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ORIGINAL ARTICLE

The A1298C Methylenetetrahydrofolate Reductase Gene Variant as a Susceptibility Gene for Non-Syndromic Conotruncal Heart Defects in an Indian Population

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Abstract Conotruncal heart defects (CTHDS) are a subgroup of congenital heart malformations that are considered to be a folate-sensitive birth defect. It has been hypothesized that polymorphisms in genes that code for key enzymes in the folate pathway may alter enzyme activity, leading to disruptions in folate metabolism and thus may influence the risk of such heart defects. This study was designed to investigate the association of six selected folate-metabolizing gene polymorphisms with the risk of non-syndromic CTHDs in an Indian population. This was a case–control study involving 96 cases of CTHDs and 100 control samples, ranging in age from birth to 18 years. Genotyping using Sanger sequencing was performed for six single nucleotide polymorphisms of genes involved in folate metabolism. Logistic regression analyses revealed that for the 5,10-methylenetetrahydrofolate (*MTHFR*) A1298C polymorphism, the CC variant homozygote genotype was associated with a significantly increased risk of CTHDs. The results of this study support an association between the inherited *MTHFR* A1298C genotype and the risk of CTHDs in an Indian population.

Keywords Deoxyribonucleic acid · Folate metabolism · Logistic regression · Sanger sequencing · Single nucleotide polymorphism

Abbreviations

CTHDS	Conotruncal heart defects
SNP	Single nucleotide polymorphisms
MTHFR	5,10-Methylenetetrahydrofolate reductase
CHD	Congenital heart disease
TOF	Tetralogy of Fallot
DORV	Double outlet right ventricle
PA-VSD	Pulmonary atresia with ventricular septal defect
TA	Truncus arteriosus
IAA	Interrupted aortic arch
DGS	DiGeorge syndrome
VCFS	Velocardiofacial
CAFS	Conotruncal and facial anomaly
MTR	Methionine synthase
MTRR	Methionine synthase reductase
VSD	Ventricular septal defect
ASD	Atrioventricular septal defect
PS	Pulmonary stenosis
CoA	Coarctation of the aorta
HWE	Hardy–Weinberg equilibrium
DNA	Deoxyribonucleic acid

Introduction

Congenital heart diseases (CHDs) encompass any structural defect of the heart which is present at birth. CHDs are the most common congenital anomalies, contributing to

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