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Association between SNPs in genes involved in folate metabolism and preterm birth risk

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ABSTRACT. We investigated the association between 12 single nucleotide polymorphisms (SNPs) in 11 genes involved in folate metabolic and preterm birth. A subset of SNPs selected from 11 genes/loci involved in the folic acid metabolism pathway were subjected to SNaPshot analysis in a case-control study. Twelve SNPs (*CBS*-C699T, *DHFR*-c594+59del19, *GST01*-C428T, *MTHFD*-G1958A, *MTHFR*-C677T, *MTHFR*-A1298C, *MTR*-A2756G, *MTRR*-A66G, *NFE2L2*-ins1+C11108T, *RFC1*-G80A, *TCN2*-C776G, and *TYMS*-1494del6) in 503 DNA samples were simultaneously tested, and included 315 preterm births and 188 controls. None of the 12 SNP genotype distributions related to the folic acid metabolism pathway showed a significant difference between preterm and term babies. The frequency of the compound mutation genotype of *MTHFD*-G1958A, *MTR*-A2756G and *RFC1*-G80A in preterm babies was 7.3%, which was significantly

higher than the 2.7% in term babies. Seven babies carried the compound mutation genotype of *MTHFD*-G1958A, *MTR*-A2756G, and *CBS*-C699T, but this was not observed in term babies. The frequency of the combined wild-type genotype of *MTHFD*-G1958A, *MTR*-A2756G, *MTRR*-A66G, *MTHFR*-A1298C, *NFE2L2*-ins1+C11108T, and *RFC1*-G80A in preterm babies was 3.17%, which was significantly lower than the 7.4% in term babies. The 12 SNPs screened in this study were not independent risk factors of preterm birth. Compound mutation genotypes, including *MTHFD*-G1958A, *MTR*-A2756G, and *RFC1*-G80A and *MTHFD*-G1958A, *MTR*-A2756G, and *CBS*-C699T, may increase the risk of preterm birth. The combined wild-type genotype *MTHFD*-G1958A, *MTR*-A2756G, *MTRR*-A66G, *MTHFR*-A1298C, *NFE2L2*-ins1+C11108T, and *RFC1*-G80A may decrease the risk of preterm birth.

Key words: Folate metabolism; Folic acid; Preterm birth; Single nucleotide polymorphism

