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Abstract Topic:- Clinical Genetics

Abstract Title:- Genetic spectrum of inherited neuropathies: a single centre experience

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Aims:-Inherited neuropathies can present as a part of a complex systemic disorder or an isolated peripheral neuropathy. The most common inherited neuropathy – Charcot Marie Tooth Disease has a prevalence of 1 in 2500. Though the overall prevalence of inherited neuropathies is unknown, it is most likely higher due to its variable clinical presentation, making them far more common and often under diagnosed.

Methods:- Clinical details, genetics, examination findings, investigations and functional outcome measures 12 individuals with genetically confirmed neuropathy was collated. Whole exome sequencing was carried out universally. Two individuals who were exome negative underwent whole genome sequencing.

Results:- 2/12 had complex phenotype and genotype for another condition with neuropathy as a feature – SNAP29 mutation associated with Cerebral Dysgenesis Neuropathy Ichthyosis Keratoderma Syndrome and STBNP4 mutation causing neurodevelopmental disorder, neuropathy and hearing impairment. 10/12 had mutations exclusively linked to peripheral neuropathy - SH3TC2, PLEKHG5, CNTNAP1, MFN2, NEFL, JAG1, and GDAP1.

3/10 had a second mutation: SLC6A19 for Hartnup in one, ATP7B for Wilson's disease in another and SMN1 for Spinal Muscular Atrophy in the third. Proband with Hartnup disease was symptomatic whereas the other two were clinically asymptomatic for the second hit. Further, there was a strong history of parental consanguinity or endogamy among these three patients.

Conclusions:- The genetic spectrum of inherited neuropathies is continuously expanding. A genetic diagnosis is crucial due to the high prevalence of parental consanguinity and endogamy in our population. This could enhance our understanding of the underlying disease pathomechanisms to help discover disease modifying strategies in the future.

Keywords:- Genetic spectrum, inherited neuropathies