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**Abstract Topic: -** Clinical Genetics

**Abstract Title: -** Genetic underpinning of childhood epilepsy- a single center observational study

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**Aims: -** Childhood epilepsy is a neurological condition with onset of seizures between 3months to 17yrs of life. It is a genetically heterogeneous condition with variable phenotype and age of onset.

Aim: To identify disease causing variants in early onset epilepsy in an Indian pediatric cohort based on whole exome sequencing.

**Methods: -** 100 individuals with seizure onset before 5 years of age were evaluated based on the clinical details, neuroimaging and metabolic testing. Following informed consent a comprehensive genetic evaluation of the patients along with the parents (Trio n=99 +1 duo) were processed for Next-generation sequencing (NGS). The sequencing data was analyzed according to GRch38 and the annotated variants were prioritized based on the clinical features. The significant variants SNvs and CNVs detected were classified as per ACMG 2015 guidelines.

**Results: -** Upon analyzing the trio data, molecular diagnosis was established for 33%. We have detected 45 pathogenic gene variants and 38 variants of uncertain significance matching the clinical presentation of the patient. 6 patients were detected with pathogenic variants in SCN1A, 3 patients with ALDH7A1 and ADGRG1 respectively; 2 patients with DEPDC5 and TSC2 variants. 19% of the variants are de novo in nature. We also detected 63% novel variants which were not previously reported.

**Conclusions: -** Genetics of epilepsy is an evolving field with new gene-phenotype association reported every year. High throughput sequencing data has led to identification of novel variants associated with epilepsy and further studies with larger cohorts will help us to understand the prevalence of these variants.

**Keywords: -** Upon analyzing the trio data, molecular diagnosis was established for 33%. We have detected 45 pathogenic gene variants and 38 variants of uncertain significance matching the clinical presentation of the patient. 6 patients were detected with pathogenic variants in SCN1A, 3 patients with ALDH7A1 and ADGRG1 respectively; 2 patients with DEPDC5 and TSC2 variants. 19% of the variants are de novo in nature. We also detected 63% novel variants which were not previously reported.