

Association of maternal folate with methylene tetrahydrofolate reductase polymorphism relationship in infants <3 months with Down syndrome

Sir,

This is in reference to our article published in Indian Journal of Human Genetics titled "Evaluation of C677T polymorphism of the methylenetetrahydrofolate reductase (MTHFR) gene and its association with levels of serum homocysteine, folate, and Vitamin B12 as maternal risk factors for Down syndrome (DS)".^[1] We found a genuine relationship between maternal folate and MTHFR gene polymorphism in <3 months infants, which was not analyzed in the original article. In DS mothers with baby <3 months, red blood cell (RBC) folate were significantly lower than controls, but not in case of serum folate. Though association with polymorphism was not statistically significant, but gave us a trend [Table 1].

Lower RBC folate in mothers with baby <3 months possibly denotes status at conception.^[2] RBC folate is a preferred marker to assess long-term folate status. Data's from the selected randomized controlled trials showed that folic acids with dietary folate supply exerted a significant effect on all the markers of folate status, especially for RBC folate.^[3] Similarly, a meta-analysis by Mohamed^[4] showed that routine folate supplementation in pregnancy resulted in a substantial reduction in the incidence of low serum and

RBC levels. Folate requirements during pregnancy are 5- to 10-fold higher than in the nonpregnant condition due to uterine growth, placental enlargement and the growth of the developing fetus.^[3] Therefore, folate supplementation during periconceptional period is very essential as shown by our statistics as well. In our study, we failed to get a statistically significant association with MTHFR polymorphism may be due to low sample size. Study with larger sample size with adequate power can prove an association. Folate supplementation may overcome the mutation of MTHFR gene and would therefore may reduce DS.

In conclusion, mothers of infants (<3 months) with DS have very low folate status and have an increasing trend of developing polymorphism (MTHFR).

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Table 1: Maternal folate and MTHFR polymorphism relationship-infants <3 months

	Case (%)	Control (%)	95% CI	P value	P _a value
Low RBC folate	12 (80)	3 (20)	9.3 (1.46-59.48)	0.034	0.03
Lowserum folate	8 (80)	2 (20)	4.57 (0.71-29.1)	0.21	0.20
	MTHFR polymorphism	Normal gene	95% CI	P value	P _a value
Low RBC folae	8 (53.3)	7 (46.7)	4.57 (0.72-29.1)	0.22	0.21

CI: Confidence interval; MTHFR: Methylene tetrahydrofolate reductase; RBC: Red blood cell, P_a: Adjusted P value

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