MUTATIONAL SPECTRUM OF THE GJB2 GENE AS THE LEADING GENETIC CAUSE OF NON-SYNDROMIC SENSORINEURAL HEARING LOSS IN CHILDREN

Madrimova A.G. Tashkent State Medical University, Tashkent, Uzbekistan

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Background. Hereditary hearing impairment accounts for 50–60% of all congenital hearing loss cases worldwide, with non-syndromic sensorineural hearing loss (NSSNHL) representing the most prevalent form (70–80%). Mutations in the GJB2 gene encoding Connexin 26 are recognized as the predominant cause of autosomal recessive NSSNHL across European and Central Asian populations. Despite growing international evidence, population-specific mutation frequencies in Uzbekistan remain insufficiently characterized.

Objective. To determine the frequency and spectrum of pathogenic GJB2 variants (c.35delG, c.235delC, c.167delT, c.313_326del14) in children with bilateral NSSNHL and to establish their correlation with audiological phenotype.

Materials and Methods. A total of 120 children aged 2–5 years with confirmed bilateral NSSNHL were enrolled. Molecular genetic analysis was performed using allele-specific Real-Time PCR targeting four GJB2 variants. Audiological assessment included pure-tone audiometry, auditory brainstem response (ABR/ASSR), and tympanometry.

Results. Pathogenic GJB2 genotypes were identified as follows: c.35delG — 23.3% (28/120), c.167delT — 13.3% (16/120), c.235delC — 10.0% (12/120); variant c.313_326del14 was not detected. GJB2-associated cases were predominantly characterized by symmetric bilateral grade IV hearing loss with ABR thresholds exceeding 90 dB in 78% of patients, representing a significantly more severe audiological phenotype compared to cases of perinatal etiology ($p<0.05$).

Conclusion. GJB2 mutations, particularly c.35delG, represent the leading identifiable genetic cause of bilateral NSSNHL in the studied pediatric cohort. Targeted allele-specific Real-Time PCR screening constitutes a cost-effective first-tier diagnostic strategy, enabling early genetic verification without recourse to expensive next-generation sequencing. Implementation of GJB2 screening as part of universal neonatal hearing programs is strongly warranted.