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Abstract Title:- Clinical, Demographic and Genetic Profile Observed in a Cohort of 18 Indian Children With Rett Syndrome

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Aims:-Rett syndrome (RS) with a prevalence of 1:10,000 female births is a genetic neurodevelopmental disorder seen predominantly in females. In 90-95% of cases, it is caused by mutations in MECP2 gene. It is characterized by regression between 6-18 months of age with loss of acquired skills, speech, stereotypical hand movements, microcephaly, seizures, intellectual disability and autism spectrum disorder (ASD). We present here a case series of clinical, demographic and genetic profile observed in 18 RS cases.

Methods:- Detailed demographic, clinical and investigations data of patient diagnosed with RS were collected from different genetic centers across western India. All samples were analyzed for MECP2 gene mutation.

Results:- The female: male ratio was 15:3. The mean age for females was 4.6 years (1.7-16 years). The mean maternal and paternal age was 27.2 (21-38 years) and 29.7 years (24-40 years) respectively. 2/15 had consanguineous marriage. 8/15 mothers had a history of miscarriages. 7/15 had normal siblings.

The mean birth weight was 2.7 kg (1.58-3.25 kg) and head circumference (n=13/15) was 45.8 cms. Convulsions was reported in 6 females with one child having non-specific periventricular white matter changes on MRI. EEG reported epileptiform discharges in 9/12 females, 5 kids had ongoing convulsions. Developmentally, 4 kids had bruxism, 3 ASD, 2 ataxic gait, 5 mouthing/drooling, 1 toilet trained. 1 each had auricular tag/auricular pit/squint. All females had SNV in MECP2 gene with 14 variants in exon-3, 1 in exon-1 and 3 were novel variants.

3 male children aged 2.5, 2.7 and 13 years had MECP2 mutation. The mean maternal and paternal age (available for 2 families) was 26 and 30 years. One child had similarly affected brother. One child had an episode of convulsions. MRI, EEG and hearing exam was normal in 2 kids. Mean head circumference was 46.3. None were toilet trained. Additional features included recurrent diarrhea, oculogyris and right thumb polydactyly.

Two males had 46,XY and one had 47,XXY karyotype. All 3 had MECP2 gene mutation (2 SNV in exon 3 and 1 CNV). X-linked somatic post-zygotic, X-linked hemizygous and X-linked heterozygous due to the presence of an extra X chromosome was seen in one each.

Conclusions:- Rett syndrome is a complex neurodevelopmental disorder which can present with variable clinical findings and demographic profile. Recent availability of FDA approved medication and improvements in therapy services have raised hope about better prognostic outcomes. It is important to provide access to genetic tests and counselling to parents for long term management and understanding of the prognosis.

Keywords:- Rett syndrome, demographics, genetics