PROLOGUE

Lysosomes are the subcellular organelles of the human system to keep the cell healthy and functioning. They contain numerous acid hydrolases synthesized in the Golgi apparatus to catabolize proteins, lipids, nucleic acids, sulphatase, phosphatase, and complex carbohydrates. Thus, lysosomal enzymes are the catabolic functional that keep the cells free from unwanted cell debris. Inborn errors of metabolism are a common cause of inherited disease (Burton, 1998), of which lysosomal storage diseases (LSDs) are a significant subgroup (Platt and Walkley, 2004; Fuller et al., 2006; Ballabio and Gieselmann, 2009) with an overall incidence of 1:5000 live birth.

The lysosomal storage diseases (LSDs) comprise a heterogeneous group of 50 disorders that are caused by genetic defects in a lysosomal acid hydrolase, receptor, activator protein, membrane protein, or transporter, causing lysosomal accumulation of substrates that are specific to each disorder (Wang et al., 2011). Most LSDs result from acidic hydrolase deficiencies (Winchester, 2004), a considerable number of these conditions result from defects in lysosomal membrane proteins or non-enzymatic soluble lysosomal proteins (Saftig and Klumperman, 2009). Therefore, LSDs offer a window into the normal functions of both enzymatic and non-enzymatic lysosomal proteins. The accumulation is progressive, ultimately causing deterioration of cellular and tissue function. Lysosomal accumulation activates a variety of pathogenetic cascades that result in complex clinical pictures characterised by multisystemic involvement. The combined incidence of LSDs is estimated to be approximately 1:5,000 live births (Fuller et al., 2006), but the true figure is likely to be greater when undiagnosed or misdiagnosed cases are accounted for. These disorders are seem to be under diagnosed due to overlapping phenotypes, non-availability of diagnostic facility in a majority of the centers and lack of awareness among clinicians. So far, the available data are for case reports, anecdotal study from few centers about the occurrence representing a small community of the country and very few molecular reports. India being the second largest populous country with ethnical diversity; LSDs are likely to be more common than thought in the country. The present study proposes to carry out biochemical and molecular studyin children suspected to have GD (Gaucher disease). The prevalence of GD in India is unknown;it is likely to be the same as in other population or may be higher due to genetically heterogeneous

population and consanguineous marriages in many parts of the country. Our recent study showed that GD is the most common storage disorder. In present study we have used three tier screening approach like screening by plasma chitotriosidase followed by study of lysosomal enzyme β-Glucoosidase from leucocytes and identification of molecular pathology involved therein.

After enzymes study, molecular pathology is very important in GD to identify common molecular marker, to screen large population for carrier frequency and prenatal diagnosis. GD has the variable phenotype associated with genotype therefore identification of molecular pathology will be of help in deciding therapeutic preferences.