# Spectrum of genetically determined movement disorder in Indian Cohort

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## INTRODUCTION

- New nomenclature was proposed in 2016 for genetically determined movement disorders against the system of locus symbols.
- This method utilised causative genes which could be tested with proven genotype-phenotype correlation.
- Phenotype suffix with gene suffix is used. Where more than one phenotype coexist, a double prefix is assigned

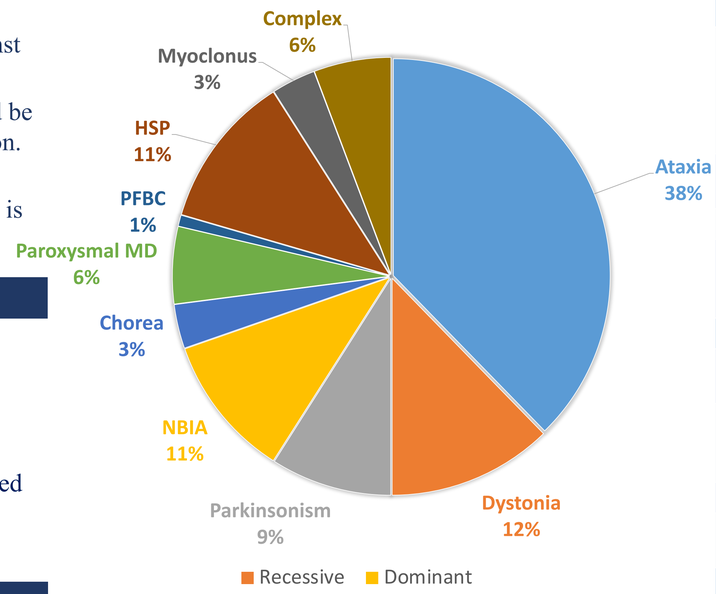
## OBJECTIVES

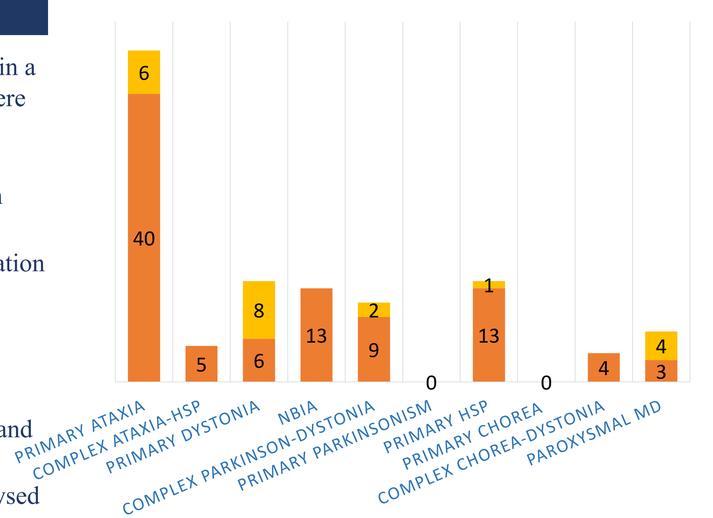
- To determine prevalence of genetic diagnoses in patients with pediatric movement disorders using genetic investigations in this retrospective cohort study
- To identify the common genetic mutations associated with primary movement disorders in Indian population

## METHODS

- All patients with primary movement disorder seen in a single tertiary centre Pediatric Neurology Clinic were reviewed retrospectively.
- We reviewed electronic clinical, neuroimaging, biochemical and molecular genetic features of each patient.
- Genetic investigation included targeted next-generation sequencing and whole exome sequencing. Parental segregation was done whenever required.
- The variants were classified according to ACMG guidelines.
- The genetic testing was done privately by patients and reports were shared with us.
- New nomenclature was applied and data was analysed

## RESULTS




| Movement disorder | Genes |
|---|---|
| **ATAXIA** | |
| Recessive ataxia (n=27) | ATX-ATM (11), ATX-APTX (2), ATX-CC2D2A (2), ATX-HEPACAM (1), ATX-GRM1 (1), ATX-NPC1 (1), ATX-SIL1 (1), ATX-CWF19L1 (1), ATX-SNX14 (1), ATX-MAN2B1 (1), ATX-NPHP1 (1), EXOSC3 (1), EIB25 (1), TCTN2 (1), ATX/MYC-TPP1 (1) |
| Dominant Ataxia (n=2) | SCA-ITPR1 (2) |
| ATX/HSP (n=5) | ATX/HSP-POLR3A (2), ATX/HSP-SACS (2), ATX/HSP-HEXA (1) |
| Genes not yet classified (n=11) | EEF2 (2), ATCAY (2), ACO2 (1), RAB3GAP2 (1), NGLY (1), ELAC2 (1), KCNC3 (1), TRPC3 (1), CREBBP (1) |
| **DYSTONIA/ PARKINSONISM/ NBIA** | |
| Primary Dystonia (n=7) | DYT-SGCE (2), DYT-THAP1 (1), DYT-TUBB4A (1), DYT-KMT2B (1), DYT-DDC (1), DYT-ANO3 (1), DLD (1) |
| Dystonia-Parkinsonism (n=11) | DYT/PARK-TH (3), DYT/PARK-GLB1 (2), DYT/PARK-ATP1A3 (2), DYT/PARK-GCH1 (2), DYT/PARK-SPR (1), DYT/PARK-QDPR (1) |
| NBIA (n=13) | NBIA/DYT-PANK2 (8), NBIA/DYT/PARK-PLA2G6 (5) |
| Genes not yet classified (n=7) | TREX1 (2), SLC18A2 (2), IFIH1 (2), TREX1(1) |
| **HEREDITARY SPASTIC PARAPARESIS** | |
| Recessive (n=11) | HSP-KIAA1840 (4), HSP-ALDH3A2 (1), HSP-C12orf65 (1), HSP-ZFYVE26 (1), HSP-SPG7 (1), HSP-AP4B (1) |
| Dominant (n=1) | HSP-ATL1 (1) |
| not yet classified (n=4) | CYP2U1 (1), TACO1 (1), ALS2 (1), SEPSECS (1) |
| **PAROXYSMAL MOVEMENT DISORDER** | |
| Classified genes (n=5) | PxMD-CACNA1A (4), PxMD-GLDC (1) |
| Genes not yet classified (n=2) | ABAT (2) |
| **PFBC** (n=1) | PFBC-SLC20A2 |
| **Chorea** (n=4) | DYT/CHOR-HPRT (2), DYT/CHOR-GCDH |
| **Myoclonus** (n=4) | MYC-CLN6 (3), ATX/MYC-TPP1 (1) |
| **Complex movement disorders** (n=7) | GNAO1 (3), SYNGAP1 (1), GPAA1 (1), PIGN (1), NACC1 (1) |

## CONCLUSIONS

- Of 178 patients tested, 56 (31%) had no significant gene identified.
- Of 122 (69%) with positive genetic result, the distribution was as shown.
- Ataxia telangiectasia (ATX-ATM) was the most common gene identified.
- Of 11, 9 presented with classical phenotype, 1 patient presented with Dopa-responsive dystonia and 1 patient presented with tremors.
- Of the dystonia genes not yet classified 5/7 patients had genes positive for Aicardi Goutiere's syndrome.
- All the parkinsonism patients presented with complex parkinsonism-dystonia phenotype.
- Given the rapid pace of evolving knowledge and continued genetic research, the new nomenclature provides a comprehensive and uniform method for classification of genetically determined movement disorders.
- **Benefits**: incorporates phenotype and genotype, potential for easy expansion
- **Limitations**: more complicated, cumbersome to use, need for further research

## REFERENCES

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