

PP-03: DNA methylation in methylenetetrahydrofolate reductase (MTHFR) gene promoter and 5-formyl-tetrahydrofolate (5-formyl-THF) levels in folic acid supplemented pregnant women

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Introduction: DNA methylation is an epigenetic modification critical for gene expression regulation. Folate metabolism cycle is intricately regulated to provide methyl groups for DNA methylation. The genetic and epigenetic influences on folate metabolism and on the levels of different folate forms are yet unclear. Methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism that determines the availability of methyl groups. The study aims were to assess the methylation status of MTHFR gene promoter and to investigate the association between DNA methylation status of MTHFR promoter and concentrations of 5-formyl-tetrahydrofolate in folic acid supplemented Sri Lankan pregnant women.

Methods: Methylation Specific PCR was used to analyse methylation status of MTHFR promoter (n=20) at two time points: baseline (before FA supplementation) and delivery (after FA supplementation). Available data on 5-formyl-THF levels of these pregnant women were compared with the methylation status. Wilcoxon rank test was performed to compare the change in DNA methylation status at baseline and delivery, while one-way ANOVA was performed to compare the mean change of 5-formyl-THF level from baseline to delivery between groups.

Results: At baseline, twelve pregnant women had fully-methylated status, seven had partially-methylated status and one had unmethylated status. All women with partially-methylated and unmethylated status at baseline were fully-methylated at delivery. Interestingly, of the twelve women with fully-methylated status at baseline, one changed to partially-methylated status at delivery. Although 5-formyl-THF levels significantly increased from baseline to delivery following FA supplementation, the mean change was not significantly different between fully and partially-methylated groups ($p=0.541$).

Conclusions: Results indicate that DNA methylation in MTHFR gene promoters increased in partially methylated and unmethylated groups after FA supplementation while the majority of the fully methylated group at baseline have maintained their methylation at delivery too. The fully-methylated status of MTHFR gene promoter may indicate the direction of metabolism towards 5-formyl-THF formation to maintain the stability of folate mediated 1C metabolism.

Keywords: DNA methylation, folic acid, MTHFR gene