Abstract

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

Shadab Ahamad 1,*, Prachi Kukshal 1, Ajay Kumar 1 and Subramanian Chellappan 2

1 Sri Sathya Sai Sanjeevani Research Foundation, Palwal 121102, Haryana, India; prachi7k@gmail.com (P.K.); ajay.kumar@srisathyasaisanjeevani.org (A.K.)
2 Sri Sathya Sai Sanjeevani International Centre for Child Heart Care & Research, Palwal 121102, Haryana, India; drsubramanian.chellappan@srisathyasaisanjeevani.com
* Correspondence: shadab1997ansari@gmail.com
† Presented at the 3rd International Electronic Conference on Biomolecules, 23–25 April 2024; Available online: https://sciforum.net/event/IECBM2024.

Keywords: congenital heart disease; NKX2-5; sanger sequencing; north India; genetic variant; case-control association

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 ($\chi^2 = 4.47; p = 0.03; \text{risk score} = 0.33$), along with a trend of association for rs3729753 ($\chi^2 = 3.73; p = 0.053; \text{risk score} = 1.68$) 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.

Author Contributions: Conceptualization, S.A. and P.K.; methodology, S.A.; software, S.A.; validation, S.A. and P.K.; formal analysis, S.A.; investigation, S.A.; resources, A.K. and S.C.; data curation, S.A.; writing—original draft preparation, S.A.; writing—review and editing, P.K.; visualization, S.A.; supervision, P.K.; project administration, P.K.; funding acquisition, P.K. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Ethics Committee of SRI SATHYA SAI SANJEEVANI RESEARCH FOUNDATION, Palwal, Haryana (protocol code: PSR00007/1/IEC/2/2019 and date of approval: 15 November 2019).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.
Data Availability Statement: The datasets used and/or analysed during the study are available from the corresponding author upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.