2.1 RATIONAL

Tay-Sachs disease (TSD) has been reported in children of virtually all ethnic and racial groups. It is considered to be very rare and not studied in Indian context till date. Considering birth incidence and autosomal recessive transmission of the disease, it can be predictable that more than expected children are likely to be born in the country every year. In the absence of confirmed diagnosis, the disease will put a tremendous trauma, psychosocial stress and financial burden on the family. Currently there is no cure of the disease except symptomatic support. Our study has shown that glycolipid storage disorders that include TSD emerge as the second most common storage disorder amongst the majority of LSDs studied in India (Sheth et al., 2014a). It can be prevented only by prenatal diagnosis. The prerequisite is the confirmation of diagnosis of an affected child by enzyme study and to understand the molecular pathology involved in disease phenotype. Therefore, the present study was aimed at developing an enzyme based diagnosis for patients with TSD, to identify the disease causing mutations and its genotype-phenotype correlations further confirmed by molecular study. Further, the study will help in developing simple cost effective DNA chips for most commonly prevalent mutations that can be used to identify carrier frequency in the population.

2.2 OBJECTIVES

This work is divided into three following objectives:

Objective-1:

To standardize enzyme based study from leucocytes or plasma for postnatal diagnosis and uncultured chorionic villus (CVS) and/or cultured trophoblats (CT Cells) and cultured amniotic fluid cells (Amniotic fibroblasts) for prenatal diagnosis of Tay-Sachs disease (TSD) and Sandhoff disease (SD).

Objective-2:

To study the mutational spectrum of *HEXA* gene in Indian patients with Tay-Sachs disease and elucidate the pathogenic effect of novel mutations

Objective-3:

To understand influence of genotype on phenotype development

Objective-4:

To provide genetic counseling to affected families and prevent the disease through prenatal diagnosis

Objective-5:

To evolve a cost effective DNA based diagnosis for prevalent mutations in our population through identification of the carrier frequency by mass screening