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Mutational analysis of Gaucher disease patients in Pakistani population

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Background & Aim: Gaucher disease (GD) is an autosomal recessive lysosomal storage disease caused due to deficient activity of glucocerebrosidase, which leads to the accumulation of the glucocerebroside in lysosomes of macrophages leading to pancytopena, organomegaly, mental retardation and skeletal deformation. The disease is not well studied in Pakistan. Patients are clinically diagnosed and symptomatically treated. The present study aimed to identify the mutations with a causative role in the onset of Gaucher disease in patients residing in different cities of Punjab.

Material & Methods: Blood samples were obtained from patients along with parents and normal siblings after informed consent. Available clinical history was recorded. DNA was extracted through organic method. All exons of GBA gene were sequenced using Big Dye terminator v3.1 Cycle sequencing kit.

Results: In affected members of 6 out of 9 families mutation c1448C (L444P) was present in homozygous state. In three families, L444P mutation was not detected and hence, the whole GBA gene comprising 11 exons was PCR amplified and sequenced to target rare mutations. In one family the patient was compound heterozygote with two heterozygous mutations; c1184C (S356F) in exon 8 in one allele and c703T (S196P) in exon 6 on another allele. In other two families, R120W was found in heteroallelic state. SNPs 155, 204, 885 (exon 11) in PKGD 04, rs28559737 (intron 9) in PKGD 01, PKGD 05, PKGD 08 and PKGD 09; 155, 208, 183 (intron 5) in PKGD 03, 04, 06 and 07 and 155, 208, 545 (intron 5) in PKGD 02, 08 and 09 were also observed.

Conclusion: The most prevalent mutation among the studied subjects was L444P. The mutational analysis enabled carrier screening of the normal members of the families with history of Gaucher disease and molecular classification of the Gaucher disease.

Biography

Khitab Gul has an academic background of MSc in Biotechnology from University of Karachi, Pakistan. He has obtained his PhD degree in Molecular Biology from University of the Punjab, Lahore. In his doctoral work, he found pathogenic mutations of gene associated with hearing impairment. After completion of his doctorate, he went to USA for Post-doctorate at University of Cincinnati to gain further expertise in his field. He has 02 research publications to his credit with an overall impact factor of 9.718. His recent research interests include investigation of genetic aspects of hearing impairment, vision impairment, infertility and rare genetic diseases in Pakistani population.

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