Methylenetetrahydrofolate Reductase (MTHFR) Gene Polymorphisms as Risk Factors for Down Syndrome in Jordan

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Abstract

Down Syndrome (DS), or trisomy 21, is the most commonly identified chromosome abnormality in humans. It is caused by the presence of a third copy of 21st chromosome. Two common genetic variants in the methylenetetrahydrofolate reductase (MTHFR) gene involving a cytosine to thymidine (C > T) transition at nucleotide 677, and a substitution of adenosine to cytosine (A > C) at nucleotide 1298. This study examined the frequencies of MTHFR C677T and MTHFR A1298C polymorphisms among the Jordanian mothers with DS children and to test the presence of any association between MTHFR polymorphisms and the risk for appearance of sporadic DS in the children of young Jordanian mothers. The frequencies of both MTHFR C677T and MTHFR A1298C polymorphisms were evaluated in 53 mothers with DS children and 29 controls. Total homocysteine and methionine in the plasma and lymphocyte methotrexate toxicity were measured as indicators of functional folate metabolism. Results showed that the frequency of MTHFR C677T is significantly higher in young DS mothers than in both old DS and control mothers, but there was no significant difference in the frequency of MTHFR A1298C between DS and control mothers. A significant increase was observed in the plasma total homocysteine and toxicity of methotrexate in lymphocytes of young and old mothers than in the control mothers, while there was a significant decrease in the methionine concentrations in young and old mothers compared to those of the control groups. This study has established an association between DS and the different polymorphisms of MTHFR in the Jordanian population, where the presence of MTHFR C677T polymorphism is associated with a high risk for having children with trisomy 21 in the Jordanian mothers, contrary to the A1298C polymorphism, which did not show any association with DS when present alone. However, the concomitant
presence of this polymorphism with the MTHFR C677T polymorphism enhanced the risk for having DS children significantly.