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ABOUT COVER

Editorial Board Member of *World Journal of Clinical Pediatrics*, Tuna Kenar, MD, MSc, Assistant Professor, Department of Otolaryngology & Audiology, Private Denizli Cerrahi Hospital, Zeytinköy Ave. No:5 Pamukkale, Denizli, 20070, Türkiye. tuna.kenar@cerrahi.com.tr

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MINIREVIEWS

Various aspects of hearing loss in newborns: A narrative review

Raid M Al-Ani

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Raid M Al-Ani, Department of Surgery/Otolaryngology, University of Anbar, College of Medicine, Ramadi 31001, Anbar, Iraq

Corresponding author: Raid M Al-Ani, MBChB, Academic Editor, Consultant Physician-Scientist, Full Professor, Researcher, Science Editor, Department of Surgery/Otolaryngology, University of Anbar, College of Medicine, Al-Andulus, Ramadi 31001, Anbar, Iraq. med.raed.alani2003@uoanbar.edu.iq

Abstract

Hearing loss is considered the most common birth defect. The estimated prevalence of moderate and severe hearing loss in a normal newborn is 0.1%-0.3%, while the prevalence is 2%-4% in newborns admitted to the newborn intensive care unit. Neonatal hearing loss can be congenital (syndromic or non-syndromic) or acquired such as ototoxicity. In addition, the types of hearing loss can be conductive, sensorineural, or mixed. Hearing is vital for the acquisition of language and learning. Therefore, early detection and prompt treatment are of utmost importance in preventing the unwanted sequel of hearing loss. The hearing screening program is mandatory in many nations, especially for high-risk newborns. An automated auditory brainstem response test is used as a screening tool in newborns admitted to the newborn intensive care unit. Moreover, genetic testing and screening for cytomegalovirus in newborns are essential in identifying the cause of hearing loss, particularly, mild and delayed onset types of hearing loss. We aimed to update the knowledge on the various aspects of hearing loss in newborns with regard to the epidemiology, risk factors, causes, screening program, investigations, and different modalities of treatment.

Key Words: Newborns; Hearing loss; Deafness; Sensorineural hearing loss; Congenital hearing loss; Universal hearing screening program in newborns

Core Tip: Hearing loss in newborns is a common problem worldwide. Hearing is responsible for the acquisition of language, speech, cognition, and learning. Deaf individuals have a great negative impact on public health and the economic state. Early detection and prompt intervention lead to better outcomes. The universal hearing screening program, genetic testing, and cytomegalovirus detection are useful tools for the early detection of hearing loss in newborns. Rehabilitation of deaf infants with hearing aids or cochlear implants, gene therapy, and treatment of cytomegalovirus infection are satisfactory methods of treatment. However, researchers are focused on resolving the ambiguities regarding the diagnosis and treatment of hearing loss.

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INTRODUCTION

Hearing loss is the most common sensory deficit and one of the most common congenital abnormalities [1,2]. It affects 432 million adults and 34 million children across the globe (https://www.who.int/en/news-room/fact-sheets/detail/deafness-and-hearing-loss). It was estimated that the prevalence of bilateral moderate to severe hearing loss ranged from 1-3/1000 normal newborns and 2-4/1000 in high-risk group newborns[3,4].

Hearing loss in newborns can be caused by a genetic factor in 50% of cases, while acquired hearing loss is related to many causes in the prenatal, natal, and postnatal periods[5]. Hearing is essential for the acquisition of speech, language, and learning development[6]. Therefore, hearing loss particularly of bilateral severe to profound severity harms the development of newborns and results in them living with a significant handicap if not detected and treated early[7].

Early detection of hearing loss and prompt intervention are of utmost importance to minimize the negative impact of hearing loss and at the same time to maximize healthy development of the auditory pathway during the critical period of neural growth. Hence, the Joint Committee on Infant Hearing (JCIH) recommends that all newborns must be screened for hearing and the diagnosis should be established by the age of three months of life, and deaf infants treated at the age of six months[8]. Of course, timely fitting of hearing aids or cochlear implants is useful for deaf children[9].

The diagnosis of hearing loss depends on the doctor or family's suspicion and cannot diagnose all cases of significant hearing impairment. Besides, hearing screening of high-risk newborns (such as a family history of congenital hearing loss) can detect approximately 50% of cases with significant hearing loss. Therefore, it is essential to perform universal hearing screening of all newborns[3].

Otoacoustic emissions as well as auditory brainstem response tests are the usual screening tools for hearing screening in newborns. However, Universal Newborn Hearing Screening is not able to detect mild or delayed onset hearing loss in newborns, in addition, the cause of hearing loss cannot be identified using this program[10]. Therefore, nowadays genetic testing of hearing loss is a useful adjunct to the Universal Newborn Hearing Screening in the early identification of a significant number of newborns with hearing loss[10].

Owing to the importance of hearing and early detection and treatment of hearing loss in newborns, we conducted this comprehensive review to update and summarize the various aspects of hearing loss in newborns (a critical period of human life).

ANATOMY OF THE EAR AND AUDITORY PATHWAY

The hearing pathway consists of the peripheral (structural) and the central component (sensorineural). These differ in their function and timeline development. The peripheral part consists of the external, middle, and internal ear. The functions of the external and middle ear are to collect and conduct the sound waves into the Organ of Corti of the inner ear. Then, these mechanical waves are converted into electrical energy which is transmitted through the auditory nerve fibers to the auditory cortex[11]. This cortex is tonotopically arranged in areas 22, 41, and 42 of the temporal lobe[12].

The labyrinth or inner ear starts to form at the 4th gestational week and is completely developed in the 20th gestational week[11-13]. Also, the auditory cortex is fully developed at the 20th gestational week[14].

The cochlea and temporal lobe are the most important sensitive parts of the auditory pathway. There are many deleterious conditions affecting these components including, for example, prenatal and postnatal infection, postnatal antibiotic, and noise exposure in the newborn intensive care unit[15]. This deleterious effect starts from full development of the neurosensory component at the 20th week of

intrauterine life until the 5th month of extra-uterine life[11].

The auditory pathway can transmit sound waves to the developing brain of the fetus during the period from the 25th to the 29th gestational week. The uterus acts as a protective barrier from deleterious factors to fetal development and protects the auditory pathway from high-intensity sounds[12,16]. However, the developing fetus can recognize various sounds (both attenuated and distorted sounds), particularly the mother's speech[17]. Furthermore, intrauterine sound stimulation helps the tonotopic development of the inner ear hair cells and auditory higher center[18]. The cortical auditory center continues to develop due to surrounding sound stimuli in the neonatal period. Therefore, this period is considered the time of the continuous auditory development process to fetal life[11]. This is supported by evidence from a study that compared vision and hearing development. Sight develops only in extra-uterine life, while hearing develops during the last 10th to 12th gestational weeks as well as after birth [11].

NEWBORN LIFE

The neonatal period is defined as the first 28 d of life[19]. The transition from intrauterine life (fetus) to extra-uterine life (newborn) is a complex process. This process is affected by certain factors, including gestational age, the health of the mother and chronic medical problems, placenta state, congenital anomalies, and care level in the delivery room. Despite the majority of infants passing this stage smoothly, around 10% need adequate resuscitation in the newborn intensive care unit to pass this process[20].

Actually, in many nations, there is a lack of contact between the mothers and their newborns and the health services with around 50% of deliveries across the globe occurring in the home without proper postnatal care[21]. This factor might harm the general health of newborns, in general, and hearing development, in particular.

The maturation of the auditory pathway might be affected by many factors including prematurity, admission to the intensive care baby unit, gestational age, and the gender of the newborn[22,23]. Therefore, great care is necessary during this critical period of life to prevent any preventable causes of hearing loss or to reduce the effect of hearing impairment by early detection of hearing loss and prompt intervention.

EPIDEMIOLOGY

Hearing loss is the 4th leading cause of handicap worldwide[24]. Hearing loss of more than 40 dB in the better ear can be considered disabling for adulthood (≥ 15 years), while, in children (0-14 years), a deficit of > 30 dB in the better ear has a disabling effect[25].

There was an increment in the number with disabling hearing loss across the globe from 42 million in 1985 to 360 million in 2010[26]. This included 7.5 million children less than 5 years old. At present, there are 466 million individuals with disabling hearing loss across the globe (https://www.who.int/en/news-room/fact-sheets/detail/deafness-and-hearing-loss). Of note, the actual number is more than the reported number with an expected continuous rising with time. This might be due to increased life span of people[27,28]. It is expected that 630 million individuals will have disabling hearing loss by the year 2030 and approximately 900 million by 2050 if no counter-measures are taken[29].

There is no gender predilection for hearing loss in newborns. However, there is a geographical variation concerning the prevalence of hearing loss. The highest prevalence was seen in Asia Pacific, South Asia, and Sub-Saharan Africa[30].

CAUSES

There are two main reasons for congenital hearing loss in newborns; genetic and environmental. According to recent investigations in developed countries, 80% of the causes are genetic, while the remaining 20% of cases are acquired or due to environmental reasons[31].

There are three reasons for genetic hearing loss; (1) Non-syndromic and syndromic; (2) Autosomal dominant/recessive/X-linked; and (3) Mitochondrial inheritance patterns[32].

The classification of syndromic and non-syndromic hearing loss depends on whether other systemic manifestations are associated with hearing loss. It is very important to diagnose syndromic hearing loss early and this depends on clinical assessment and molecular diagnostic tools. The advantages of early diagnosis include; predicting the progress of hearing impairment, looking for other systemic abnormalities, and guidance of treatment. Otolaryngologists are the first physicians to deal with children with syndromic hearing impairment and cooperate with other specialties for prompt management[33].

The non-syndromic and autosomal recessive cases outnumber the cases of syndromic and autosomal dominant cases. This means that congenital hearing loss can occur with a negative family history of hearing loss or without systemic abnormalities, which might be an unexpected aspect of the family[32]. Several investigations studied adding genetic testing to the current universal newborn hearing screening. However, only 1.4% of newborns who passed the hearing screening had a positive genetic screening test[10,34]. DFNB1 is the most prevalent form of congenital hearing loss in developed countries. DFNB1 results from mutations in the gap junction protein beta 2 (GJB2) gene[35]. GJB2 is expressed between the supporting cells and spiral ligament, stria vascularis, and spiral limbus of the cochlea. It is included in the potassium recycling mechanism, that hair cells utilize to produce an action potential to external sound waves[36]. Hence, GJB2 gene mutations are considered a cause of sensorineural hearing loss (SNHL). The common causes of hereditary hearing loss are shown in Table 1 [37,38].

Although the environmental causes of hearing loss in newborns are relatively low in number, great attention should be paid to prevent the significant sequel of hearing loss in the individual, family, and population. Another issue should be mentioned here, that is infections (such as cytomegalovirus infection) might lead to delayed onset hearing loss[39].

Generally, the causes of hearing loss are divided into three groups; prenatal, natal, and postnatal causes. In the prenatal period, TORCH infections include toxoplasmosis, others (syphilis, hepatitis B), rubella, cytomegalovirus, herpes simplex infections are groups of congenital infections and caused by *Toxoplasma gondii*, *Treponema pallidum*, *Hepatitis B* virus, *Rubella* virus, *cytomegalovirus*, and *herpes virus simplex* (HSV) viruses, respectively. If these infections occur in the first trimester, the severity of the infection is worse[40]. These infections cause different congenital anomalies and SNHL is one of them. In the era of coronavirus disease 2019 (COVID-19), the maternal-fetal transmission of severe acute respiratory syndrome coronavirus 2 could occur and harm the fetal ear[41]. Maternal smoking may have a deleterious effect on the inner ear of the fetus[42]. A pregnant woman with cardiovascular diseases, diabetes mellitus, ototoxic drugs such as aminoglycoside antibiotics, loop diuretics, and immunosuppressive drugs, and other conditions might have teratogenic effects on the well-being of the developing fetus including development of the ear[43].

During parturition, many factors might affect the hearing of newborns such as vertical transmission of infection from the mother to the fetus, birth asphyxia (Apgar score ≤ 6 at 5 min), meconium aspiration, and trauma[44].

In the neonatal period, several causes lead to hearing impairment including, but not limited to, prematurity, low birth weight, severe hyperbilirubinemia, ototoxic drugs like aminoglycosides, bacterial meningitis, respiratory distress, assisted ventilation > 5 d after delivery, long stay in the newborn intensive care unit (more than 5 d), and head trauma or intracranial hemorrhage[44].

TYPES AND SEVERITY OF HEARING LOSS

Hearing loss is a difficulty in hearing. Many classifications of hearing loss depend on the laterality of the hearing loss (unilateral or bilateral), symmetry (symmetrical or asymmetrical), affected frequencies (low, moderate, or high), involved site of the auditory pathway (conductive, sensorineural, or mixed), and the onset of hearing loss (congenital or acquired)[45].

In conductive hearing loss, the lesion involves the conductive hearing pathway, namely the external and middle ear, such as stenosis or atresia of the external ear, otitis media with effusion, or dislocation of ossicles. In SNHL, there is an abnormality in the cochlea, or auditory nerve fibers, or in the auditory cortex, or a combination of them. The majority of congenital cases of hearing loss are due to genetic causes, as seen in the United States and other developed nations (around 80%). Other causes of hearing loss include, but are not limited to, prenatal and postnatal infections, noise exposure, hyperbilirubinemia, and hypoxia[31].

Regarding severity, hearing loss is divided according to the degree of hearing loss into slight (where the hearing loss of 16-25 dB), mild (26–40 dB), moderate (41–55 dB), moderately severe (56–70 dB), severe (71–90 dB), and profound (> 90 dB)[45].

EVALUATION OF HEARING IN NEWBORNS

Currently, three screening programs are useful in detecting the majority of causes of hearing loss in newborns[39].

Newborn hearing screening program

In the past, hearing screening in the infant was performed by distraction or other behavioral tests[46]. These tests are usually performed in high-risk groups of hearing loss in newborns or depend on parental concern for their infants.

Table 1 Common causes of hereditary hearing loss

Type	Mode of inheritance	Gene or syndrome	Type of deafness	Laterality	Severity of deafness	Systemic disorders
Non-syndromic	Autosomal dominant	WFS1	Mostly SNHL	Uni- or bilateral	Variables	No
		TECTA	Mostly SNHL	Uni- or bilateral	Variables	No
		COCH	Mostly SNHL	Uni- or bilateral	Variables	No
		KNCQ4	Mostly SNHL	Uni- or bilateral	Variables	No
	Autosomal recessive	GJB2	Mostly SNHL	Uni- or bilateral	Variables	No
		SLC26A4	Mostly SNHL	Uni- or bilateral	Variables	No
		MYO15A	Mostly SNHL	Uni- or bilateral	Variables	No
		OTOF	Mostly SNHL	Uni- or bilateral	Variables	No
		CDH23	Mostly SNHL	Uni- or bilateral	Variables	No
		TMC1	Mostly SNHL	Uni- or bilateral	Variables	No
Syndromic	Autosomal dominant	Neurofibromatosis 2	High frequency SNHL	Bilateral	Mild to profound	Facial nerve paresis or paralysis; Tinnitus; Vertigo
		Branchio-oto-renal syndrome	Mixed (50%), Conductive (30), SNHL (20%)	Bilateral	Severe and progressive	Otological problems (*e.g.* cochlear dysplasia), Branchial anomalies *e.g.* lateral cervical fistulae, Renal such as agenesis
		Treacher Collins	Conductive; Sensorineural or mixed hearing loss less common	Unilateral or bilateral	Various severities	Craniofacial abnormalities such as hypoplastic facial bones and external auditory canal atresia
		Stickler syndrome	Conductive; SNHL; Mixed	Unilateral or bilateral	Various severities	Ophthalmological such as vitreous anomaly. Joint hypermobility; Craniofacial anomalies such as hypertelorism
		Waardenburg syndrome				Dystopia canthorum, heterochromia iridium, white forelock, synophrys, broad nasal root, hypoplasia of, the alae nasi, patent metopic suture line, and a square jaw
	Autosomal recessive	Pendred syndrome	SNHL			Goiter and a partial defect in iodide organification
		Jervell and Lange–Nielsen syndrome	SNHL		Severe to profound	Marked prolongation of the QT interval, and multiple syncopal attacks induced by exercise or emotion
		Usher syndrome	SNHL	Bilateral	Various severities	Vestibular dysfunction, retinitis pigmentosa
		Refsum disease	SNHL		Severe and progressive	Peripheral polyneuropathy; Cerebellar ataxia; Retinitis pigmentosa; Ichthyosis
	X-linked dominant	Alport syndrome	SNHL	Bilateral	Progressive	Hemorrhagic nephritis; Vision changes
	Mitochondrial	MELAS	SNHL	Bilateral	Progressive	Short stature; Nausea; Migraines; Seizures; Alternating hemiparesis; Hemianopia; Cortical blindness
		MERRF				Myoclonic epilepsy; Ataxia; Dementia; Optic atrophy; Short stature; Neuropathy

SNHL: Sensorineural hearing loss.

In 1982, the Joint Committee on Infant Hearing of the United States recommended that detection of hearing loss should be screened in newborns. This early identification has a crucial role in achieving an optimum outcome of rehabilitation[47]. Despite the benefit of early detection of hearing loss in newborns and early infantile life having been recognized for 80 years, the real efforts on a country level to detect congenital hearing loss were started at the beginning of the last decade of the 20th century[48]. Currently, the national universal newborn hearing screening program was practiced in all developed countries and some developing nations[32,45,49]. Unfortunately, Iraq is one of the developing countries that still have not practiced this vital program[50]. A recent large global survey reported that 38% of the world's neonates and infants had no or minimal hearing screening and 33% screened approximately 85% of newborns[51].

As a rule of thumb, a screening test for hearing should have the following characteristics; cheap, easy to learn and apply by screeners, quick to administer, not invasive, high compliance, and high specificity and sensitivity. There are two screening tests used in the newborn hearing screening program; otoacoustic emission (records responses from the outer hair cells of the cochlea) and automated auditory brainstem response (measures response to sound based on the neural transmission of a signal from the cochlea to the brainstem) or a combination of both screening tests[31]. Owing to the high validity of the tests, they are accepted across the globe. These screening tests give either pass or fail, the latter indicates the possibility of hearing loss in the screened newborn who requires a referral for further audiological evaluation to detect the type, severity, and configuration of hearing loss[31].

If the above-mentioned step is unable to detect the cause of hearing loss, genetic testing, radiological evaluation, laboratory tests, and consultation from other specialists are necessary depending on the case under the evaluation process[52].

Application of the universal hearing screening program in newborns is cost-effective[53].

Genetic testing

Genetic screening is an adjuvant to Universal Newborn Hearing Screening as the latter fails to identify syndromic hearing loss, risk factors for aminoglycoside-related hearing loss, auditory neuropathy, mild hearing loss, and delayed-onset hearing loss[10,45].

There are 124 identified genes implicated in non-syndromic congenital SNHL (https://hereditary-hearingloss.org).

There are three main technologies for genetic testing: Direct sequencing, Microarrays, and Next-generation sequencing. Direct sequencing can identify the exact order of nucleotide bases in an examined gene or the part of interest[54]. Sanger Sequencing is the most widely used technique of direct sequencing. The benefits of this technique are its ability to detect the vast majority of mutations (including novel mutations) present in a sequence, and it is the most accurate method. The drawbacks are as follows; costly, time-consuming, and labor-intensive. Therefore, this technique is used mainly in the identification of novel mutations or to confirm the results of other experimental screening methods [10].

Microarrays or mutation chips can be used for screening multiple mutations at one time. Microarrays are easily adjusted according to a specific population depending on the frequencies of the gene mutations. The benefits of this method over direct sequencing are low cost and speed as multiple genes can be screened at the same time. However, this technique cannot determine novel mutations as the direct sequencing method can. Despite the many mutations that can be screened simultaneously, this technique is limited by increasing the mutations without a significant increment in the time and cost [54]. At present, there are 15-300 mutations in 4-31 common hearing loss-related genes[55].

Next-generation sequencing or high-throughput sequencing techniques or massively parallel sequencing is now available and able to test all hearing loss-related genes in children with congenital hearing loss[37].

Cytomegalovirus testing

Congenital cytomegalovirus infection is considered the main non-hereditary reason for hearing loss at birth, the estimated incidence is approximately 10% of all causes of congenital hearing loss and 15%-20% in all children with hearing loss[56]. Approximately 6% of newborns who fail the hearing screening tested positive for cytomegalovirus[57].

Newborns with cytomegalovirus infection are divided into asymptomatic (90%) and symptomatic (10%). The most common symptomatic conditions are premature delivery, intrauterine growth restriction, and dysfunction of multiple organs. Approximately 50% of symptomatic newborns can develop SNHL[58]. Unilateral hearing loss is mostly seen among asymptomatic newborns with cytomegalovirus infection which is detected during screening. Owing to the high possibility of late occurrence of hearing loss in childhood, therefore, long-term follow-up of those children with cytomegalovirus infection is of utmost importance to detect late-onset hearing loss[59].

It is not necessary to test all neonates for cytomegalovirus because the test is not useful or cost-effective, as the majority of the infected neonates are asymptomatic. The correct timing of testing for congenital cytomegalovirus is either during pregnancy or during the first 21 d of neonatal life[60]. There are two methods for testing cytomegalovirus in the fetus; culture and polymerase chain reaction (PCR) testing of the amniotic fluid through amniocentesis[61]. Amniocentesis is not recommended for routine

screening testing as there is a 0.49% risk of demise in the fetus. The best samples used for the detection of cytomegalovirus by PCR are saliva or urine because they have sensitivities and specificities reaching 100%[58]. In newborns, detection of IgM antibodies against cytomegalovirus is not recommended as only 70% of those with positive cytomegalovirus infection can be detected using this serological test. There is limited value of cytomegalovirus detection using PCR of dried blood spots due to low sensitivity (28.3%)[62].

A recent study adopted a comprehensive hearing screening of newborns which comprised hearing screening, genetic testing, and cytomegalovirus testing[45]. The benefits of this program include; detection of the causes of hearing loss in newborns who were not detected on the routine hearing screening program, providing the etiological pattern of the hearing loss, reducing the number of children that might be lost to follow-up, and reducing the cost by decreasing the cases that need later testing.

Table 2 shows certain studies from various countries using the above-mentioned investigations in the diagnosis of neonatal hearing loss.

TREATMENT

Successful treatment depends on early detection of hearing loss in newborns as well as prompt intervention. The main treatment modalities are discussed below.

Hearing aid and cochlear implant

A multidisciplinary team is necessary for audiological, educational, and medical management. The team consists of an otolaryngologist, audiologist, pediatrician, specialist in genetics, and others[39]. The main factors that affect the development of language in a deaf infant are early detection and intervention[63]. It is critical to start intervention in a deaf infant at the age of 6 mo for better acquisition of language. At this age, the infant gets similar results to normal-hearing infants[64].

There are two options for the rehabilitation of hearing-impaired infants; hearing aids and cochlear implants. The hearing aid is the treatment of choice for mild-to-moderate congenital SNHL, while those with severe-to-profound SNHL can benefit from cochlear implants[65].

Gene therapy

Due to the developments in genetic sequencing technology in the last several years, there have been significant advancements in the molecular and biochemical pathways concerning the treatment of congenital hearing loss[66]. Following the first clinical approval protocol of human gene therapy by the Food and Drug Administration in 1990[67], there has been a significant increase in the acceptance of human gene therapy as a treatment option for different clinical problems including hearing loss.

There are four methods of human gene therapy; gene suppression, cell replacement, gene replacement, and targeted gene editing[68]. The application of these methods in cases of hearing loss faces difficulty in their administration to the inner ear as it is not an easily accessible structure and is covered by a strong bony labyrinth. Besides, most treated cases of hearing loss are severe and associated with irreversible destruction of the hair cells (outer and inner). However, many hearing loss-related genes have been successfully treated with curative gene therapy in an animal model[39].

Novel gene therapy in humans to prevent or restore SNHL is still under investigation[68].

Treatment of cytomegalovirus infection

The recommended treatment for symptomatic cytomegalovirus infection is either parenteral use of ganciclovir or oral valganciclovir. The triphosphate derivative of ganciclovir can inhibit cytomegalovirus DNA replication[69]. A previous clinical trial in 2003 reported that there was preservation of hearing in infants at 6 mo and one year following treatment with ganciclovir for symptomatic cytomegalovirus infection for those infants who received treatment during the neonatal period. The study also reported that 63% of the infants (29/46 treated group) had grade 3 or 4 neutropenia following antiviral treatment with ganciclovir[70].

Recently, three randomized controlled clinical trials studied the efficacy of valganciclovir antiviral therapy on the severity and course of cytomegalovirus-related SNHL[39].

CONCLUSION

Hearing is vital for speech, language, cognition, and learning. Hearing loss is the most common sensory abnormality. Hearing loss harms the person, family, and community. Early identification and intervention of hearing loss in newborns can result in an excellent outcome. Early detection of hearing loss in newborns can be accomplished by the hearing screening program, genetic testing, and cytomegalovirus infection testing. The rule of 1, 3, and 6 should be applied to hearing loss in newborns and

Table 2 Studies from various nations using different tools to diagnose hearing loss in newborns

Authors	Country	Year	Sample size	Study method	Data type	Diagnostic tool	Predictor(s)
Malesci *et al*[7]	Italy	2022	318878	Longitudinal retrospective study	Newborns	UNHS	UNHS is feasible and effective
Chu *et al*[34]	Taiwan	2015	15345	Retrospective study	Newborns	UNHS; Genetic testing	A genetic profile of the connexin genes and SLC26A4 gene among infants with hearing impairment detected by a UNHS program in Taiwan
Durante *et al*[42]	Brazil	2021	105	Comparative study	Newborns	Transient-evoked otoacoustic emissions and distortion product otoacoustic emissions	The impact of smoking exposure could be analyzed through transient-evoked otoacoustic emissions in newborns.
Bielecki *et al*[44]	Poland	2011	5282	Comparative study	Newborns	UNHS	Most common risk factors for hearing loss; Ototoxic drugs; Premature birth; Low birth weight; Intensive care in excess of 7 d
Pitathawatchai *et al*[53]	Thailand	2023	126	A decision analytical model with a 78-year time horizon	Newborns	UNHS; TNHS	Both tools are cost-effective
Rawlinson *et al* [57]	Australia	2018	1669	Cohort study	Newborns, Infants	UNHS; CMV testing	Congenital CMV (5.9%) in infants with permanent hearing loss and who did not pass the UNHS
Boppana *et al* [62]	United States	2010	20448	Comparative study	Newborns	CMV testing	Saliva rapid culture had low sensitivity in comparison with CMV testing with DBS real-time PCR

UNHS: Universal newborn hearing screening; TNHS: Targeted newborn hearing screening; CMV: Cytomegalovirus; PCR: Polymerase chain reaction.

infants. Number 1 means that the assessment of hearing should be started at the first month, number 3, accomplish the diagnosis at three months, and number 6, intervention should be started at 6 mo of life. Rehabilitation of deaf infants with hearing aids or cochlear implantation, gene therapy, and antiviral therapy for cytomegalovirus infection are recommended treatment modalities for hearing loss. Further investigations are necessary to solve the many ambiguities concerning hearing loss in newborns.

FOOTNOTES

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ORCID number: Raid M Al-Ani 0000-0003-4263-9630.

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