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Short Communication

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Molecular characterization of families affected with autosomal recessive primary microcephaly

Sarah Sabir

Kinnaird College for Women, Pakistan

Abstract:

Statement of the Problem: Cousin Marriage is very common in part of world and there have been proven association with the degree of consanguineous marriages and prevalence of autosomal recessive genetic disorders. It is reported that 60% of cousin marriages in Pakistan is the subject of prevalence of most rare genetic disorders in our population. Microcephaly which is present at birth and causes non-progressive mental retardation is called autosomal recessive primary microcephaly (MCPH), whereas which develops postnatally is secondary microcephaly. It is a neurogenic mitotic disorder which results in small brain size compared to one third of normal brain. Affected patients have normal neuronal migration, neuronal apoptosis and neuronal function. Sixteen MCPH loci have been reported by different scientist from various populations around the world containing the following genes Microcephalin, WDR62, CDKRAP2, CASC, ASPM, CENPJ, STIL, CEPH135, CEPH152, ZNF335, PHC1, CDK6, CENPE, SAS6, MFSD2A and ANKLE2. Mutations in any one of the gene will lead to disease phenotype due to premature chromosomal condensation, disturbed mitotic spindle orientation, signaling response as a result of DNA damage.

Methodology & Theoretical Orientation: In the current study, the molecular genetics of five families affected with autosomal recessive primary microcephaly from Pakistani origin were studied. By taking the head circumference of the affected individual these families were identified from different cities of Pakistan. Clinical information was collected with the help of a carefully designed questionnaire. Venous blood sample of the affected families was collected and genomic DNA was extracted using standard phenol-chloroform method. Four loci i.e. MCPH5 (ASPM), MCPH2 (WDR62), MCPH1 (Microcephalin) and MCPH6 (CENPJ) were selected for initial screening bring the most prevalent loci reported from Pakistan. Linkage analysis of the affected families was done by Polymerase Chain Reaction (PCR) using specific microsatellite markers flanking the selected gene. 8% native Polyacrylamide Gel (PAGE) was used to identify PCR results.

Conclusion & Significance: Five families affected with autosomal recessive primary microcephaly were mentioned in this study. These families were screened for ASPM, WDR62, CENPJ genes. These families showed no linkage to the initial screening done for the three most prevalent loci reported from this region. Hence, it can be concluded that disease phenotype in these families is apparently not due to mutations in these three genes, however further screening using more markers and mutation screening of these families will give confirmed results. The aim of this study is to elucidate the molecular genetics of this disorder in five affected families. Linkage analysis will be initially done followed by mutations screening of the families linking to any of the known loci. The current project will enable us to offer carrier screening and genetic counseling, which will be our meager contribution towards reducing the prevalence of this disease our parent population. Results: The gel analysis revealed that two of the families are linked with ASPM gene, whereas the rest of three were not found linked with ASPM, WDR62, CENPJ and Microcephalin genes.

Biography:

Sarah Sabir has completed her MPhil (Master in Philosophy) in Biochemistry in 2016 from Kinnaird College, Pakistan. Her research interests are in molecular genetics of various diseases, retrovirus biochemistry, neurodevelopmental disorders, cell division, cell biology and structural biological studies of proteins. She has published her Bachelors research work entitled "Molecular Studies on preproinsulin gene" in Matec web of conference 2016 6th International Conference on Chemistry and Chemical Process, ICCCP 2016. She also did Internship at Chagatai's Lahore lab for six months and worked in the departments of hematology, microbiology, molecular biology and biochemistry and learned about testing of blood samples, streaking and culturing of the samples of blood and urine, doing PCR on HCV samples and performing LFTs and RFTs on various blood samples. Currently she is working as a High School Science Assistant in Lahore American School. She has plans to pursue her PhD in Biochemistry from a well-known institute.