Comprehensive genetic testing gives a high diagnostic yield in the Indian sub-continent compared to the western population

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BACKGROUND

- 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

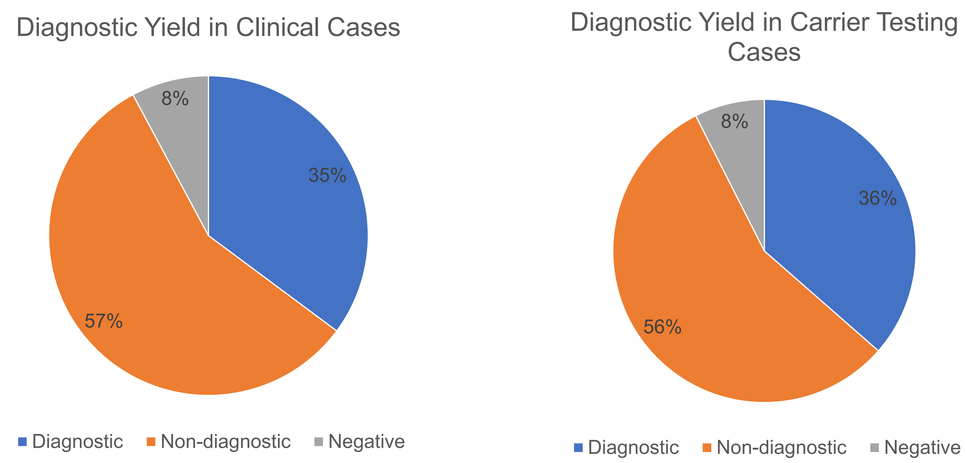

Fig 1: Overall Diagnostic Yield of FOCEX Test

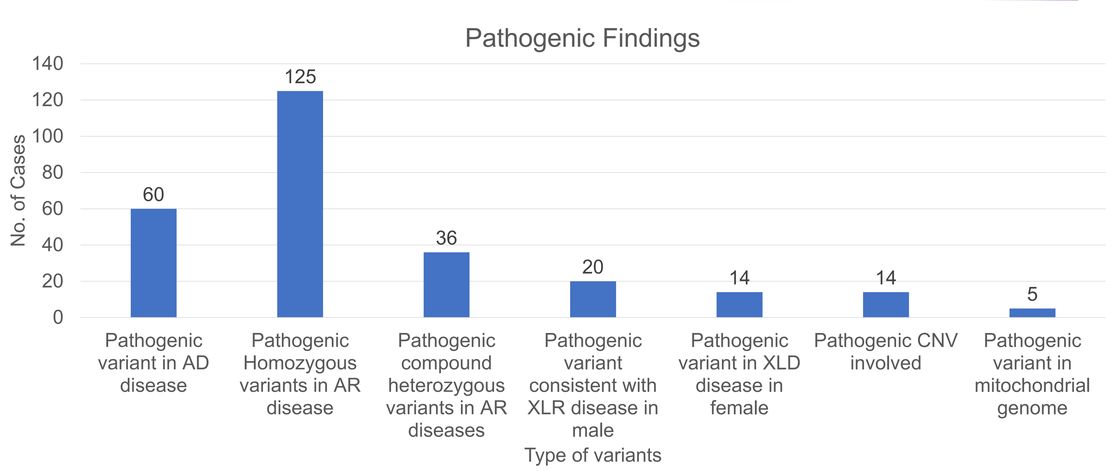

Fig 2: Pathogenic Variants in different types of cases

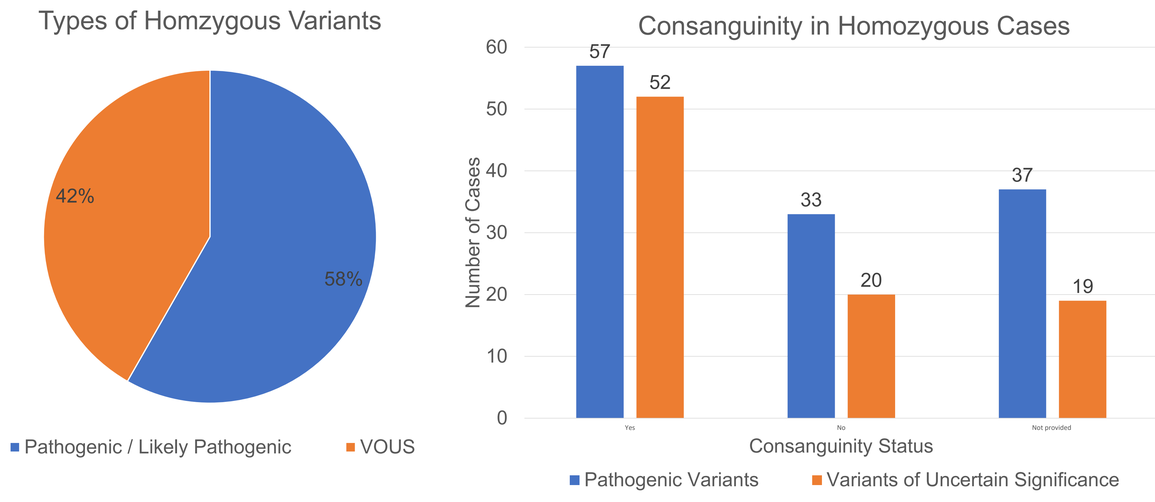

Fig 3: Findings in homozygous cases and consanguinity

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.