

Genetic Disorders among Egyptian Population: Experience from Epidemiologic & Molecular Data

Sherifa Ahmed Hamed (M.D.)

Consultant Neurologist, Associate Professor

Department of Neurology & Psychiatry, Assiut University Hospital, Assiut, Egypt.

Epidemiologic studies have characterized the magnitude of genetic disorders among Egyptian communities & emphasized the fact that they are responsible for the major proportions of mortality, morbidity & handicap. Our clinical & molecular studies reported that 11% of birth defects are due to single-gene disorders, 31% are chromosomal in origin & 56% are due to multifactorial etiology. Neuropsychiatric disorders constitute 9.9% of the non-fatal burden of disability in the Egyptian population. The prevalence figures from large-sized epidemiologic studies from Upper Egypt are as follow: 50/1000 for idiopathic nocturnal enuresis, 5.18/1000 for idiopathic/cryptogenic epilepsy, 110/3000 for MCA/MR (multiple congenital anomalies & mental retardation), 11/3000 for inborn errors of metabolism, 3/3000 for Down's syndrome, 1/3000 for Fragile X syndrome, 102.4/100,000 for Parkinson's disease, 21/100,000 for Huntington chorea, 26/100,000 for idiopathic dystonia, 37.5/100,000 for muscular dystrophies & 3.2/100,000 for Friedreich's ataxia. Incidence rates are 3.7-6.96% for neural tube defects. It has been estimated that 1:75 of Egyptians are carriers for the gene of PKU. Several factors are responsible for the high prevalence of genetically determined disorders among Egyptians, which include: high coefficient of inbreeding or consanguineous marriages (~28-60%) which favors expression of complex genotypes, high fertility rate, large family size & rapidly growing population size (~80 millions), The complex & poorly organized health care system, & patchy, selective & inadequate genetic service (WHO & Egypt report 2005-2009). Our epidemiological data emphasize the need to announce collaboration with the international service of HVP. Here, I will present a keynote on the magnitude of the neurogenetic problem in Egypt through demonstrating some epidemiologic statistics of neurogenetic disorders from Upper Egypt together based on clinical & molecular analysis. I will demonstrate our facilities to carry out genetic services together with our obstacles for the high throughput genetic work in the region. I will also express our initial steps to build up a phenotype-genotype database together with our future plans for collaboration with HVP & strengthening up the regional clinical & functional phenotypic data. As an initial step, we will collect & catalogue our mutations for single-gene neurogenetic disorders as **1**) primary muscular dystrophies [Duchenne & Becker muscular dystrophies (DMD/BMD), severe childhood autosomal recessive muscular dystrophy (SCARMD) or sarcoglycanopathies, calpainopathies & other primary muscular dystrophies], **2**) Hereditary Familial Ataxia (as Friedreich's Ataxia and Vitamin E responsive cerebellar ataxia).

Dystrophin gene mutations in Egyptian patients with Duchenne & Becher Muscular Dystrophy

Sherifa Ahmed Hamed (M.D.)

Consultant Neurologist, Associate Professor

Department of Neurology & Psychiatry, Assiut University Hospital, Assiut, Egypt.

Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are allelic disorders caused by mutations within the dystrophin gene. Large variations in the proportion of intragenic deletion in the dystrophin gene have been observed in different populations. Although dystrophin gene deletion was extensively studied all over the world, only few studies were done on Egyptian population. We present the results on the pattern of dystrophin gene mutations among a group of Egyptian population using quantitative multiplex PCR technique. 141 DMD/BMD patients were included in this meta-analysis. The diagnosis was based on detailed clinical assessment, CK level, neurophysiologic study and muscle biopsy. DNA was extracted & multiplex PCR was done for deletion mutation analysis of the dystrophin gene using both Chamberlin & Beggs sets of primers amplifying 18 exons covering the two main dystrophin gene hot spots. DNA from cases with no detectable deletion was analyzed for detection of dystrophin gene duplication using quantitative PCR technique. A percentage of 61.1 deletions were detected & spanning multiple exons. Those deletions were localized in the major hotspot region between exons 44 and 52. The remainder 40% which mainly involved exon 45. 5% of cases had duplications. This study concluded that employment of the 18 exon analysis is cost effective & highly accurate (97%). Comparing these findings with frequencies of other countries, ours fall within the reported ranges. Distribution of deletions in our & other studies was variable & specific ethnic differences do not apparently account for specific deletions.