عنوان مقاله:

Risk of Atrioventricular Septal Defects in Down syndrome : Association of MTHFR C۶۷۷T and RFC۱ A۸۰G polymorphisms in Indian Bengali cohort

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خلاصه مقاله:

Background : Etiology of Congenital heart defects (CHD), especially Atrio-Ventricular Septal Defect (AVSD) among the individuals with Down syndrome (DS) is enigmatic and may differ across the population divides owing to ethnicity and sociocultural differences. The polymorphisms of folate pathway regulators MTHFR and RFC۱ as risk of AVSD among DS individuals from Indian Bengali cohort has not been explored yet. Objectives : Aim of the present study is to investigate the association of MTHFR C۶۷۷T and RFC۱ A۸۰G polymorphisms with the incidence of AVSD among individuals with DS in the Indian Bengali cohort. Methods : Genotyping was done by bi-directional Sanger sequencing of DNA samples from DS with AVSD (N=۴۷۹; 'DS-AVSD'), DS without AVSD (N=۵۴۰; 'DS'), karyotypically confirmed euploid with AVSD (N=۳۲۱; 'Control-AVSD') and euploid without AVSD (N=۴۰۹; 'Control'). Odds ratio (OR) was calculated to infer degree of risk imposed by alleles and genotypes. Functional implications of polymorphisms were inferred using Project HOPE server. Results : RFC۱ A۸۰G polymorphisms was found to be significantly associated with DS-AVSD when compared with control (p = ۰.۰۰۰۱; p< ۰.۰۰۰۱), control-AVSD (p=۰.۰۰۰۴; p< ۰.۰۰۰۱) and DS (p< ۰.۰۰۰۱) groups. MTHFR C۶۷۷T showed significant association with DS-AVSD in comparison to control only (p=۰.۰۰۰۴; p< ۰.۰۰۰۱). We also found elevated risk of AVSD among DS when both the polymorphisms are present together. In-silico analyses suggest probable amino acid replacement and subsequent compromised functions of the genes that may results in AVSD. Conclusion : Our study suggests the RFC۱ A۸۰G polymorphism is a significant risk for developing AVSD among the individuals with DS from Indian Bengali population. .The MTHFR C۶۷۷T polymorphism increases risk when present together with RFC۱ A۸۰G polymorphism

کلمات کلیدی:

.Down syndrome, Atrio-ventricular Septal Defect, MTHFR, RFC۱, genetic polymorphisms