Disease is as old as life itself with almost all having a genetic component. About 5000 human disease phenotypes are documented, although, many still remains to be described. The discovery of disease causing genes has been increasing with time, however, about 1000 of them are noted till date. Congenital malformations are being described since the times of ancient primitive man (30,000 years ago) and are the most common diseases which increase the rate of mortality and morbidity in a population (Savona and Grech 1999). In total population, it has been estimated that 4-6% is suffering with genetic defects. About 7.5% of all conceptions have a chromosomal abnormality, most of which are not compatible with survival and 50% of first-trimester spontaneous abortions have a chromosomal abnormality. In general, 0.5-1% of liveborn infants have a chromosomal abnormality (Gardner et. al., 1996).

One such common single group of congenital abnormalities is congenital heart disease which is the leading cause of birth defect - related deaths in the first year of life (http://www.fi.edu/biosci/develop.html). Tremendous advances in the diagnosis and treatment of congenital heart malformations have occurred in the last five decades since the surgical interventions of patent ductus arteriosus and coarctation of aorta, way back in early 1990s. Lethal and severely morbid anomalies can be surgically treated with an increased success rates for most lesions (Noonan 2004). However, despite the advances in diagnosis and treatment, understanding of the etiologies of congenital heart disease, which is
essential for the prevention and more physiological treatments, has until very recently been limited. However, in the last decade, the role of genes, their critical timing of expression and the understanding of important downstream pathways which are required for optimizing normal development and control of the left-right symmetry of the heart have emerged (Garg 2006). In India, although few studies on the epidemiology of congenital heart disease are carried out, not many studies on the genetic aspects have been done. In view of this, in the present investigation, an attempt has been made to understand the genetics of congenital heart disease in Mysore. The findings and implications of this study are compiled as follows:

Section I reviews what is already known about congenital heart disease. It also brings about the existing gap in understanding the genetics of congenital heart disease in India, particularly Mysore.

Section II presents the overall genetic analysis of congenital heart disease in Mysore population.

Section III summarizes the findings and brings out the future prospects of these investigations.

Section IV deals with appendices and literature cited in this thesis.

Section V includes the list of publications from this work.