Novel Mutations in Cyclin-Dependent Kinase-Like 5 (CDKL5) Gene in Indian Cases of Rett Syndrome.
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This is the first report from India on the identification of mutations in the CDKL5 gene in children who had presented with atypical Rett syndrome. There were 44 cases presenting with features of atypical Rett syndrome. On screening, 5 children were found to have CDKL5mutations with one child having 2 mutations. All the mutations were substitutions, 3 were novel while 3 were known. Details of these children are presented. Various clinical features are described including delayed milestones, hand stereotypies, hand wringing, clapping and mouthing. Only 4 of the children had seizures and in one child seizures did not start until 8 months of age. One child is described as having a severe degree of mental retardation while another showed a milder phenotype but with global developmental delay. This latter child was also the one without seizures and both children had mutations in exon 21. There was a third child with a mutation in exon 21, who also had a mutation in exon 12, which is described as being silent. The last 2 children had mutations affecting exons 15 and 16. The child with a mutation of exon 15 developed severe gastro-oesophageal reflux and also had changes on an MRI scan of her brain. The authors use an interesting on-line tool, PolyPhen-2, that predicts the effects of a substitution on the structure and function of a human protein. They also assessed the degree of X-inactivation but found no relation between this and the severity of the phenotype.

Note -this is a small study and some of the clinical detail described is a little vague and not presented in a way that allows for easy or adequate comparison with known data from other studies. It is also worth noting that mutations beyond intron 18 may not be clinically significant if you consider the paper by Sarah Williamson et al. However, having said all that, this paper can only help improve the recognition of theCDKL5 disorder around the world, and that can only be good for those children affected.