**CONGENITAL HEART DISEASE IN INDIA**

R. Bhardwaj1, A. Kumar2, D. Agrawal3, **B. Mohapatra4**

1. Dept. of Zoology, Inst. of Science, BHU, Varanasi, India

2. Dept. of Pediatrics, Inst. of Med Science, BHU, Varanasi, India

3. Dept. of CTVS,Inst. of Med Science, BHU, Varanasi, India

4. Dept. of Zoology, Inst. of Science, BHU, Varanasi, India

Congenital Heart Defects (CHDs) are the major cause of infant mortality and morbidity worldwide with an estimated prevalence of 9 per 1000 live births. The burden of CHD is huge in developing countries like India especially due to high birth rate. Despite of its higher prevalence and utmost clinical significance, etiology of these defects is not completely understood. Our objective is to assess the pattern and prevalence of congenital heart defects in India and to decipher underlying genetic cause by screening cardiac specific transcription factors (TFs) and functional validation of genetic variants by in siico as well as in vitro studies.

A five-year study (2011-2015), in North-central region of India revealed a prevalence of approximately 19 per 1000 individuals. VSD (33%) was the most common, followed by ASD (19%) and TOF (16%). We screened 280 non-syndromic CHD cases for 12 genes NKX2-5, GATA4, BMP2, BMP4, BMP7, NODAL, CITED2, TGFB1, TGFB2, TBX20, SRF and CRELD1. Out of these genes, GATA4 and NKX2-5 were noted to be most frequently associated with CHD in this population. We identified 5 novel sequence variants (A8D, A9T, E128V, S133C and W228R) and 4 known variants (A75S, S358T, P407Q and T355S) in 20 CHD cases (7.1%) in GATA4. Parallely, NKX2-5 as revealed 5 non-synonymous genetic variants (A61G, R95L, E131K, A148E and P247A) in 5 CHD cases (1.78%). None of these variants were found in 200 ethnic matched controls (400 Chromosomes). These mutants also exhibited in silico and in vitro functional deficits demonstrated by western blot, immunocytochemistry and inhibition of down stream promotor (ANF/cActin) activity. The prevalence of CHDs in our cohort was high. NKX2-5 and GATA4 are also most frequently mutated genes in CHD patients in Indian population. Functional validation of mutations listed for these two genes, indicate their possible role in disease manifestation.