Summary and Conclusion
6. Summary and Conclusion

6.1 Summary

Individual with congenital malformations place a heavy burden on the society and affected families. Among malformations, neural tube defect (NTD) is a major malformation in the Indian subcontinent which has become highly amenable to primary and secondary prevention (Dubey et al., 2005; ICMR, 2009). Primary prevention of genetic diseases is emerging as an important area to improve quality of life and prevent disease burden. Hence, the causes of birth defects and developmental disabilities should be found.

The primary focus of antenatal care has been health of the mother during pregnancy and safe delivery of the child. Fetal medicine is now emerging as an equally important component of the antenatal care. Hence, the scope of antenatal care needs to be enlarged to include fetal health. Advances in medical and surgical care during childhood, increases the number of survivors with complex CHD. Therefore, the number of adults with a CHD is on the rise. This new and growing population of adolescents and adults reaching reproductive age group and their recurrence risk to offspring represent a challenge to the health service.

Antenatally diagnosed cases of CHD should be investigated for Karyotyping and 22q11.2 deletion syndrome. Increased NT, IUGR and other non-cardiac malformations of 22q11.2 deletion syndrome should be screened carefully for thymus hypo or aplasia and fetal echo including vascular ring. Chromosome analysis along with the FISH studies to be carried out in patients with the DGS/VCFS spectrum. Other chromosomal abnormalities can help in detecting new gene loci similar to all other genes which were identified based on chromosomal
abnormality. Even though the deletion on 10p is relatively rare deletions of DGSI and DGSII result in similar phenotypes, and hence, it is still beneficial to screen patients referred for DGS and VCFS for DGSII loci, if DGSI is normal (Berend et al., 2000). There is a possibility of involvement of other cardiac genes apart from GATA4 gene involved in chromosome 8p23 deletion syndrome as observed in case CHD1. Recent studies also suggest that mutation in GATA4 and NKX2-5 are responsible for CHDs and may not be the microdeletion.

All fetuses with congenital diaphragmatic hernia (CDH) should be investigated for chromosomal analysis. In case of normal karyotype, CDH can be corrected by Percutaneous Fetoscopic Endoluminal Tracheal Occlusion (FETO) antenatally or delivery should be planned at a tertiary care center where CDH can be managed postnatally.

All fetuses with Agenesis of corpus callosum (ACC) should be carefully looked for any other CNS abnormalities and Non-CNS features. Fetal MRI can be performed to confirm the diagnosis and to demonstrate some additional cerebral anomalies. Isolated ACC picked up in antenatal with normal karyotype poses a great challenge in counseling. Further research is necessary in understanding the etiology and pathogenesis of the ACC and its effect in the fetuses.

6.2 Conclusion

Thus this study highlights the need and benefit of screening women during pregnancy for birth defect. It requires targeting pregnant women or those with increase risk for prevention by suitable screening strategies. There is a need for
uniform national protocols for preventive genetic services to be implemented in the National Family Welfare Programme.

All women planning for family should take periconceptional (before conception) folic acid which reduces the risk of NTD, cleft lip and CHD in the fetus. All expectant mothers should undergo level II USG at 11-14wks for NT scan and 18-20 wks of pregnancy for anomaly scan. If any abnormality is detected, it should be investigated in detail.

All cardiac defects should be investigated for deletion 22q11.2 syndrome in addition to aneuploidies. Parents should be also examined with detailed history. All cases of congenital abnormality picked up during antenatal period with normal karyotype should be stored for further studies. In case, the couple decides to terminate the pregnancy infantogram and fetal autopsy should be conducted to look for any other abnormalities.

Carefully monitoring early infant and child development, particularly social and emotional development, is important for ensuring early diagnosis and intervention for developmental problems, such as autism. Right now prevention is through early identification and diagnosis of the birth defects. Because of complex condition and poor prognosis most of the couple opts for termination of the pregnancy.

Finally, the completion of the human genome project has provided a range and depth of information. It has brought lot of importance and challenge to understand the genetic disease. Further challenges include utilizing this information to improve diagnosis and treatment of children with CHDs. We need to extend the ability of fetal medicine specialist to find heart defects as early as possible so that,
they can be treated while the heart is still forming (Ramegowda and Ramchandra, 2005).

In the near future whole genome sequencing will not only be achievable, but also come within reach for advanced clinical diagnostic testing. Whole genome sequencing will generate a lot of new information and interpreting these results will be difficult. There is a need to identify approaches and means to translate knowledge into effective intervention. This information can be translated through Pre-implantation Genetic Diagnosis (PGD) and Gene therapy. PGD will help in selecting the normal embryos and prevention of the termination of the pregnancy and physical and emotional trauma associated with it. Gene therapy will help in correcting the defect at the gene level.