# CLINICAL UTILITY OF NEXT GENERATION SEQUENCING IN NEURODEVELOPMENTAL DISORDERS – EXPERIENCE FRO A TERTIARY CARE CENTRE

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## INTRODUCTION

- Neurodevelopmental disorders (NDDs) comprises phenotypically and genotypically heterogenous conditions with onset in the developmental period.
- The advent of next generation sequencing (NGS) techniques has unearthed the genetic landscape of these conditions.
- Hence, this study was planned to identify the clinical utility of NGS in NDDs.

## OBJECTIVES

- To identify the diagnostic utility of NGS in neurodevelopmental disorders.

## METHODOLOGY

- Retrospective observational analysis (June 2017 to May 2021) of children satisfying the DSM V criteria for NDDs attending the Comprehensive Care Centre for Neurodevelopmental Disorders of our Institute on whom NGS was performed.
- Relevant clinical and genetic details of the patients were recorded. American College of Medical Genetics (ACMGE) criteria were used to classify the genetic variants into pathogenic, likely pathogenic(LP) and variants of unknown significance (VOUS).

## RESULTS

- 75 patients were included in the study with median age of 4.2 years (8 months – 16 years) of which 39 patients were males.
- In 15 patients ,NGS was negative

**Genetic Analysis**

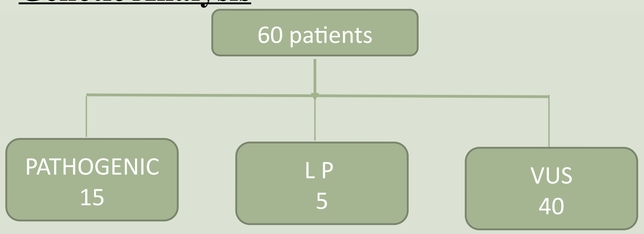



**Table 1: Pathogenic variants in NDD as per ACMG criteria**

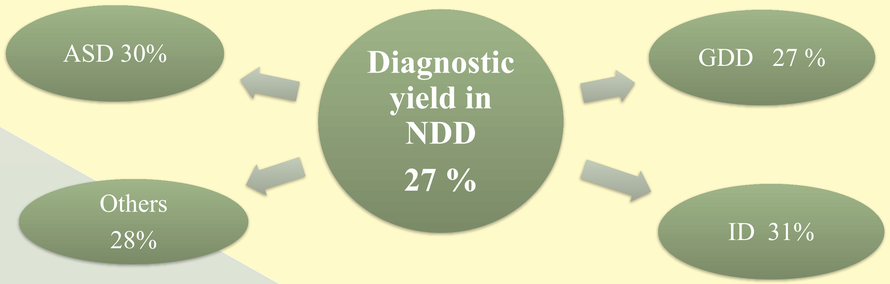
| Patient (Age/Sex) | Gene | Variants | Variant type | Zygosity | OMIM Phenotype |
|---|---|---|---|---|---|
| P1(11/F) | *SMC1A* | c.547C>T | Nonsense | Ht | #301044 |
| P2(5/F) | *MECP2* | c.1197_1222delinsAGC | Indel | Ht | #312750 |
| P3(2/F) | *CDKL5* | c.1842T>A | Nonsense | Ho | #312750 |
| P4(7/F) | *MECP2* | c.1233dup | Indel | Ht | #312750 |
| P5(5/M) | *OCRL* | c.1880-2A>G | Splice site | Hi | #309000 |
| P6(9/F) | *SLC9A1* | c.1147delC | Indel | Ho | #616291 |
| P7(7/F) | 17p11.2 del | | CNV | Ht | #182290 |
| P8(16/M) | *TTC8* | c.515delT | Indel | Ho | #615985 |
| P9 (10m/F) | *ELOVL4* | c.452_455del | Indel | Ho | #614457 |
| P10(2/M) | *GNB5* | c.538A>T | Missense | Ht | #617182 |
| P11(4/M) | *DVL3* | c.655C>T | Missense | Ht | #616894 |
| P12(9/F) | *OPA1* | c.790-2A>C | Splice site | Ho | #210000 |
| P13(11m/F) | *AHI1* | c.1152-1G>C | Splice site | Ho | #608629 |
| P14(4/F) | *MECP2* | c.433C>T | Missense | Ht | #312750 |
| P15(2/F) | *SHANK3* | c.3470_3479del | Indel | Ht | #606232 |

m - month ,CNV –Copy number variant ,Ht – Heterozygous , Hi- Hemizygous , Ho – Homozygous,M-Male , F - Female

**Table2 :Likely pathogenic variants as per ACMG criteria**
[2]

| Patient (Age/Sex) | Gene | Variants | Variant type | Zygosity | OMIM Phenotype |
|---|---|---|---|---|---|
| P16(9/M) | *SCN1A* | c.5252C>T | Missense | Ht | #607208; #604403 |
| P17(6/F) | *SPAST* | c.1496G>A | Missense | Ht | #182601 |
| P189m/F) | *GNAO1* | c.626G>A | Missense | Ht | #617493 |
| P4(1/M) | *ALDH3A2* | c.(798+1_800_1_1207+1_1396)del | CNV | Ho | #270200 |
| P5(11/M) | *NUS1* | c.852T>A | Nonsense | Ht | #617831 |

**Diagnostic Yield**




## CONCLUSION

The diagnostic yield from NGS among NDDs are high and should be considered during their clinical evaluation.

## REFERENCES

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2.Hanly C, Shah H, Au PYB, Murias K. Description of neurodevelopmental phenotypes associated with 10 genetic neurodevelopmental disorders: A scoping review. Clin Genet. 2021 Mar;99(3):335-346.