Title: Association of C677T and A1298C polymorphisms of the MTHFR gene with maternal risk for Down syndrome: a meta-analysis of case-control studies

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Abstract:Background: Several studies around the world support the hypothesis that genetic polymorphisms involved in folate metabolism could be related to the maternal risk for Down syndrome (DS). Most of them investigated the role of MTHFR C677T and/or A1298C polymorphisms as maternal risk factors for DS, but their results are often conflicting and still inconclusive. Methods: We conducted a systematic review and meta-analysis to clarify the association of MTHFR C677T and/or A1298C polymorphisms with the maternal risk of DS. Our search strategy selected 42 eligible case control studies for a total of 4131 case mothers and 5452 control mothers. The Newcastle–Ottawa Scale was used to assess the methodological quality of the selected studies. To assess the confidence of statistically significant associations we applied false positive report probability test, and we performed the trial sequential analysis to minimize the type I error and random error. Results:We observed significant associations between the MTHFR C677T polymorphism and maternal risk for DS for each of the genetic models investigated (dominant, recessive, codominant, and allelic contrast). Subgroup analysis by region revelated significant association in the Asian population for all the genetic models investigated. Significant associations were also found for certain genetic models in North American, South American, and Middle Eastern populations, while no association was observed in Europeans. The MTHFR A1298C polymorphism did not show any association with the maternal risk of DS, either alone or in combination with the C677T one. The results of false positive report probability to verify the confidence of a significant association suggest that the association between the MTHFR C677T polymorphism and the maternal risk for DS is noteworthy, with high confidence in Asians. Conclusion: The results of this meta-analysis support that the MTHFR C677T polymorphism, but not the A1298C one, is associated with the maternal risk for DS. Further studies are required to better characterize the contribution of gene-gene and gene-nutrient interactions aswell as those of other regional or ethnic factors that could explain the observed different effect size in different populations.

Biography: Nutritionist, Master in Health Sciences (UFRN) inserted in the Line of Biosciences Applied to Health and Phd student of Health Sciences. Have experience in Biochemistry (Experimental and Clinical), Molecular Biology and Nutrition, with emphasis on Clinical Nutrition, Evidence-Based Medicine, Systematic Review and Meta-analysis.