Abstract

Mucopolysaccharidosis IV A (Morquio A syndrome, MPS IVA) and GM1 gangliosidosis are lysosomal storage diseases (LSDs) caused by deficiencies of N-acetylgalactosamine-6-sulfatase (GALNS) and β-galactosidase (β-GAL) respectively, due to the mutations in the genes coding for these enzymes. To further characterize the phenotype and the mutation spectrum for these conditions, we analyzed the clinical profiles of Indian patients with these conditions and identified the mutations in the GALNS and GLB1 genes. All the exons and the adjacent intronic sequences of GALNS and GLB1 were amplified and sequenced. We performed in silico and structural analyses of novel mutations identified in this study. We identified 51 different mutations in GALNS in 91 families, of which 28 were novel and 23 were previously reported. We also found 36 different mutations in GLB1 in 53 families, of which 22 were novel and 14 were already reported. We identified the most common mutations in GALNS and GLB1, and noted a higher frequency of mutations in exons 1, 8 and 7 of GALNS and exons 1, 14 and 10 of GLB1. We propose a strategy to identify the mutations in GALNS and GLB1 in Indian patients with these conditions. The most frequent mutations identified in Indian patients were rare in comparison to the mutational profiles reported in other populations. These results indicate that Indian patients may have a distinct mutation spectrum when compared to those of other populations. In silico and structural analyses of GALNS and GLB1 reveal that all novel mutations affect the function and structure of the proteins. This study presents the largest series of patients with MPS IVA and GM1 gangliosidosis and is the first from India. This study has helped prenatal diagnosis and genetic counseling of affected families.