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Abstract Title:- TRIOBP gene mutation in non-syndromic hearing loss: A compelling case study with a new variant

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Aims:-South Asia countries including India have contributed 28.2% to the global burden of hearing loss. This rise over time reflects the gradual increase in people who have hearing loss due to progressive, acquired, or inherited causes. Because language abilities are still developing in babies and are not abnormal at that time, diagnostic findings for hearing loss are inconclusive; as a result, prevalence estimates for these conditions vary. Given this, an 8-year-old female patient with hearing loss, the first child of consanguineous parents visited the hospital, parents were clinically normal. No past medical history. Therefore, we aimed to determine the underlying genetic cause of her hearing loss.

Methods:- The blood samples of the patient were obtained after informed consent from the parents. The DNA was extracted and subjected to whole genome sequencing to identify a genetic abnormality. Next Generation Sequencing of Genomic DNA of the patient was enriched for the complete coding regions and splice site junctions of genes using a custom bait-capture system. Paired-End Sequencing was performed with 2x100/2x150 chemistry, on an Illumina platform. Reads were assembled and aligned to reference sequences based on NCBI RefSeq transcripts and human genome build GRCh37/UCSC hg19. Data was filtered and analyzed to identify variants of interest and interpreted in the context of a single most damaging, clinically relevant transcript for the report, indicated as a part of variant details. Clinvar, OMIM, UCSC genome browser, etc, predictive tools and disease-specific databases used. Bioinformatics pipeline version: 5.2.2 was used in the present study.

Results:- The result showed a homozygous autosomal recessive missense c.5849C>T(p.Pro1950Leu) variant in exon 16 of the TRIOBP gene. It has not been reported previously as a pathogenic variant nor a benign variant, to our knowledge. The p.Pro1950Leu variant has been reported with an allele frequency of 0.02% in gnomAD Exomes. This variant has not been reported to the ClinVar database. Bi-directional Sanger sequencing assay confirmed the presence of the heterozygous gene mutation in both the parents of the patient.

Conclusions:- A wide range of pathogenic mutations in the TRIOBP gene in families or individuals with severe or profound prelingual hearing loss has been reported. Early diagnosis, intervention, and therapy help children develop more successfully later in life. Neonatal hearing screening overlook children with progressive hearing loss as hearing loss can worsen over time. The new TRIOBP variant found in the present study broadens the range of TRIOBP mutations implicated in hearing loss and can be helpful in the early detection of hearing loss

Keywords:- Hearing loss, TRIOBP gene, congenital hearing loss, mutations, whole genome sequencing