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# Genetic Variant Screening and Association Study of *NKX2-5* in Congenital Heart Disease Patients from North India †

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**Background**: Globally, 1% of all live births are affected by some form of congenital heart defects (CHDs). Genetics and the environment both play a role in its causation, but very few of these aspects have been explored in the Indian subcontinent. One of the first and key transcription factors required for the formation of the heart during fetal development is *NKX2-5*. Several mutations in this gene have been identified for CHDs. In this study, we screened for known and novel variants to understand their role in CHDs.

**Methods**: Two exons and flanking 3′ and 5′ UTR regions of *NKX2-5* were sequenced in n= 71 CHD cases, followed by a case–control test of association and a haplotype study.

**Results**: Only three known variants, namely rs2277923 (c.63A>G), rs3729753 (c.606G>C), and rs703752 (c.61G>T), were identified in a total of n= 69 cases. The case–control test of association revealed no significant allelic or haplotypic association. A genotypic association was observed for rs703752 in a recessive model ($\chi^2 = 4.47$; $p = 0.03$; risk score = 0.33), along with a trend of association for rs3729753 ($\chi^2 = 3.73$; $p = 0.053$; risk score = 1.68) and rs703752 ($p = 0.08$).

**Discussion**: Although we did not identify any new mutations in the coding regions of *NKX2-5* gene, our findings are important observations for establishing an association between *NKX2-5* variants and cardiac defects in the context of the north Indian population. There is a need to explore the roles of other transcription factors and cardiac developmental pathways and establish their interaction and role in disease biology in the Indian subcontinent.

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

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