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Letter to the Editor

Molecular Genetics of Intellectual Disability in Kashmiri Families from Pakistan: An Overview

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Intellectual disability (ID) or cognitive impairment (CI) is a genetically mutated neuro developmental disorder in which neurons are not fully developed [1-2] and synaptic plasticity is also defective [3]. Intellectual disability frequency in percent age is usually 1-3% [4] and1.5 to 2% in Western countries [5]. Disable persons are characterized by deficient in at least two adaptive skills including conceptual, social and practical skills and onset usually occur before18yearofageorless [6-7].This brief review focuses on recent neurological disorder findings and provides a view about its prevalence in Kashmiri families and its relation to disorder based on these findings. ID prevalence is higher in males than females [8-9] and it is mainly due to presence of X specific MR genes and single X chromosome [10]. Generally this disorder showed in the developing nations where consanguineous marriage rate is high, event is less (1-3%) in United States. In current study clinical markers are utilized to decide the hereditary evidence of intellectual disability.ID caused by hereditary variable might be because of the chromosomal peculiarities (such as expansion or erasure of complete chromosome) or monogenic issue connected with sex and autosomal chromosome. Numerous X linked mental retardation genes have been distinguished, however, because of hereditary heterogeneity it is hard to pool smaller families with comparable clinical phenotype that is the reason similarly little data accessible being identified with autosomal gene [11]. Late discoveries assigned the vicinity of substantial number of genes included in autosomal recessive intellectual disability [12]. In recent years the advanced techniques like SNPs microarray and complete genome (CGH) methods are used to recognize mutations in the families having ID. In consanguineous families homozygosity mapping is used to distinguish particular gene in an affected person [13]. By utilizing this method mutation in more than 50 genes have been recognized that lead to autosomal recessive ID in families from Iran, Pakistan and other regions [14].In the current study family (ID-12) was recruited from Azad Jammu and Kashmir showing intellectual disability or learning incapacity and have autosomal recessive mode of inheritance. Affected individuals of ID-12 family were showing mild to severe type of non-syndromic ID with no other clinical appearance. Microsatellite markers were used in genotyping and no linkage was shown by ID-12to any known locus by using the homozygosity mapping technique. It might be possible that any novel gene could be responsible for this phenotype. Current studied family show the involvement of hereditary genes in ID. In the present study locus for non-syndromic ID was characterized and gave persuading proof that a portion of the hidden deformities was not uncommon and it is recommended that whole exome sequencing (WES) should be done to identify the responsible pathogenic variant in known or novel gene responsible for specific phenotype of ID. In Pakistan there is a significant burden of autosomal recessive disorders including non-syndromic intellectual disability. There is a high rate of consanguinity, which is 62.7%, of which 84% marriages are between first cousins [15]. Identification of genetic causes of ID in families may allow genetic counseling and genetic screening to reduce the number of affected individuals born by the marriages among carriers of the same genes. The current study will provide additional sustenance concerning genetic heterogeneity of ID in Pakistan.

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