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Abstract Topic: - Molecular effects of genetic variation

Abstract Title: - Exploring role of Folate gene polymorphisms in Congenital Heart Disease: A pilot study from north India

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Aims: - Micronutrients are invariably essential during conception and if inadequate may result in adverse birth outcome including congenital anomalies. One such micronutrient is Folate which is crucial for replication and is a substrate for vitamin metabolism and amino acid synthesis and its dietary supplementation is known to reduce the risk of neural tube defects (NTDs), congenital heart defects, low birth weight and preterm birth. In this study, we explore gene variants of Folate One Carbon Metabolic (FOCM) pathway with risk of CHD in a north Indian tertiary pediatric cardiac hospital.

Methods: - N=~450 Non-syndromic CHD cases with one or both parents available were analysed for selected gene variants in the FOCM pathway with Institutional Ethics Committee approval. N=100 healthy adult controls ruled out for CHD were also screened. Both CHD affected vs parents and case-control genotypes for 6 markers namely c.677C4T (rs1801133) and c.1298A4C (rs1801131) variants in methylenetetrahydrofolate reductase (MTHFR); rs526934 in transcobalamin 1 (TCN1); c.2756A4G (rs1805087) in methionine synthase reductase (MTR); G1958A (rs2236225) in methylenetetrahydrofolate dehydrogenase (MTHFD1) and an Ins/del polymorphism rs4646994 in Angiotensin-converting enzyme (ACE) were obtained either by RFLP or ARMS PCR. Since inhouse control sample data was small in number it was pooled with publicly available South East Asian population data and combined case control analysis was also performed.

Results: - Since most of the patients are from rural and lower socioeconomic background demographic data showed ~40% of the expecting mothers never took folate. Genetic data points to limited replication in our sample set with allelic association observed for rs1805087 ($p=0.044$) in transmission disequilibrium test; and a trend of association observed for rs1801133 ($p=0.06$)

Conclusions: - Our study demonstrated folate genes like MTHFR (rs1801133) and MTR (rs1805087) both on Chromosome #1 show a trend of association and might contribute to CHD susceptibility by regulating folic acid metabolism. Therefore, replication studies with larger sample sizes are required to further understand the genetic mechanisms of Folate metabolic genes in CHD development.

Keywords: - Since most of the patients are from rural and lower socioeconomic background demographic data showed ~40% of the expecting mothers never took folate. Genetic data points to limited replication in our sample set with allelic association observed for rs1805087 ($p=0.044$) in transmission disequilibrium test; and a trend of association observed for rs1801133 ($p=0.06$)