DOHaD 2026 ABSTRACT

Maternal One-Carbon Metabolism Biomarkers and Related Single Nucleotide Polymorphism (SNPs) in Relation to Spontaneous Preterm Births in New Zealand SCOPE Cohort

Presenting Author Sonia Khan[1' 2], Clare R. Wall[1], Ngaire Anderson[3], Claire Roberts[4], John M. D. Thompson[2, 3]

[1] Department of Paediatrics and Dietetics, The University of Auckland, Auckland 1010, New Zealand

[2] Department of Paediatrics, Child and Youth Health, The University of Auckland, Auckland 1010, New Zealand

[3] Department of Obstetrics, Gynaecology and Reproductive Sciences, The University of Auckland, Auckland 1010, New Zealand

4 College of Medicine and Public Health, Flinders University, Adelaide Australia

Email: sonia.khan@auckalnd.ac.nz

Background: Globally spontaneous preterm birth (sPTB) remains a major cause of neonatal mortality. One carbon metabolism (OCM) is essential for DNA synthesis, methylation and fetal development. Single nucleotide polymorphisms (SNPs) within OCM may alter association between maternal metabolites and sPTB risk. The study aimed to investigate the association between maternal OCM metabolites and related SNPs in relation to sPTB risk

Methods: This prospective SCOPE cohort conducted in 1774 New Zealand women at 15 ± 1 weeks' gestation. Six OCM related SNPs MTHFR(C677T), TCN2(C776G), MTHFD1(G1958A), MTR(A2756G), MTHFR(A1298C) and MTRR (A66G) were genotyped alongside plasma B12, folate, homocysteine, choline, betaine, cysteine and methionine. Logistic regression was performed to assess the relationship between SNPs and sPTB and interactions between SNPs and OCM levels and sPTB.

Results: MTHFR C677T significantly increased sPTB risk, while TCN2 C776G decreased it. Higher betaine levels emerged as the strongest and most consistent protective modifier of sPTB risk, with significant interactions observed among women carrying TCN2(C776G), MTHFR(C677T), MTHFD1(G1958A), and MTR(A2756G) variants. In contrast higher methionine and choline increased sPTB risk specifically among MTHFR(C677T) CT carriers. No statistically significant interactions were identified for MTHFR(A1298C).

Conclusions: SNPs modify how maternal OCM metabolites impact sPTB risk. Betaine consistently demonstrated interactions across multiple SNPs suggesting a potential protective role of adequate maternal betaine status during pregnancy to mitigate OCM disruption. These findings highlight considering genetic and nutritional factors in sPTB risk assessment. Further research in larger and more diverse populations, is needed to confirm these findings and clarify underlying biological mechanisms.