# RATIONAL AND OBJECTIVES

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## 3.1 Rational

GD has been observed in the patients of different ethnic groups. On the basis of birth incidence and autosomal recessive inheritance, every year approximately 1000children's are born with this disorderin India. GD is the second most common storage disorders among the majority of Lysosomal Storage Disorders (LSDs) studied in India and other population as well (Sheth et al., 2004 and 2013; Startz-Chacham et al., 2009). The diagnostic facility, awareness of the disease and activeness of patient advocacy group is very limited. This study is aimed to develop enzyme based diagnosis for patients with GD, and to understand the molecular pathology of the disease. This will help to understand the genotype/phenotype correlation in Indian patients and is likely to help in our understanding of the disease severity prediction. Further this study will also help in developing the DNA chips as a simple cost effective molecular screening for the most frequent mutations in Indian patients. This information will also be used for carrier identification in the population and provide comprehensive approach of enzymatic and molecular study during prenatal diagnosis. Therapeutic decisions and its prognostications can also be improved with this information.

## 3.2 Aims and Objectives

### 3.2.1 Aims

**Aim-1:** To screen patients with hepatosplenomegaly, anemia and thrombocytopenia by plasma chitotriosidase followed by confirmative study using β-glucosidase assay from leucocytes

**Aim-2:** To carry out molecular confirmative study for common mutations followed by sequencing of the *GBA* gene to identify common disease causing alleles and to identify novel mutations for GD

**Aim-3:** To understand the genotype correlation with disease phenotypes and use this information for therapeutics like ERT (Enzyme Replacement Therapy), SRT

(Substrate Reduction therapy) and chaperones

### 3.2.2 Objectives

**Objective1:** To identify patients with GDand assign type of GD based on clinical presentation

**Objective2:** To demonstrate the presence of known common mutations (N370S (c.1226A>G), L444P (c.1448T>C), R463C (c.1504C>T), Ivs2 (+1) G>A) and to identify disease specific mutant allele in patients with GD in India which will demonstrate the mutation spectrum of *GBA* gene in Indian patients with GD

**Objective 3:** To Understand the genotype correlation with phenotype and use this information for differential diagnosis of the disease and prognostication

**Objective 4:** To understand the effect of genotype on patients receiving ERT