Exploring the genetic basis of Leukodystrophies through an in-house targeted panel approach in resource-poor settings

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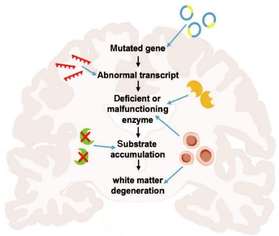
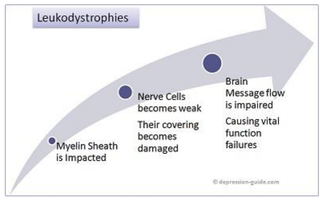
Leukodystrophies

- Genetically determined neurodegenerative disorders that affect predominantly white matter[1]
- Rare disorders: less in numbers but huge impact on families
- Diagnosis: Clinical and radiological[2]
  - Limited confirmation facilities
  - Genetic testing costly
  - Prenatal testing often missed/ignored





Objectives

- To identify genetic variations by NGS technique in children with leukodystrophies

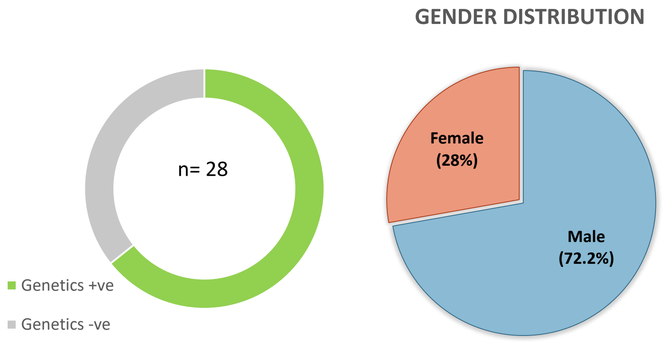
Materials and Methods

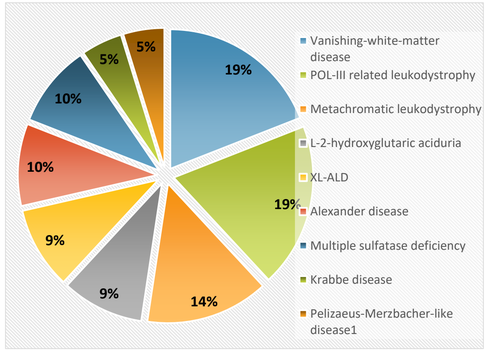
- **Study design:** Cohort study
- **Study population:** 28 children of either sex
- **Study setting:** Pediatric Neurology Clinic
- **Sample type:** peripheral blood

- Detailed evaluation, neurological examination and MRI
- Genetic analysis by an in-house Ion Torrent next-generation sequencing using customised gene panel
- *In-sillico* analysis of mutations

Results

- N=28
- Gender distribution: male 72% (n=13/18), female 28% (n=5/18)
- Mean age at presentation: 7.8 years (range 0.3 - 15 years)
- Common clinical features: developmental delay (100%), increased tone (60%), gait impairment (50%), and seizure (40%)
- Novel mutation: *GFAP gene* variation, c.1187C>T; p.Thr396Ile (Alexander disease)





Results

Predicted amino acid using HOPE software

Threonine to Isoleucine at position 396

Conclusions

- The advent of next-generation sequencing has helped in the early genetic confirmation and prenatal counselling
- Use of in-house targeted genetic panels helps in significant cost reduction and feasibility for patients in resource-poor settings

References

1. Van der Knaap MS, et al. Diagnosis, prognosis, and treatment of leukodystrophies. Lancet Neurol. 2019 Oct;18(10):962-972
2. Gulati S, et al. The spectrum of leukodystrophies in children: Experience at a tertiary care centre from North India. Ann Indian Acad Neurol 2016;19:332-8.

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