Genotype phenotype relationship in Gaucher’s disease in Egypt


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Background: Gaucher’s disease is the most prevalent of the genetic lysosomal storage disorders. It is an autosomal recessive disease which was described by French physician Philippe Gaucher in 1882. It is caused by sever deficiency of glucocerebrosidase enzymatic activity with resultant accumulation of large quantities of glycolipid, glucocerebrosidase within the lysosomes of the phagocytic cells of the monocytes-macrophage system. Gaucher’s disease is classified into three conventional types; type I: Chronic non-neuropathic form which usually found in adult especially in Jewish population, type II: infantile neuropathic form which always appears by 1 month of age as a rapidly progressive neurological affection, and type III: Juvenile sub-acute neuropathic with slowly progressive neurological disease that begins during child-hood or adolescence. The aim of this study is to investigate the genotypes of Gaucher’s disease, the most prevalent mutation in Egypt and to assess if a genotype-phenotype relationship could be elicited.

Patients and Methods: The present study included 71 Gaucher’s disease documented patients; they were 38 males and 33 females. Their ages ranged from 6 months to 65 years with of a mean of 4.37 and median of 3 years. All patients were subjected to clinical evaluation, revision of their filed clinical progress, radiological and laboratory data including full blood count, b-Glucocerebrosidase enzyme assay, liver enzymes, bone marrow and splenic aspirate. In addition, we studied the most common GBA mutations using strip assay which based on the reversed-hybridization principle. The assay covered ^ of the most frequent GBA mutations: ^GG (^277G), IVS^1^+^1 (^277G>A), N^1^V^2^S (^1^V^2^A>G), V^7^T^8^E (^7^T^8^G>T), L^1^T^2^P (^1^T^2^A>T>C), R^7^S^8^G (^7^S^8^G>A) and ^ recombinant alleles (RecNcil, Rec TL).

Results: Neither the age of patients, age of onset of the disease nor the sex showed significant relation with homozygosity Vs double heterozygosity or the different genotype groups. The most common mutations found in this study were L^1^T^2^P/L^1^T^2^P (homozygous) and L^1^T^2^P/IVS^1^+^1 (double heterozygous); ^ patients each (4.24%) followed by L^1^T^2^P/D^5^T^6^H (double heterozygous) in ^ patients (4.24%) whereas N^1^V^2^S/N^1^V^2^S (homozygous) was the least common mutation found in only ^ patient (6.55%).

Allele frequency showed that L^1^T^2^P was found in 70.85% of studied chromosomes, IVS^1^+^1 in 10.82%, D^5^T^6^H in 7.47%, whereas N^1^V^2^S was in only 6.55%. As for family history, ^% of cases had positive consanguinity; with 6.55% of patient parents being first cousins. All homozygous cases showed positive consanguinity (7 cases), where as only 7 cases of 11 of the double heterozygous showed positive consanguinity. Also all patients with the genotypes L^1^T^2^P/L^1^T^2^P and N^1^V^2^S/N^1^V^2^S were from consanguineous parents; ^ of ^ and of ^ respectively. On the other hand, the ^ patients with genotype L^1^T^2^P/D^5^T^6^H had negative consanguinity, while the genotype L^1^T^2^P/IVS^1^+^1 showed ^ of ^ cases with positive consanguinity and only ^ case with negative consanguinity.

Conclusion: The most common mutations found in our study were L^1^T^2^P/L^1^T^2^P homozygous and L^1^T^2^P/IVS^1^+^1 double heterozygous. L^1^T^2^P was the most common allele. Analysis for the most common mutation was the method of choice for identification of Gaucher’s disease carriers. Both age of the patients and onset of the disease had no significant relation with either homozygosity Vs. double heterozygosity or the different genotype groups. Gaucher’s disease occurred with equal frequency in males and females. Patients with homozygous gene mutations tend to have consanguineous parents. Neurological manifestations, growth retardation and chest symptoms were the most common clinical conditions reported in studied cases. None of the previous conditions were significantly associated with certain genotype. No correlation was detected between genotype or homozygosity Vs heterozygosity on one side and either age of patients, age of onset or clinical manifestations on other side.