Chapter 7
Conclusions,
Limitations and
Future directions
7.1. Conclusions

1) This study identified the mutations responsible for MPS IVA and GM1 gangliosidosis patients in India.

2) This is the largest cohort of patients with these conditions being molecularly characterized in literature.

3) We could find common phenotype in patients which has common mutations in GALNS and GLB1.

4) This study found great allelic heterogeneity, as observed in other populations, which hinders the establishment of genotype-phenotype correlations.

5) This study identified 28 novel mutations in GALNS and 22 novel mutations in GLB1 and reports the most common mutations in India.

6) Indian patients have different mutation spectra when compared with other populations.

7) Homozygous mutations are frequent even when consanguinity is not evident.

8) This study identified common mutations in GALNS and GLB1 in Indian patients.

9) Nearly 40% of the mutant allele’s frequency lies in exons 1, 8 and 7 of GALNS and nearly half of the mutant allele’s frequency present in exons 1, 14 and 10 of GLB1 in Indian patients and hence it may be cost-effective to initially screen these exons in Indians with these conditions.

10) This study has been very useful for providing prenatal diagnosis and genetic counseling to the affected families.

7.2 Limitations

Due to the allelic heterogeneity of mutations in GALNS and GLB1 genes, this study is unable to provide a detailed genotype and phenotype correlation.

This study does not provide plasma keratan sulfate level in Morquio syndrome patients, which is a good biomarker for this condition to correlate with genotype.

This study could not provide clinical data of 21 patients with MPS IVA and five patients with GM1 gangliosidosis as they were referred for clinical testing and carrier analysis.
7.3. Future directions

1) The mutations identified in *GALNS* and *GLB1* in this study will help to create Indian database for MPS IVA and GM1 gangliosidosis.

2) We have proposed a strategy to firstly screen the mutations in exon 1, 8, and 7 of *GALNS* and exons 1, 14 and 10 of *GLB1*. More patients need to be screened to validate the proposed strategy for identification of mutations in these exons in Indians patients with these conditions.

3) Confirmation of mutations in the patients with MPS IVA and GM1 gangliosidosis will help to provide mutation specific therapy.

4) Identification of mutations in families with MPS IVA and GM1 gangliosidosis will help to provide prenatal diagnosis in future.