




MANAGEMENT OF CONGENITAL HEARING LOSS: EARLY INTERVENTION STRATEGIES

MANEJO DA PERDA AUDITIVA CONGÊNITA: ESTRATÉGIAS DE INTERVENÇÃO PRECOCE

MANEJO DE LA PÉRDIDA AUDITIVA CONGÉNITA: ESTRATEGIAS DE INTERVENCIÓN TEMPRANA

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ABSTRACT

Congenital hearing loss affects approximately 1 to 2 per 1,000 live births, with more than 50% of cases presenting a hereditary etiology. Early recognition of these causes, combined with effective neonatal hearing screening through Transient Evoked Otoacoustic Emissions (TEOAE) and Automated Auditory Brainstem Response (AABR), allows not only timely detection of hearing impairment but also etiological characterization, with a direct impact on therapeutic decision-making, functional prognosis, and family counseling. In this context, advances in molecular genetics and the development of gene therapies have emerged as promising perspectives for the future treatment of monogenic forms of congenital hearing loss (Mey et al., 2025; Lieu et al., 2020; Taylor et al., 2021). Without appropriate treatment, congenital hearing loss can lead to deficits in the development of communication, behavior, and intellect (Lieu et al., 2020; Zhang et al., 2025). Considering this, the identification of congenital hearing loss through Transient Evoked Otoacoustic Emissions (TEOAE) and Automated Auditory Brainstem Response (AABR) in neonatal hearing screening programs is crucial to initiate early rehabilitation with hearing aids or cochlear implants (Mey et al., 2025).

Keywords: Congenital Hearing Loss. Congenital CMV Infection. Neonatal Screening.

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RESUMO

A perda auditiva congênita acomete aproximadamente 1 a 2 a cada 1.000 nascidos vivos, sendo mais de 50% dos casos aqueles que apresentam etiologia hereditária. O reconhecimento precoce dessas causas, aliado à triagem auditiva neonatal eficaz por meio de Emissões Otoacústicas Evocadas e da Resposta Auditiva Automática do Tronco Encefálico, permite não apenas a detecção oportuna da deficiência auditiva, mas também a caracterização etiológica, com impacto direto na escolha terapêutica, no prognóstico funcional e no aconselhamento familiar. Nesse contexto, os avanços em genética molecular e o desenvolvimento de terapias gênicas despontam como perspectivas promissoras para o tratamento futuro de formas monogênicas de perda auditiva congênita. (Mey et al., 2025; Lieu et al., 2020; Taylor et al., 2021). Sem o tratamento necessário, a perda auditiva congênita é capaz de causar déficits no desenvolvimento da comunicação, do comportamento e do intelecto. (Lieu et al., 2020; Zhang et al., 2025) Considerando isso, a identificação da perda auditiva congênita por meio de Emissões Otoacústicas Evocadas Transientes (TEO) e Resposta Auditiva Automática do Tronco Encefálico (AABR) em programas de triagem auditiva neonatal é crucial para iniciar a reabilitação precoce com aparelhos auditivos ou implantes cocleares (Mey et al., 2025).

Palavras-chave: Perda Auditiva Congênita. Infecção Congênita por CMV. Triagem Neonatal.

RESUMEN

La pérdida auditiva congénita afecta aproximadamente a 1 a 2 de cada 1.000 nacidos vivos, siendo más del 50% de los casos de etiología hereditaria. El reconocimiento temprano de estas causas, junto con una evaluación eficaz mediante programas de cribado auditivo neonatal a través de Emisiones Otoacústicas Evocadas Transitorias (TEOAE) y la Respuesta Auditiva Automática del Tronco Encefálico (AABR), permite no solo la detección oportuna de la discapacidad auditiva, sino también su caracterización etiológica, con un impacto directo en la elección terapéutica, el pronóstico funcional y el asesoramiento familiar. En este contexto, los avances en genética molecular y el desarrollo de terapias génicas surgen como perspectivas prometedoras para el tratamiento futuro de formas monogénicas de pérdida auditiva congénita (Mey et al., 2025; Lieu et al., 2020; Taylor et al., 2021). Sin el tratamiento adecuado, la pérdida auditiva congénita puede ocasionar déficits en el desarrollo de la comunicación, el comportamiento y el intelecto (Lieu et al., 2020; Zhang et al., 2025). Considerando esto, la identificación de la pérdida auditiva congénita mediante Emisiones Otoacústicas Evocadas Transitorias (TEOAE) y la Respuesta Auditiva Automática del Tronco Encefálico (AABR) en los programas de cribado auditivo neonatal es fundamental para iniciar la rehabilitación temprana con audífonos o implantes cocleares (Mey et al., 2025).

Palabras clave: Pérdida Auditiva Congénita. Infección Congénita por CMV. Cribado Neonatal.



1 INTRODUCTION

Congenital hearing loss represents a clinical and social challenge of great relevance, affecting approximately 1 to 2 per 1,000 live births (Mey et al., 2025). Early identification of this condition is vital, as hearing plays a key role in the development of language, speech, and social integration of the child. The causes of hearing loss at birth are varied, being divided primarily between genetic and infectious etiologies (Mey et al., 2025). Among genetic factors, inherited mutations account for more than 50% of cases, including syndromes such as recurrent deletion 16p11.2, which is associated with motor speech disorders and language delays (Taylor et al., 2021).

The continuous advance in the identification of genes associated with hearing has significantly expanded the spectrum of known genetic etiologies, evidencing the complexity of the mechanisms involved and the clinical heterogeneity observed in these patients. This scenario reinforces the importance of a comprehensive diagnostic approach, capable of integrating clinical, audiological and genetic data from the first months of life. (Mey et al., 2025; Morton & Nance, 2006)

Congenital hearing loss of genetic origin can be divided into non-syndromic, when it occurs in isolation, and syndromic, when associated with other clinical manifestations. Approximately 70% of genetic cases are non-syndromic (Morton; Nance, 2006).

Among the genes most frequently associated with non-syndromic hearing loss is *GJB2*, which is responsible for encoding connexin 26. Mutations in this gene represent one of the main causes of hereditary deafness in several populations (Kelsen et al., 2018). Other relevant genes include *GJB6*, *SLC26A4*, *OTOF*, and *MYO7A*.

In syndromic cases, hearing loss may be part of complex clinical conditions, such as Usher syndrome, Waardenburg syndrome, and Pendred syndrome, each associated with specific genetic mutations and distinct systemic manifestations (Nussbaum; Mcinnes; Willard, 2016).

Among the chromosomal alterations associated with congenital hearing loss and neurodevelopmental disorders, the recurrent deletion 16p11.2 stands out, recognized as one of the most frequent genetic causes of neuropsychiatric conditions. The clinical phenotype is characterized by motor speech disorders, language disorders, motor coordination difficulties, psychiatric conditions, and autism spectrum traits, with significant variability in severity. Although most individuals do not have intellectual disabilities, mild to moderate cognitive deficits and learning difficulties are common, in addition to systemic



manifestations such as early obesity, seizures, and, in some cases, hearing impairment (Taylor et al., 2021; Chung et al., 2021).

Regarding infectious causes, congenital cytomegalovirus (cCMV) stands out as the main viral cause of non-hereditary sensorineural hearing loss (Pesch et al., 2021; Zhang et al., 2025). In addition to cCMV, congenital toxoplasmosis is also a significant etiology, capable of resulting in permanent auditory sequelae if there is no adequate pharmacological management during pregnancy or in the first months of life (Santos et al., 2025). The advent of universal neonatal hearing screening has allowed for a faster diagnosis, enabling therapeutic interventions aimed at minimizing neurodevelopmental damage and optimizing functional prognosis (Mey et al., 2025; Zhang et al., 2025). This study aims to analyze the current diagnostic strategies and therapeutic interventions for the management of congenital hearing loss.

Congenital cytomegalovirus (CMVc) is transmitted to the fetus through maternal blood circulation, the virus crosses the placenta during the period of viremia. After reaching the circulation of the fetus, it spreads to susceptible cells, such as endothelial cells, fibroblasts, and smooth muscle cells. This process usually occurs through direct contact between infected and non-infected cells, and can also occur through free viral particles present in the circulation (Lawrence et al., 2024).

Regarding congenital toxoplasmosis, the risk of placental transmission varies according to the period of pregnancy in which maternal infection by *Toxoplasma gondii* occurs, with the risk being lower in the first trimester and reaching up to 90% risk in the third trimester. However, the manifestations in children usually occur more severely when the infection occurred in the early stages of pregnancy (Bollani et al., 2022).

In addition, advances in molecular genetics and pediatric infectious diseases have expanded the understanding of the mechanisms involved in congenital hearing loss, allowing the identification of alterations associated with genetic mutations and congenital infections, such as cytomegalovirus and toxoplasmosis (Mey et al., 2025; Pesch et al., 2021). The incorporation of genetic tests and expanded neonatal screening protocols favors the etiological and prognostic definition, in addition to enabling early therapeutic interventions capable of reducing the progression of hearing loss and minimizing impacts on child neurodevelopment (Taylor et al., 2021; Chung et al., 2024; Santos et al., 2025).

Thus, recent evidence indicates that the absence of integrated protocols can result in underdiagnosis and delay in the initiation of interventions, compromising the child's



auditory and linguistic development (Mey et al., 2025). From this perspective, the articulation between neonatal auditory screening, directed etiological investigation, and systematic longitudinal follow-up is an essential strategy for reducing functional sequelae and optimizing neurodevelopmental outcomes in childhood (Zhang et al., 2025).

2 METHODOLOGY

The present study is characterized as a narrative literature review, developed with the objective of synthesizing and analyzing the most recent scientific evidence related to the management of congenital hearing loss and its intervention strategies. The search was conducted by searching the PubMed database, using the descriptors "Hearing Loss", "Congenital", "Treatment" and "Diagnosis", duly integrated by the Boolean operators AND and OR, following the standardized terminology of Medical Subject Headings (MeSH). Articles published in the last twenty years, available in full and written in Portuguese or English, which directly addressed the proposed theme, were selected. Studies that did not have a direct relationship with the central theme, duplicate publications, narrative reviews with low methodological rigor, and articles not indexed in the database used were excluded. The selection of studies was carried out in two stages: screening of titles and abstracts, followed by the evaluation of full texts to confirm scientific relevance. The information extracted was organized and presented in a descriptive way.

3 RESULTS AND DISCUSSION

3.1 NEWBORN DIAGNOSIS AND SCREENING

Neonatal hearing screening is the gateway to early intervention. Knowledge of the specific cause of hearing loss, obtained through genetic testing and imaging tests such as Magnetic Resonance Imaging (MRI), is crucial to define prognosis and treatment (Mey et al., 2025). In the case of cCMV, screening often occurs after the ear test has failed, using the dried bloodspot test to confirm viral infection (Chung et al., 2024).

The efficacy of neonatal hearing screening through Evoked Otoacoustic Emissions and Automatic Auditory Brainstem Response goes beyond the early identification of hearing loss, since it enables the subsequent etiological characterization, especially of genetic causes. Defining the molecular basis of hearing loss contributes to functional prognosis and allows for the selection of patients potentially eligible for future targeted



therapies, including gene therapy approaches targeting specific monogenic causes of congenital hearing loss (Mey et al., 2025).

Newborn hearing screening was introduced in Denmark in 2005 to identify congenital hearing loss and initiate timely and correct treatment of this loss, as well as to prevent developmental delays related to hearing loss. Previously, the BOEL («Guided Look After Sound») test was used between seven and nine months of age by the healthcare professional as a hearing screening, but the BOEL test is not specific or sensitive enough to identify hearing loss in children. Currently, the screening methods Transient Evoked Otoacoustic Emissions (TOAE) or Distortion Product Otoacoustic Emissions (DPOAE) and Automatic Auditory Brainstem Response (AAAR-TE) are used to identify congenital hearing loss (Mey et al., 2025).

With regard to the Transient Evoked Otoacoustic Emissions (TOAE) screening method, this test allows the detection of hearing loss by sending a sound stimulus that provokes a response in the hair cells of the cochlea. If the response signal of these cells is adequate, the test will be negative and, if it is different from what is expected, the TOAE test will be positive. Since most hearing loss involves outer hair cells in the cochlea, the test is a quick and effective way to detect moderate and severe hearing loss. Sensitivity and specificity are usually $> 80\%$ for TEOAE (Mey et al., 2025; Lieu et al., 2020).

And in relation to the Brainstem Automatic Auditory Response (AAR-TE) test, it is known that it has greater sensitivity than the test previously presented. It emits sound waves into the ear canal, measuring the neurophysiological response by detecting an action potential that is physiologically generated in the auditory nerve and that travels through the brainstem. This signal is detected with the help of electrodes. Due to its more complete analysis of the auditory pathway, the RAA-TE test allows the detection of damage to both the inner and outer hair cells of the cochlea (Mey et al., 2025).

3.2 INTERVENTIONS IN INFECTIOUS ETIOLOGIES

The management of cCMV has evolved to the use of antivirals in neonates. Oral valganciclovir has been administered to infants with hearing loss and clinically apparent or unapparent infection, demonstrating efficacy in stabilizing or improving hearing in the better ear at long-term follow-ups (Chung et al., 2024; Zhang et al., 2025). However, pharmacological treatment requires safety monitoring due to potential side effects.



Regarding congenital toxoplasmosis, early pharmacological treatment is essential to minimize sensorineural auditory sequelae. The persistence of hearing deficits in some of the treated children suggests the influence of factors such as the virulence of *Toxoplasma gondii*, the parasite load, and, especially, the gestational period in which the maternal infection occurred, with infections in the first trimester being associated with more severe conditions (Santos et al., 2025). Studies indicate that timely drug intervention significantly reduces the risk of permanent damage to the auditory system, reinforcing the need for strict prenatal care protocols (Santos et al., 2025).

Another option for managing congenital hearing loss is the use of hearing devices, such as the Cochlear Implant – it directly stimulates the auditory nerve through electrical signals, in addition to being able to amplify ambient sound and emit it into the ear canal. Studies already indicate that bilateral hearing aids contribute to better cognitive performance when compared to unilateral devices. (Litovsky et al., 2016 ; Lieu et al., 2020). Thus, it is imperative that the use of such technologies be combined with the pharmacological treatment already presented.

Thus, the literature highlights that, in both congenital cytomegalovirus and congenital toxoplasmosis, pharmacological interventions should be understood as part of an integrated approach, which includes systematic auditory screening and longitudinal follow-up (Pesch et al., 2021.). Children exposed to these infections may have late-onset or progressive hearing loss, even after appropriate treatment and normal initial results in neonatal hearing screening, which reinforces the need for continuous audiological monitoring throughout childhood (Pesch et al., 2021; Chung et al., 2024). Thus, the effectiveness of therapies does not depend exclusively on infection control, but also on the ability of health systems to ensure prolonged surveillance and timely access to rehabilitative interventions, with the aim of minimizing impacts on language and communication development (Mey et al., 2025).

3.3 GENETIC AND FUTURE PERSPECTIVES

For hearing loss of genetic origin, current management focuses on hearing aid devices, such as amplification devices and cochlear implants. However, the field of gene therapy is expanding, with promising clinical trials aimed at repairing specific genetic defects in the cochlea, which could transform the treatment of hereditary hearing loss in the near future (Mey et al., 2025). In complex syndromes, such as the 16p11.2 deletion,



the approach should be multidisciplinary, integrating speech therapy and psychiatric support to address the associated speech and coordination disorders (Taylor et al., 2021). In this scenario, the diagnostic accuracy provided by genetic tests is decisive in the therapeutic multidisciplinary intervention. The early molecular identification of the alterations involved favors the effectiveness of treatment strategies and ensures their implementation in a decisive period of neuronal plasticity in childhood, an essential stage for adequate linguistic development and for the full social integration of the child (MEY et al., 2025).

The identification of the gene responsible for congenital hearing loss has not only diagnostic value, but also prognostic and therapeutic value. Different genetic variants are associated with predictable clinical patterns, which allows us to anticipate the progression of the loss and guide the choice between hearing aids and cochlear implants. Mutations in GJB2, for example, usually cause severe congenital deafness with excellent response to cochlear implantation, while deletions in STRC usually course with mild to moderate and stable losses, adequately managed only with amplification. Variants in SLC26A4 are associated with fluctuating and progressive loss, requiring earlier planning for implantation. Thus, genetic testing directly contributes to the individualization of the segment and to the optimization of the timing of interventions (Mey et al., 2025).

The discovery of genetic variants, the significance of which is still unknown, poses a challenge in explaining to parents of children with hearing loss what to expect from the future (Mey et al., 2025).

In the evolutionary scenario of interventional therapies, current evidence indicates a promising contribution of technological innovation associated with gene therapy. Experimental studies in animal models use adeno-associated viral vectors (AAVs), reformulated to cross the plasma membrane of hair cells. The main objective of this strategy is to restore fundamental structural proteins, such as connexin-26, recovering cochlear homeostasis and ensuring the processing of auditory stimuli. (Mey et al., 2025). In this context, the studies demonstrated consistent results related to the partial recovery of auditory functions, evaluated by the auditory potentials of the brainstem (ABR). The efficient transduction of the GJB2 gene, responsible for connexin-26, showed an improvement of 20 to 30 dB in the auditory thresholds of mice. In the morphological context, histological samples also confirmed that the preservation of the cochlear structure and the restoration of intercellular communication by gap-type junctions,



indicating that the ions essential for auditory transduction were reestablished in a balanced way, capable of generating action potential and carrying the necessary information to the central nervous system. Despite the advances and findings identified, the study also highlighted limitations regarding the durability of gene expression, suggesting the need for additional adjustments in clinical application (Wang et al., 2025).

When it comes to deleterious dominant alleles, in which the pathological phenotype manifests itself even in heterozygosis, the therapeutic perspectives shift to genome editing via the CRISPR/Cas9 system. Unlike conventional replacement therapies, this approach uses selective inhibition or targeted silencing of the mutated allele. The main objective is to block the synthesis of cytotoxic proteins beforehand, mitigating the progressive degeneration of the auditory neuroepithelium before irreversible tissue damage to the cochlear structure occurs. (ZHU et al., 2023). Functional trials in the animal models demonstrated that hearing thresholds were preserved over 12 weeks, measured by both ABR and DPOAE, compared to the control group that did not receive the treatment, evidencing its sustained neuroprotective effect (Ding et al., 2021).

At the same time, regenerative medicine has expanded the understanding of the mechanisms of cellular reprogramming of the auditory system. Through the modulation of molecular signals, associated with the control of the expression of transcription factors, such as ATOH1, it is possible to induce the conversion of remaining support cells into functionally active hair cells. This therapy allows the rearrangement of cellular microarchitecture in Corti's organ, reestablishing the integrity of mechanoreceptor transduction, allowing the auditory system to convert mechanical stimuli into neural signaling. In adult animal models, the sensory epithelium was partially regenerated, accompanied by a modest 10-15 dB improvement in auditory thresholds, as assessed by ABR. Despite the less significant benefits compared to other gene therapies, these findings reinforce the potential of this approach in restoring cochlear architecture in advanced stages of auditory degeneration (MCGOVERN et al., 2024).

Among the most promising prospects for the management of congenital hearing loss is gene therapy, which aims to correct or compensate for mutations responsible for hearing dysfunction. Experimental studies in animal models have shown positive results in partial hearing restoration through viral vector-mediated gene transfer (Akil et al., 2019).



In addition, gene editing-based approaches, such as CRISPR-Cas9 technology, have the potential for accurate correction of pathogenic mutations, although they still face challenges related to safety and clinical application (Gao et al., 2018).

Regenerative medicine, including the use of stem cells for the regeneration of hair cells in the cochlea, is also emerging as an area of intense scientific interest. Although it is still in the experimental phase, this strategy may represent a paradigm shift in the treatment of hearing loss (Gelfand; Lentz, 2020).

4 CONCLUSION

Thus, the consolidation of effective neonatal hearing screening programs, associated with systematic genetic investigation, is an essential strategy not only for early rehabilitation intervention, but also for the future incorporation of innovative etiological therapies. Although gene therapies are still in the experimental phase, recent advances suggest the possibility of reducing or even eliminating hearing loss in specific subgroups of patients, highlighting the importance of early etiological diagnosis and appropriate genetic counseling for families, especially in the face of the identification of variants of uncertain clinical significance. (Mey et al., 2025; Taylor et al., 2021)

Congenital hearing loss is of great relevance to public health, as it directly interferes with the development of language, cognition, and social skills during childhood. Among the main non-genetic causes, congenital cytomegalovirus (CMV) infection stands out as the most frequent etiology. Despite this, this condition remains largely underdiagnosed, especially in newborns who do not have evident clinical signs at birth (ZHANG et al., 2025).

One of the greatest challenges in the management of hearing loss associated with congenital CMV is related to its late and often progressive nature. Children who have normal initial neonatal hearing screening may develop hearing impairment throughout the first years of life, which reinforces the need for longitudinal audiological follow-up and continuous surveillance in populations considered at risk (Zhang et al., 2025).

In this context, the early diagnosis of congenital hearing loss becomes decisive for the success of intervention strategies. Evidence indicates that the timely introduction of rehabilitative measures — such as the use of individual sound amplification devices, the indication of cochlear implants, and the early initiation of speech-language pathology



intervention — is associated with better outcomes in communication and language development when compared to late diagnosis (Zhang et al., 2025).

Additionally, the current scientific scenario seeks to consolidate molecular biological interventions as a complementary therapeutic pillar for this condition. Although success in experimental models and initial clinical trials are promising, the definitive transition to its global application faces critical obstacles, requiring refinement of genomic techniques and improvement of their clinical applicability in a safe and reproducible way. (Akil et al., 2019).

In addition to rehabilitative approaches, etiological treatment should be considered in specific situations. In newborns with congenital CMV and moderate to severe hearing impairment, antiviral therapy has the potential to stabilize or slow the progression of hearing loss, especially when started early. However, its indication still requires caution, especially in asymptomatic cases or with isolated hearing loss, which reinforces the need for individualized decisions and specialized follow-up (Zhang et al., 2025).

Finally, the care of children with congenital hearing loss should be understood as a continuous and multidisciplinary process. Integrated action between different health professionals is essential to ensure timely diagnosis, adequate follow-up, and support for families. At the same time, prenatal education and the training of health professionals play a strategic role in the recognition of congenital CMV and its auditory repercussions, contributing to earlier interventions and the promotion of a better quality of life for affected children (Pesch et al., 2020).

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