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Predictive metabolomic profiling within a diverse population of pregnant women at low or high risk of gestational diabetes

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While gestational Diabetes Mellitus (GDM) affects up to 1 in 7 pregnancies worldwide, its burden is far from uniform [(1)]. Notably, the prevalence in women of South Asian descent is estimated to be 15%, twice that observed in white European women. This increased prevalence in South Asian women appears to be independent of BMI and the differences in adiposity between the two ethnicities [(1)]. Most surprisingly, although aetiologically similar to T2D, the metabolic traits that result in an elevated risk of GDM are poorly understood [(2–4)]. This study aimed to apply multivariate statistical methods to highlight common and unique metabolites and metabolic features that characterise and distinguish GDM risk in British Pakistani or white Caucasian women.

146 serum metabolites from 3,877 white Caucasian and 4,299 British Pakistani pregnant women (median gestational age of 184 days) from the Born in Bradford (BiB) cohort were included within this analysis. Data were pareto scaled prior to unsupervised principle component analysis (PCA) and supervised partial least squares discriminant analysis (PLSDA). Following the analysis of the full metabolite panel, subgroup analyses were performed based on metabolite class including lipoprotein subclasses, glycerides and phospholipids, and amino acids.

No apparent differences in the metabolomes of White Caucasian and Pakistani women in early pregnancy were observed by GDM status, age, parity, BMI, smoking or gestational age alone. However, a composite profile based upon ethnicity, BMI status, and future GDM diagnosis suggested that Pakistani women of normal weight who later develop GDM present a distinct metabolic profile in early pregnancy. This remained after smoking status and the mother's history of diabetes were accounted for. Glycolysis-related metabolites, branched and unbranched amino acids, and ketone bodies were identified as potential key drivers of these differences (Variable Importance in Projection $\geq$1.75).

British Pakistani GDM cases of a healthy weight were found to have a distinct early metabolic profile compared to overweight and obese Pakistani mothers and all white Caucasian mothers. The investigation continues, and we are now examining specific metabolites and pathways, which may be important in discerning the aetiology of GDM in high risk ethnicities. The identification of key dietary related metabolites in this high-risk group could be utilised to develop dietary interventions to reduce GDM disease burden in high risk global regions.

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