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Genetic polymorphisms involved in folate metabolism and elevated plasma concentrations of homocysteine: maternal risk factors for Down syndrome in Brazil

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ABSTRACT. The aim of the present study was to investigate the effect of polymorphisms C677T and A1298C in the methylenetetrahydrofolate reductase (*MTHFR*) gene, A2756G in methionine synthase reductase (*MTR*) gene and A80G in reduced folate carrier 1 (*RFC1*) gene, and plasma homocysteine (Hcy), on the maternal risk for Down syndrome (DS). Seventy-two DS mothers and 194 mothers who had no children with DS were evaluated. The investigation of the *MTHFR* C677T, *MTR* A2756G and *RFC1* A80G polymorphisms was performed by polymerase chain reaction and enzyme digestion and the *MTHFR* A1298C polymorphism by allele-specific polymerase chain reaction. Hcy quantification was carried out by liquid chromatography-tandem mass spectrometry. The median number of polymorphic alleles for the four loci tested was greater in DS mothers compared to the control group, and the presence of three or more polymorphic alleles increased the risk for having a child with DS 1.74 times. Elevated maternal risk for DS was also observed when plasma Hcy

concentration was higher than 4.99 μmol/L. In conclusion, the presence of three or more polymorphic alleles for *MTHFR* C677T, *MTHFR* A1298C, *MTR* A2756G, and *RFC1* A80G, and plasma Hcy concentrations higher than 4.99 μmol/L are maternal risk factors for DS.

Key words: Trisomy 21; Down syndrome; Nondisjunction; Genetic polymorphism

