The genetically isolated yet heterogeneous and highly consanguineous Indian population has shown a higher prevalence of rare genetic disorders. However, there is a significant socioeconomic burden for genetic testing to be accessible to the general population.

In the current study, we analyzed next-generation sequencing data generated through a focused exome sequencing from individuals with different phenotypic manifestations, referred for genetic testing to achieve a molecular diagnosis and assess the clinical utility of the assay.

**Highlights of Focused Exome Sequencing performed at PKIG:**
- Complete coverage of >99% of the exome, including over 5,400 disease-associated genes
- Reliable detection of intragenic deletions and duplications in clinically relevant genes as well as large-scale CNV events and structural rearrangement events
- Include the analysis of the mitochondrial genome

**RESULTS**

- We reported pathogenic or likely pathogenic variants in 274 out of 779 cases with a diagnostic yield of 35.2%.
- Carrier testing of asymptomatic individuals with a family history of disease through focused exome also achieved diagnostic yield of 36.4% in 39 of 107 cases tested.
- We identified five pathogenic variants in the mitochondrial genome with different degree of heteroplasmy.
- No relevant findings related to reported phenotype were identified in 7.8% of the cases.
- Homozygous variants were found as diagnostic findings in 125 cases owing to the high consanguinity in the Indian population.
- Approximately 5.1% of cases had copy number variations (CNV) ranging from single exon deletion to large copy number with or without a SNV

**CONCLUSION**

- The diagnostic yield achieved through Focused exome sequencing in Indian patients is higher than those reported in patients from Western countries.
- Proprietary bioinformatics pipelines helps in enhanced detection of sequencing variants (SNVs), copy number variants (CNVs) and mitochondrial DNA (mtDNA) in a single assay, making PerkinElmer Genomics' Focused Exome Sequencing one of the most comprehensive testing options available in Indian markets.
- We suggest Focused Exome sequencing test as a good lower-cost alternative for whole exome and whole genome sequencing as a first-tier approach to genetic testing.