with disease duration, as β-cell function was lost. Of note, the decrease in levels of IGF1 and IGF2 was seen in participants who had a single AAb^+, which is early in the progression of the disease (before loss of β-cell function and mass is detectable). In addition, the researchers showed that the decline in levels of IGF1 was quicker in patients with young onset T1DM than in those who were older at disease onset.

"Importantly, we report novel evidence of IGF1 and IGF2 levels showing longitudinal stability in single AAb^+ participants, with IGF1 levels decreasing over time in participants with multiple AAb and

IMMUNOMETABOLISM

Obesity-linked inflammation tied to glutamine levels

Low-grade, chronic inflammation occurs in white adipose tissue (WAT) in obesity; however, the causative mechanisms are unclear. A study in *Cell Metabolism* now reports that the levels of glutamine in human WAT are linked with obesity-associated inflammation.

"As part of a European consortium, our work was focused on mapping the metabolites dysregulated in WAT of well-phenotyped clinical cohorts including individuals with obesity and insulin resistance," explains corresponding author Mikael Rydén. "This collaboration is how we discovered glutamine as the main polar metabolite altered in obesity."

The polar metabolome released from subcutaneous abdominal WAT was mapped; samples were obtained by biopsy from a cohort of 52 women with obesity and 29 women without obesity. Notably, glutamine release from WAT showed an inverse relationship with BMI and was decreased in obesity.

Next, transcriptomic data from a previously described cohort of 56 women with and without obesity was analysed. These data showed that in obesity, WAT is characterized by altered expression of glutamine-metabolizing genes, with the biggest difference observed for glutamine synthetase (*GLUL*) expression, which was decreased. Interestingly, further analysis showed that low *GLUL* expression was associated with pro-inflammatory pathways in human WAT. Furthermore, administering glutamine to high-fat diet-fed mice attenuated the associated adipose tissue inflammation.

In vitro studies of human adipocytes showed that high glutamine levels reduce glycolysis and inflammation. These studies also suggest a nuclear *O*-GlcNAcylation mechanism linking glutamine to inflammation in WAT.