MEDS Basic Medicine (2024)
Clausius Scientific Press, Canada

DOI: 10.23977/medbm.2024.020211
ISSN 2616-2091 Vol. 2 Num. 2

Research on the progress of newborn hearing screening combined with deafness gene testing

Xiaolong Wu[1,a], Yazhen Wu[1,b,*], Jiannan Liu[2,c], Dandan Yang[1,d]

[1]Qinghai University Affiliated Hospital, Qinghai University, Xining City, Qinghai Province, China
[2]Qinghai Maternal and Child Health Hospital, Qinghai University, Xining City, Qinghai Province, China
[a]wuxiaolong45@qq.com, [b]514332846@qq.com, [c]1287336775@qq.com, [d]958503485@qq.com
[*]Corresponding author

Keywords: Newborn; Hearing screening; Deafness gene testing; Newborn hearing combined with genetic screening for deafness

Abstract: Deafness is one of the most common birth defects in newborns, ranking at the top of the five major disabilities. It is essential to perform rapid and precise genetic screening for combined hearing and deafness in newborns immediately after birth. In recent years, due to the rapid advancements in molecular biology technology, research into deafness genes has deepened significantly. Selecting the appropriate genetic tests enhances the detection rate of deafness genes. Choosing suitable intervention strategies can effectively avoid the progression from deafness to muteness. This ensures that children with congenital hearing impairments receive timely and effective interventions and treatments, reducing the incidence of neonatal deafness and enhancing the quality of life for deaf children. This review summarizes the current state of hereditary hearing loss, aiming to offer optimal guidance for advancing combined newborn hearing and genetic screening in clinical practice.

1. Introduction

The most common cause of neonatal deafness is genetic. In clinical practice, universal newborn hearing screening is performed after birth; however, it cannot identify the cause at an early stage. Performing genetic testing for deafness in the neonatal period allows for early detection of carriers, clarification of the molecular causes, and timely, targeted interventions and treatments. This can effectively prevent the onset of deafness and enhance the quality of life for deaf children in later stages. The most common deafness genes in China are GJB2, GJB3, SLC26A4, and mitochondrial 12SrRNA[1]. Genetic testing methods include DNA sequencing, gene chip analysis, polymerase chain reaction (PCR) with flow-through hybridization, matrix-assisted laser desorption ionization time-of-flight mass spectrometry, multiplex displacement amplification and single nucleotide polymorphism (SNP) typing, denaturing high-performance liquid chromatography, and high-throughput sequencing (NGS)[2]. All these methods are applicable for deafness gene testing. This article reviews the current state of congenital hearing impairment, aiming to offer optimal guidance for the clinical advancement of combined neonatal hearing and deafness gene screening.

2. Background and significance

The implementation of newborn hearing screening gradually began in China in the late 1990s and has been progressively improved and promoted over the following years. After years of effort, significant progress has been made, and newborn hearing screening is now widely conducted across the country. In 2004, the Ministry of Health issued the "Technical Specifications for Newborn Hearing Screening," which was revised by an expert group in 2010. It explicitly requires that all newborns who do not pass the screening should undergo comprehensive audiological and medical evaluations within three months of birth. Infants diagnosed with permanent hearing loss should receive intervention treatment as soon as possible within six months to maximize their auditory and speech communication abilities and cognitive development[3].

Newborn hearing screening is an important clinical method for diagnosing hearing loss and has shown significant clinical effectiveness. However, its effectiveness in diagnosing drug-induced and delayed-onset hearing loss is relatively poor. At present, scholars suggest that combining hearing screening with genetic testing for deafness can effectively prevent the occurrence and development of hearing loss and improve prognosis. In 2007, Qiuju Wang[4] and her team first proposed the concept of "combined newborn hearing and deafness gene screening" in China, which has since been gradually carried out nationwide. Beijing took the lead in 2012, and now many provinces and cities across the country, including Chengdu, Dalian, Suzhou, Shenyang, Zhengzhou, Changsha, Jinan, Nanjing, Tianjin, and Wuhan[5], have implemented combined newborn hearing and deafness gene screening. Quality control systems for this combined screening are gradually being established nationwide.

With the development of the combined newborn hearing and deafness gene screening system, many newborns with hearing loss are being detected within a few weeks after birth, significantly the diagnosis age to 2-3 months. Early diagnosis and intervention can significantly improve their language and developmental outcomes. Although the incidence of hearing loss in children is lower than in adults, the consequences are more severe. If unaddressed, hearing loss in children can affect their speech development, reading abilities, and academic performance, further impacting their cognitive abilities and social development. Early identification and timely intervention can reduce adverse outcomes.

In 2019, Professor Qiuju Wang[6] and her research team followed up with 1.2 million newborns who had completed genetic screening in China. The results showed that combined newborn hearing and genetic screening significantly reduced the incidence of hearing loss. A study by Shihao Zhou[7] and others on 152,676 newborns in Changsha, which included testing for four or more deafness-related genes, found a mutation carrier rate of 4.57%, with 438 newborns (0.29%) having a risk of drug-induced hearing loss that could not be detected by hearing screening alone. Therefore, combined newborn hearing and deafness gene screening is of great significance.

3. Overview

3.1. Etiology and classification

Congenital deafness refers to hearing loss caused by abnormal maternal pregnancy, abnormal delivery processes, or genetic factors, and it can be categorized into two major types: genetic and non-genetic. The causes of hearing loss include various environmental factors such as infections and ototoxic medications. However, in developed countries, genetic factors account for 50%-60% of hearing loss in children[8]. Genetic hearing loss can be further divided into syndromic hearing loss (SHL) and non-syndromic hearing loss (NSHL), with NSHL accounting for approximately 70%[9]. In terms of inheritance patterns, genetic hearing loss can be classified into autosomal

dominant, autosomal recessive, X-linked, and mitochondrial maternal inheritance[10]. NSHL is more commonly associated with autosomal recessive inheritance.

3.2. Epidemiology

According to reports, the prevalence of congenital deafness in newborns is about 1.8/1000, increasing to approximately 2.7/1000 by age five, and reaching around 3.5/1000 during adolescence[11]. Based on 2024 statistics from the World Health Organization, over 5% of the global population (approximately 430 million people) have hearing disabilities. It is estimated that by 2050, more than 700 million people, or one-tenth of the global population, will experience disabling hearing loss[12]. Epidemiological studies suggest that the majority of nonsyndromic hearing loss (NSHL) cases are monogenic, with the primary causes in China being mutations in the genes GJB2, GJB3, SLC26A4, and mitochondrial 12SrRNA[1]. Therefore, genetic testing for hearing loss in newborns can determine if they carry deafness-related genes, which can inform the need for early intervention to ensure children do not miss the optimal period for language learning. Combining newborn hearing screening with genetic screening for deafness can complement each other and significantly improve the early detection rate of-risk factors for hearing loss., the World Health Organization advocates for early diagnosis and detection of the disease, as timely intervention can reduce the risk of hearing loss[12]. According to the "Technical Specifications for Newborn Screening" and the "Specifications for Genetic Screening of Hereditary Deafness," it is recommended that all newborns undergo combined hearing and genetic screening for deafness within three days of birth[13].

3.3. High risk factors

The high-risk factors for hearing loss primarily include[3.14]:

1) Neonatal intensive care unit (NICU) stay of more than 5 days;
2) Family history of hereditary childhood hearing loss;
3) Intrauterine infections caused by cytomegalovirus, rubella virus, herpes virus, syphilis, toxoplasmosis, etc.;
4) Viral or bacterial meningitis;
5) Neonatal asphyxia (e.g., Apgar score of ≤7 at 1 minute or 5 minutes, accompanied by umbilical artery blood gas pH <7.2);
6) Neonatal respiratory distress syndrome;
7) Mechanical ventilation;
8) Extracorporeal membrane oxygenation (ECMO);
9) Neonatal hyperbilirubinemia requiring exchange transfusion;
10) Maternal use of ototoxic drugs or loop diuretics during pregnancy, or substance abuse and alcohol consumption;
11) Extremely low birth weight infants;
12) Craniofacial anomalies (e.g., malformations of the auricle or ear canal, cleft lip, cleft palate, etc.).

4. Main research methods

4.1. Newborn hearing screening

The commonly used method for newborn hearing screening is Otoacoustic Emission (OAE)[15]. OAE is a series of distortion signals generated when the cochlea is simultaneously stimulated by

two initial pure tones with a certain frequency ratio, due to the nonlinear modulation effect of the basilar membrane. These signals are transmitted to the external ear canal through the ossicular chain and tympanic membrane, and the audio energy is recorded. However, OAE cannot reflect the condition of the auditory neural pathway beyond the cochlea, so it should be combined with the Auditory Brainstem Response (ABR). ABR is another rapid detection method for evoked potentials, using a specialized probe for quick newborn hearing screening. It can detect not only conductive hearing loss but also post-cochlear lesions, and ABR has higher specificity[16]. The degree of hearing loss in infants is mainly assessed through ABR, which represents the current clinical gold standard[17]. Combining both methods can more effectively reduce the rate of missed diagnoses. The combination of OAE and ABR leverages each other's strengths to comprehensively reflect the physiological functions and pathological phenomena of the auditory pathway from the cochlea to the brainstem[18]. Yangping Zhuang[16] and teams reported that in newborn hearing screening, the combined use of OAE and ABR has higher value compared to using either method alone, thereby improving screening accuracy.

4.2. Genetic testing methods

Currently, commonly used gene detection methods include DNA sequencing technology, gene chip technology, high-throughput gene genotyping detection technology, PCR + flow-through hybridization technology, and matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS)[2]. The first three are often used for hearing loss gene detection. Gene chip technology, introduced in 1995, is widely used in clinical applications for hearing loss gene detection due to its high throughput, relatively simple operation, and easy interpretation of results[18]. Next-generation sequencing (NGS), introduced in 2005, offers extensive detection capabilities for known genes and the ability to identify unknown genes, thereby providing effective assistance for early diagnosis. Sanger sequencing, known for its high accuracy, is considered the gold standard for gene diagnosis. However, due to its low throughput, time-consuming process, and high cost, it is not routinely used and is only employed for further validation of homozygous mutations and abnormal mutations (where both normal and mutant points are not colored). Sanger sequencing is commonly used for gene mutations at specific sites[2]. Gene chip technology is often used for large-scale population screening and multi-gene mutation detection[18]. High-throughput sequencing technology is commonly used for detecting rare hearing loss gene mutations and single-gene heterozygous mutation patients[19].

5. Common deafness genes in China

5.1. GJB2 gene

With the progress of extensive research, the most common deafness susceptibility genes in China have been identified[1]. Among the deafness susceptibility genes in China, the highest detection rate is for the GJB2 gene. The GJB2 gene, located on chromosome 13 at 13q11-q12, is primarily inherited in an autosomal recessive pattern, with the gene locus designated as DFNB1. The GJB2 gene encodes the protein Gap Junction Protein 26 (Connexin 26, Cx26), which is mainly expressed in the non-sensory epithelial cells and connective tissue cells of the cochlea. The Cx26 protein forms intercellular channels on the surface of adjacent cells and is involved in the potassium ion cycle from hair cells to the stria vascularis. It is responsible for regulating the lymph fluid that flows back into the cochlea from the inner ear hair cells. Through these channels, potassium ions are pumped back into the cochlear endolymph, thereby maintaining the endolymphatic potential of the cochlea and sensing incoming sounds. Mutations in the GJB2 gene result in disturbances of inner

ear electrolyte balance and retention of metabolic by-products, leading to apoptosis of hair cells. The c.235delC mutation in GJB2 is a common mutation site causing Sensorineural Hearing Loss (SHL) and is associated with autosomal recessive Non-Syndromic Hearing Loss (NSHL) and auditory neuropathy spectrum disorders[20-21]. Research by Guo Xuehong[22] and others has found that the GJB2 gene is a pathogenic factor associated with congenital deafness or severe-to-profound sensorineural hearing loss, and it is also the first hereditary deafness gene to be cloned and identified in humans. Dai Pu[23] and others discovered that the proportion of NSHL caused by GJB2 gene mutations in different regions of China ranges from 4% to 30%, with c.235delC being the main mutation site, having a mutation rate of 13% to 21%, followed by the c.299-300delAT mutation. Research by Wang Leilei[24] and others showed that the detection rate of GJB2 gene mutations in 117 non-syndromic deaf patients was 21%; therefore, it is believed that the synergistic effect of the compound heterozygous mutations c.235delC + c.299-300delAT is the pathogenic gene mutation causing deafness in patients.

5.2. SLC26A4 gene

The SLC26A4 gene is the second most common gene associated with hearing loss susceptibility. This gene is located on chromosome 7 at position 7q31 and follows an autosomal recessive inheritance pattern, with its locus designated as DFNB4. The SLC26A4 gene encodes the Pendrin protein, and is therefore also known as the PDS gene. Pendrin protein is widely expressed in the thyroid gland, kidneys, and inner ear. In the inner ear, it is primarily expressed in the endolymphatic duct, endolymphatic sac, saccule, and macula. Its main function is anion transport. Mutations in the SLC26A4 gene primarily cause NSHL (non-syndromic hearing loss) and Pendred syndrome, which is characterized by hearing loss and thyroid goiter. Both conditions manifest as bilateral sensorineural hearing loss and inner earformations, but these are rarely detected in newborns because thyroid function is normal at birth. Most children with Pendred syndrome do not develop goiter until around age 20, making early diagnosis challenging. Chinese patients with large vestibular aqueduct syndrome (LVAS) have a higher mutation rate at the c.919-2 site of the SLC26A4 gene[25]. The vestibular aqueduct is a bony channel that connects the cochlea to the cerebrospinal fluid in the posterior cranial fossa. It helps maintain the metabolic environment balance by allowing unidirectional flow of endolymph within the endolymphatic duct, essential for the metabolic homeostasis of inner ear hair cells (auditory cells). An enlarged vestibular aqueduct leads to an enlarged endolymphatic, causing endolymph reflux, disrupting the metabolic environment of hair cells, and resulting in sensorineural hearing loss due to toxic damage to the hair cells. The molecular mechanism for the enlargement of the endolymphatic duct may involve impaired absorption of sodium ions, chloride ions, and water by the endolymphatic sac during development. LVAS is the most common inner ear malformation in newborns. Most children with LVAS do not show symptoms at birth but develop hearing loss due to triggers such as colds, fevers, high decibel exposure, or head trauma, commonly referred to as "sudden slap-induced deafness." Liu Licui[26] et al. analyzed the audiological phenotypes and deafness gene mutation characteristics in 558 children with NSHL, finding that SLC26A4 gene mutations were detected in 22.2% of patients with severe hearing loss and 14.8% of those with profound hearing loss. Huang Lihui[27] et al. studied 18 children (36 ears) with hearing loss caused by SLC26A4 gene mutations, finding that 50.00% had profound hearing loss and 36.11% had severe hearing loss. Therefore, hearing loss in children with SLC26A4 gene mutations is predominantly severe to profound.

5.3. Mitochondrial DNA genes

The earliest discovered mutation site in mitochondrial DNA (Mitochondrial DeoxyriboNucleic

Acid, mtDNA) related to hereditary deafness is the A1555G mutation. mtDNA mutations primarily occur in the 12SrRNA gene and tRNASer gene[28]. The mechanism of deafness may be due to the A1555G mutation in the 12SrRNA of mtDNA, which affects the normal synthesis of ribosomal proteins and the production of adenosine triphosphate. The A1555G mutation causes ribosomes to resemble bacterial ribosomes, making individuals with the 12SrRNA-A1555G mutation more susceptible to damage by aminoglycoside antibiotics. This impacts the function of inner hair cells and the organ of Corti, leading to hearing loss after using aminoglycoside antibiotics. Even minimal or therapeutic doses of aminoglycoside drugs can induce tinnitus or more severe hearing damage. This constitutes a significant molecular basis for hearing loss induced by aminoglycoside antibiotics[22]. The 12SrRNA-A1555G mutation is characterized by maternal inheritance and a mitochondrial disease threshold effect[29]. The higher the proportion of mutant mtDNA, the more significant the hearing loss. Changes in the quality and quantity of mtDNA are crucial factors in determining clinical phenotypes. Some other variations may significantly increase the response and sensitivity to drug toxicity, leading to NSHL. The prevalence of hearing loss following aminoglycoside treatment is estimated to be between 2%-25%[30]. Therefore, genetic testing for deafness can effectively reduce the incidence of hearing loss induced by aminoglycoside antibiotics.

5.4. GJB3 gene

Professor Xia Jiahui first discovered the mutation of the GJB3 gene related to hearing loss in 1998[31]. The GJB3 gene is located on autosome 1p33-p35 and encodes the translated protein Connexin31 (Cx31). Genetic hearing impairment types within this gene can result in both autosomal recessive and autosomal dominant inheritance patterns[32], primarily manifesting as acquired high-frequency hearing loss. Mutations in the GJB3 gene can cause NSHL (Non-Syndromic Hearing Loss). The 538C>T mutation directly leads to a sudden termination of coding at the 180-base connection. The corresponding protein expression is located at the second transmembrane region of the gap junction protein, which is a critical area forming the voltage-gated channel. This gene mutation at the site is likely to directly reduce the permeability of the gated channel. Guoxue Hong[22] et al. found that the pathogenic mutation sites 538C>T and 547G>A of the GJB3 gene are closely related to acquired high-frequency sensorineural hearing loss.

6. Intervention

The primary goal of hearing loss treatment is to restore or partially restore lost hearing. Treatment for hearing loss begins with ruling out any underlying primary diseases, followed by methods such as drug therapy. In the acute phase (within 14 days) of pediatric hearing loss, administering glucocorticoids promptly is effective. If systemic treatment fails to significantly improve the condition, hearing aids become necessary. Cochlear implantation is also an effective treatment, with surgery ideally performed before the age of 6 to maximize outcomes. Cochlear implants are specifically designed for patients with sensorineural hearing loss and, when combined with speech training, can help improve language functions to some extent.

However, the most ideal treatment for hereditary deafness is gene therapy, which involves compensating for defective genes with normal ones. The basic principle is to correct or replace the gene mutations causing deafness using gene editing, gene replacement, and other techniques, thereby fundamentally restoring or improving hearing in a single intervention. Recently, Professor Shu Yilai and his research team at Fudan University employed the gene therapy "RRG-003" to permanently restore hearing in children with congenital deafness caused by OTOF (Otoferlin) gene mutations leading to otoferlin deficiency. This represents a significant advancement in gene therapy. Continuous progress in gene therapy offers new hope for treating hearing loss[33].

7. Conclusion

A deaf patient used significant social resources, thereby making early detection and intervention crucial to minimize such waste. As gene sequencing costs decline, genetic testing has become more widely adopted in clinical practice. Early genetic screening can significantly reduce costs associated with deafness, which is of great significance to society. Prospective studies conducted across various provinces and cities in China have demonstrated that this integrated approach can promptly identify newborns with hearing abnormalities, enabling early intervention and the prevention of birth defects. Therefore, it is crucial to vigorously promote combined hearing and deafness gene screening in clinical practice, enhance genetic counseling, and ensure regular follow-up. This approach ensures that infants carrying deafness genes receive early and effective prevention and intervention, and provides scientific guidance for marriage and childbearing to prevent the occurrence of deafness-related birth defects.

References

[1] Expert Consensus on Genetic Variation Screening Technology for Hereditary Deafness "Expert Group, Inter laboratory Quality Evaluation Expert Committee for Prenatal Screening and Diagnosis Laboratory of Clinical Laboratory Center of National Health Commission, Inter laboratory Quality Evaluation Expert Committee for Neonatal Genetic Metabolic Disease Screening Laboratory of Clinical Laboratory Center of National Health Commission Expert consensus on genetic mutation screening technology for hereditary hearing loss [J]. Chinese Journal of Medical Genetics, 2019(03):195-198.

[2] Yuan Yongyi, Dai Pu. Discussion on Standardized Screening and Diagnosis of Hereditary Deafness [J]. Chinese Journal of Otology, 2019, 17(05):611-615.

[3] National Health and Family Planning Commission Newborn Disease Screening Hearing Diagnosis and Treatment Group. Guidelines for Diagnosis and Intervention of Hearing Loss in Infants and Young Children [J]. Chinese Journal of Otolaryngology Head and Neck Surgery, 2018, 53(3):181-188.

[4] Wang Qiuju, Zhao Yali, Lan Lan, et al. Implementation Plan and Strategy of Gene Screening for Neonatal Deafness [J]. Chinese Journal of Otolaryngology Head and Neck Surgery, 2007, 42(11):809-813.

[5] Zhang Jiao, Wang Dayong, Han Bing, et al. A systematic review and meta-analysis of combined screening of newborn hearing and genetics [J]. Chinese Journal of Otology, 2020, 18(02):216-224.

[6] Wang Q, Xiang J, Sun J, et al. Nationwide population genetic screening improves outcomes of newborn screening for hearing loss in China. Genet Med. 2019 Oct; 21(10):2231-2238.

[7] Zhou Shihao, Hou Da, Chen Jing, et al. Clinical study on combined screening of hearing and deafness genes in newborns in Changsha area [J]. Chinese Journal of Otology, 2023, 21(03):307-314.

[8] Bi Q, Huang S, Wang H, et al. Preimplantation genetic testing for hereditary hearing loss in Chinese population. J Assist Reprod Genet. 2023 Jul;40(7):1721-1732.

[9] Garc á-Garc á G, Berzal-Serrano A, Garc á-D áz P, et al. Improving the Management of Patients with Hearing Loss by the Implementation of an NGS Panel in Clinical Practice. Genes (Basel). 2020 Dec 7; 11(12):1467.

[10] Sheffield AM, Smith RJH. The Epidemiology of Deafness. Cold Spring Harb Perspect Med. 2019 Sep 3; 9(9): a033258.

[11] Neumann K, Chadha S, Tavartkiladze G, Bu X, White KR. Newborn and Infant Hearing Screening Facing Globally Growing Numbers of People Suffering from Disabling Hearing Loss. Int J Neonatal Screen. 2019 Jan 18; 5(1):7.

[12] Deafness and hearing loss. World Health Organization. Page publishing date: February, 2024.Reference date: August, 2024.https://www.who.int/news-room/fact-sheets/detail/deafness-and-hearing-loss.

[13] China Deafness Gene Screening and Diagnosis Clinical Multi Center Research Collaboration Group, National Technical Guidance Group for Prevention and Treatment of Deafness Genetic screening standards for hereditary hearing loss [J] Chinese Journal of Medicine, 2021, 101(2):97-102.

[14] Hardani AK, Goodarzi E, Delphi M, Badfar G. Prevalence and Risk Factors for Hearing Loss in Neonates Admitted to the Neonatal Intensive Care Unit: A Hospital Study. Cureus. 2020 Oct 27; 12(10):e11207.

[15] Zhuang Yangping. The impact of different screening techniques on the effectiveness of newborn hearing screening [J]. Chinese Medical Guidelines, 2023, 21(11):45-48.

[16] Wroblewska-Seniuk KE, Dabrowski P, Szyfter W, Mazela J. Universal newborn hearing screening: methods and results, obstacles, and benefits. Pediatr Res. 2017 Mar; 81(3):415-422.

[17] Wen Cheng, Huang Lihui, Wang Xianlei, Zhao Xuelei, Deng Kui, Li Xiaohong, etc. Meta analysis of the efficacy of OAE and AABR in detecting hearing loss in neonatal hearing screening [J]. Journal of Audiology and Speech Disorders, 2020, 28(2): 201-206.
[18] Han GY, Xu Z, Li QS, et al. Detection of hereditary hearing loss gene by DNA microarray. Eur Rev Med Pharmacol Sci. 2017 Aug; 21(16):3538-3542.
[19] Wang Cuicui, Yuan Huijun. Application and research progress of high-throughput sequencing technology in genetic hearing loss research [J]. Genetics, 2017, 39(03):208-219.
[20] Lin YF, Lin HC, Tsai CL, Hsu YC. GJB2 mutation spectrum in the Taiwanese population and genotype-phenotype comparisons in patients with hearing loss carrying GJB2 c.109G>A and c.235delC mutations. Hear Res. 2022 Jan;413:108135.
[21] Xia H, Huang X, Xu H, et al. GJB2 c.235delC variant associated with autosomal recessive nonsyndromic hearing loss and auditory neuropathy spectrum disorder. Genet Mol Biol. 2019 Jan-Mar; 42(1):48-51.
[22] Guoxue Hong, Zhang Di, Lu Hong. Analysis of Susceptible Gene Mutations for Hereditary Hearing Loss in Newborns in Southwest Guizhou and Its Clinical Significance [J]. Technology and Health, 2023(1):28-31.
[23] Dai Pu, Yu Fei, Han Bing, et al. Study on the distribution and frequency of hotspot mutations in severe sensorineural hearing loss populations in different regions and ethnicities of China [J]. Chinese Journal of Otolaryngology Head and Neck Surgery, 2007, 42(11):804-808.
[24] Wang Leilei, Gu Ying, Yang Shuting, etc. Mutation analysis of 117 non syndromic hearing loss patients [J]. Chinese Journal of Medical Genetics, 2019, 36(2):108-111.
[25] Danilchenko VY, Zytsar MV, Maslova EA, et al. Insight into the Natural History of Pathogenic Variant c.919-2A>G in the SLC26A4 Gene Involved in Hearing Loss: The Evidence for Its Common Origin in Southern Siberia (Russia). Genes (Basel). 2023 Apr 17;14(4):928.
[26] Liu Licui, Wang Xia, Li Yongjing, et al. Analysis of auditory phenotypes and genetic mutations in 558 children with non syndromic hearing impairment [J]. Maternal and Child Health Care in China, 2020, 35(6):1089-1092.
[27] Huang Lihui, Zhao Xuelei, Cheng Xiaohua, etc. Genotyping and Phenotypic Analysis of 850 Newborns with Single Heterozygous SLC26A4 Mutations in Deafness Gene Screening [J]. Chinese Journal of Otorhinolaryngology Head and Neck Surgery, 2023, 58(2):117-125.
[28] Qu Chunyan, Wang Jing, Shen Min et al. Analysis of Hearing Screening and Diagnosis Results of Newborns Carrying mtDNA 12SrRNA Gene Mutation [J]. Journal of Audiology and Speech Diseases, 2022, 30(02):198-199.
[29] Finsterer J. Variant m.1555A>G in MT-RNR1 causes hearing loss and multiorgan mitochondrial disorder. Medicine (Baltimore). 2020 Feb;99(6):e18488.
[30] O'Sullivan ME, Perez A, Lin R, et al. Towards the Prevention of Aminoglycoside-Related Hearing Loss. Front Cell Neurosci. 2017 Oct 18; 11: 325.
[31] Xia JH, Liu CY, Tang BS, et al. Mutations in the gene encoding gap junction protein beta-3 associated with autosomal dominant hearing impairment. Nat Genet. 1998 Dec;20(4):370-373.
[32] Aliazami F, Farhud D, Zarif-Yeganeh M, Salehi S, Hosseinipour A, Sasanfar R, Eslami M. Gjb3 Gene Mutations in Non-Syndromic Hearing Loss of Bloch, Kurd, and Turkmen Ethnicities in Iran. Iran J Public Health. 2020 Nov; 49(11):2128-2135.
[33] Jiang L, Wang D, He Y, Shu Y. Advances in gene therapy hold promise for treating hereditary hearing loss. Mol Ther. 2023 Apr 5; 31(4):934-950.