

## **DBT-NIBMG study to help detect congenital muscular dystrophy better**

New Delhi, Nov 03: More than 70 million persons in India are affected by some rare disease or the other. So far, around 450 rare diseases have been recorded in India of which congenital muscular dystrophy (CMD) and congenital myopathy (CM) are common. The two are part of a group of genetically and clinically heterogeneous degenerative primary muscle disorders, with onset at birth or during infancy.



The group of disorders is characterized by progressive muscle weakness and degeneration, diminished muscle tone, contractures, spinal rigidity and delays in reaching motor milestones. In India, the prevalence of CMD is estimated to be 0.89/100,000.

Clinicians often face a challenge in accurately diagnosing these complex muscle disorders due to the lack of systematic investigation on the inter-connectivity between disease genotype and clinical phenotype. The scenario is further compounded by multifactorial inheritance such as multiple variants, multiple genes as well as epigenetic and environmental factors. In many cases, no mutation is found in known candidates, implying the involvement of unknown causal genes. Fortunately, with the advances in genomic technologies in the past few years, addressing the complexity of the genotype-phenotype relationship has become possible.

A team of researchers at DBT-National Institute of Biomedical Genomics (DBT-NIBMG) has been working to improve the diagnostic rate of CMD and CM in India as well as to identify new disease-causing genes to increase specificity and identify changes in the DNA that may be responsible for the disease phenotype.

In a new work, they sequenced all the protein coding regions of the genes, also called whole exome sequencing (WES), in a cohort of 36 difficult-to-diagnose Indian CM and CMD patients, for whom protein-based analyses and clinical examination were insufficient to enable an accurate diagnosis. They could accurately diagnose 54% patients (n=12/22) in the

CMD group and 35% patients (n=5/14) in the CM group. They found causative mutations in both, previously reported genes and in novel genes.

A vast overlap of disease phenotypes was observed in the cohort and in most of the cases, ancillary investigations such as muscle biopsy, MRI, clinical examination were required to further validate the WES findings and support the diagnosis. Transferring such WES findings to clinical practice will help boost guided clinical care of the patients as well as have informed genetic counselling.

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