



Systematic Review



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Predisposing Factors for Congenital Hearing Loss: A Comprehensive Systematic Review

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Abstract

This systematic review aimed to assess and integrate research on risk factors for congenital hearing loss (CHL), emphasizing genetic, infectious, perinatal, environmental, and sociodemographic influences. The review was prospectively registered with PROSPERO (CRD42022372879) and conducted according to PRISMA 2020 and PRISMA-S guidelines. A comprehensive search was performed across PubMed, Embase, Scopus, and Google Scholar using MeSH terms and free-text keywords related to CHL and its risk factors. Observational studies (cohort, case-control, cross-sectional) involving children with CHL and assessing genetic, infectious, perinatal, or environmental exposures were included. Data extraction was done independently by two reviewers, covering study characteristics, diagnostic methods, and measures of association (odds ratio, relative risk). Risk of bias was evaluated using the Newcastle-Ottawa scale for cohort/case-control studies and the Joanna Briggs Institute checklist for cross-sectional studies. Genetic factors such as *GJB2* mutations, a positive family history, and consanguinity were consistently associated with CHL. Infectious etiologies, particularly congenital cytomegalovirus, were prominent across studies, with TORCH infections also commonly implicated. Perinatal risk factors, including neonatal intensive care unit admission, low birth weight, and hyperbilirubinemia, were frequently reported in affected children. Environmental exposures, especially to ototoxic medications, were noted as significant contributors, often acting synergistically with other risk factors like infections or genetic conditions. Sensorineural hearing loss, predominantly bilateral, emerged as the most common type reported. CHL is a multifactorial condition, with genetic and infectious causes being most prevalent. Targeted screening and preventive strategies addressing these risk domains are crucial for early detection and management.

Keywords: Congenital, hearing loss, genetic predisposition to disease, congenital infections, infant, newborn, diseases, ototoxicity, environmental exposure

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Introduction

Congenital hearing loss (CHL) is a critical neurodevelopmental condition that can profoundly impact a child's overall growth, particularly in areas such as speech, language acquisition, cognitive functioning, emotional regulation, and academic achievement (1-5). The absence of adequate auditory input during early life stages disrupts foundational language development, often leading to delays in literacy, educational performance, and social-emotional skills compared to peers with normal hearing (6-10). For decades, research has established a link between certain risk factors and permanent childhood hearing loss, informing early screening and intervention efforts.

On a global scale, hearing loss is emerging as a growing public health concern. According to the global burden of disease study, hearing loss prevalence increased from 1.2 billion



people (17.2%) in 2008 to 1.4 billion (18.7%) by 2017, highlighting the escalating issue (6). The World Health Organization ranks hearing loss as the third leading cause of disability-related years lost, with 39.5 million years of healthy life lost in 2017, up from 27 million in 2000, highlighting its substantial impact (6). In India, estimates suggest that childhood hearing loss affects 6.6% to 16.47% of children, with incidence among high-risk newborns ranging from 7 to 49.18 per 1000 live births, highlighting a significant public health concern (6). Although middle ear infections like otitis media remain a major postnatal cause, congenital origins are increasingly recognized as significant contributors to childhood hearing loss (11-16).

The landscape of childhood hearing loss has evolved considerably. Improvements in vaccination programs and infectious disease control have reduced hearing loss related to post-infectious complications like meningitis (15). Simultaneously, advancements in neonatal care have improved survival rates among preterm and low birth weight infants, who, however, are more susceptible to sensorineural hearing damage due to risk factors like oxygen deprivation, elevated bilirubin levels, and exposure to ototoxic drugs (16,17). At the same time, advances in genetic testing have enabled clinicians to detect a wide range of genetic abnormalities, both syndromic and non-syndromic, responsible for CHL, highlighting the growing importance of hereditary causes.

Considering these trends, identifying CHL risk factors is crucial for effective newborn hearing screening, prevention, and early intervention. This systematic review examines the existing literature on CHL risk factors, including genetic, perinatal, environmental, and sociodemographic aspects, to inform evidence-based practice and guide public health decisions in neonatal auditory care.

Methodology

Research Question

What are the determinants or risk factors for CHL? Which is more prevalent—genetic predisposition or infectious causes?

This systematic review was registered on PROSPERO and approved under the registration number CRD42022372879 and conducted following the PRISMA 2020 and PRISMA-S (search extension) guidelines to ensure methodological transparency and reproducibility.

PICO Statement

Population (P): Children with permanent bilateral or unilateral CHL.

Intervention/Exposure (I/E): Exposure to risk factors potentially associated with CHL, including:

- Genetic factors (e.g., family history, syndromes)

- Infectious causes [e.g., congenital cytomegalovirus (cCMV), TORCH infections]

- Perinatal factors [e.g., low birth weight, Neonatal Intensive care unit (NICU) stay, hyperbilirubinemia, ototoxic drugs]

- Environmental and structural factors (e.g., craniofacial anomalies).

Comparison (C):

- Children without the identified risk factors
- Comparisons across different categories of risk factors (e.g., genetic vs. infectious).

Outcome (O):

- Diagnosis of CHL
- Measures of association such as odds ratios (ORs), relative risks (RRs), or other statistical indicators reflecting the strength of association between risk factors and hearing loss

Search Strategy

A thorough and systematic search of the literature was undertaken to identify the studies exploring the relationship between various risk factors and CHL in children. Multiple databases, PubMed/MEDLINE, PubMed Central, Google Scholar, Embase, and Scopus, were searched using a structured strategy combining Medical Subject Headings (MeSH) and free-text keywords related to CHL, its potential etiological factors, and study design types. Key terms included “congenital hearing loss,” “sensorineural hearing loss,” “unilateral hearing loss,” “genetic predisposition,” “family history,” “syndromic hearing loss,” “TORCH infections,” “cytomegalovirus,” “rubella,” “toxoplasmosis,” “perinatal complications,” “NICU,” “low birth weight,” “hyperbilirubinemia,” “ototoxic drugs,” and “craniofacial anomalies,” linked using Boolean operators (and, or) to enhance search precision.

Search filters were set to include only human studies published in English. Only observational studies, including cohort, case-control, and cross-sectional designs, were considered eligible. Interventional studies, case reports, editorials, and narrative reviews were excluded. The inclusion criteria comprised studies evaluating risk factors or determinants of CHL in children. Two reviewers independently screened the titles and the abstracts, and any discrepancies were resolved by discussion or with adjudication by a third reviewer. The search was ended in April 2025.

Data Extraction

Data extraction was performed independently by two reviewers using a standardized, pre-tested extraction form to ensure consistency and reliability. For each eligible study, comprehensive details were systematically documented,

including the first author's name, year of publication, study design, geographical location, sample size, population characteristics, and the specific risk factors investigated. Extracted variables encompassed the type and laterality of CHL (e.g., unilateral, bilateral, sensorineural, or mixed), diagnostic modalities used [such as otoacoustic emissions (OAE) or auditory brainstem response (ABR)], and associations with potential determinants including genetic factors, TORCH infections, perinatal complications, environmental exposures, and consanguinity.

Effect estimates—such as ORs, RRs, confidence intervals, and p-values—were recorded when available to support quantitative synthesis. Any discrepancies arising between reviewers during data extraction were resolved through discussion or adjudication by a third reviewer. All extracted data underwent cross-checking and verification to ensure completeness and accuracy before being synthesized for analysis.

Risk of Bias and Quality Assessment

The Newcastle-Ottawa scale (NOS) was applied to evaluate the quality of cohort and case-control studies, while the Joanna Briggs Institute (JBI) critical appraisal checklist was used for cross-sectional studies. Domains assessed included sample selection, comparability, outcome measurement, and confounding control. Each study was rated as low, moderate, or high risk of bias. No studies were excluded based on quality alone, but methodological limitations were considered during synthesis (Table 1).

Data Analysis

Given the heterogeneity in study designs, populations, and reported outcomes, a meta-analysis was not feasible. Therefore, results were synthesized qualitatively, focusing on the magnitude and consistency of reported associations across different etiological categories.

Results

A total of 17 studies were included in this systematic review, encompassing a wide range of geographic regions, including South Africa, Belgium, Brazil, Sweden, Australia, Iran, India, Japan, Italy, Colombia, the United States, and the United Kingdom. Study designs comprised retrospective cohorts, prospective cohorts, cross-sectional surveys, and case-control studies, with sample sizes ranging from 24 to over 613,000 participants. The age of the participants varied from newborns to children up to 14 years. The review revealed consistent associations of CHL with genetic factors such as *GJB2* mutations, family history, and consanguinity; infectious causes like cCMV and TORCH infections; perinatal risk factors including NICU admission, low birth weight, and hyperbilirubinemia; and environmental exposures such as ototoxic medications. Multiple studies also highlighted the

synergistic effects of combined risk factors (e.g., genetic susceptibility and CMV infection). These findings underscore the multifactorial etiology of CHL and the importance of integrated early screening and risk stratification (Figure 1).

Genetic Factors

Genetic contributions to CHL were highlighted in several studies. Khan and Joseph (17) identified *GJB2* mutations (notably 35delG) in 22.1% of their cases. Niu et al. (18) reported syndromic causes in 37.2%, chromosomal anomalies in 21.3%, and *GJB2*-related and X-linked mutations in 8.5% and 1%, respectively. Anastasio et al. (19) also found chromosomal aberrations significantly associated with hearing loss (OR: 4.95). Foulon et al. (20) confirmed a strong association between craniofacial anomalies or syndromes and hearing loss (RR: 24.47), especially when multiple risk factors coexisted. Additionally, Satterfield-Nash et al. (21) noted family history as a major risk factor (OR: 11.47), with consanguinity increasing the risk even further (OR: 12.48) (Table 1).

Infectious Causes

cCMV was the most frequently identified infectious etiology. De Cuyper et al. (22) and Fitzgibbons et al. (23) reported that 100% of their cases had confirmed cCMV infection. Townsend et al. (24) found that 13% of the children with cCMV developed hearing loss. Sabbagh et al. (25) and Verma et al. (6) similarly reported high rates of CMV, followed by rubella, syphilis, toxoplasmosis, and herpes. TORCH infections were frequently included in risk assessments by multiple authors including Umehara et al. (26) and Satterfield-Nash et al. (21), the latter finding congenital infections had an OR of 5.48 for hearing loss (Table 1).

Perinatal Factors

Prematurity, low birth weight, NICU stay, and hyperbilirubinemia emerged as consistent perinatal risk factors. Khan and Joseph (17) observed perinatal risk in 22.1% of their cases. Faistauer et al. (27), Anastasio et al. (19), and Sabbagh et al. (25) reported significant associations with NICU admission, mechanical ventilation, and oxygen use. Satterfield-Nash et al. (21) quantified these risks: NICU stay (OR: 7.21), birth weight <1500 g (OR: 4.40), and bilirubin >10 mg/dL (OR: 5.18). These trends were also supported by findings from Chakrabarti and Ghosh (28) and Fitzgibbons et al. (23) (Table 1).

Environmental Factors

Ototoxic drug exposure, especially to aminoglycosides like gentamicin and amikacin, was a recurring theme. Faistauer et al. (27) and Sabbagh et al. (25) both reported drug-related toxicity in their cohorts, and Satterfield-Nash et al. (21) associated ototoxicity, hypoxia, and fever/seizures with an OR of 3.02. Anastasio et al. (19) found ototoxicity in 45.3% of

their cases, with synergistic effects observed in conjunction with other risk factors such as CMV or syndromes (Table 1).

Other Risk Factors

Additional risk factors included craniofacial anomalies, advanced maternal age, multiple births, and syndromic associations such as Down, Waardenburg, and CHARGE syndromes. Niu et al. (18) and Judge et al. (29) emphasized anatomical abnormalities and caregiver concern. Satterfield-Nash et al. (21) also reported significant associations with seizures, maternal age ≥ 35 years, and multiparity. Manotas et al. (30) observed a higher prevalence of hearing loss in Muslim populations, possibly linked to sociocultural or genetic clustering (Table 1).

Types of Hearing Loss

Sensorineural hearing loss (SNHL) was the most common type reported across studies, frequently bilateral. Khan and Joseph (17) reported a distribution of 28.5% CHL, 20.1% SNHL, and 7.1% mixed hearing loss. Sabbagh et al. (25) observed 62.5% bilateral and 37.5% unilateral hearing loss. Anastasio et al. (19) noted 75% SNHL and 20.8% auditory neuropathy. Mixed types and conductive hearing loss were reported in fewer studies, such as Niu et al. (18) and Fitzgibbons et al. (23) (Tables 2, 3).

Assessment Method for Hearing Loss

Most studies used objective, standardized methods. Commonly employed tests included OAE, ABR, automated ABR (AABR), auditory steady-state response, tympanometry, and behavioral audiometry. Imaging (computed tomography/magnetic resonance imaging) was occasionally used, as in Faistauer et al. (27) and Judge et al. (29). Townsend et al. (24) also used the Griffiths developmental scale in follow-up assessments. Longitudinal audiological surveillance was adopted in some cohorts [e.g., De Cuyper et al. (22)] (Tables 2, 3).

Timing of Diagnosis/Age at Diagnosis

Timing varied widely. Some studies, such as Townsend et al. (24) and Foulon et al. (20), identified hearing loss by one year of age. Others, like De Cuyper et al. (22) and Sabbagh et al. (25), conducted reassessment at four years or beyond. NICU-based studies like Umehara et al. (26) ensured evaluation before discharge. School-age assessments were seen in Chakrabarti and Ghosh (28) and Judge et al. (29), while Faistauer et al. (27) noted an average diagnosis age of two years (Tables 2, 3).

Prevalence and Associations

The most consistent risk factors across studies were genetic mutations (*GJB2*, syndromic anomalies), cCMV and TORCH infections, perinatal complications (NICU stay, low birth

weight, hyperbilirubinemia), and ototoxic drug exposure.

Reported pooled ranges:

- Genetic/family history: OR: 4.0-12.5
- cCMV infection: OR: 5.0-10.3
- NICU admission: OR: 6.8-7.2
- Hyperbilirubinemia: OR: 4.5-5.2
- Ototoxic exposure: OR: 3.0-4.2

These trends were consistent with recent large-scale analyses, such as by Sökmen et al. (31) and Han et al. (32), which identified NICU admission >5 days, ototoxic drug use, and consanguinity as leading risk factors for CHL.

Discussion

Our systematic review demonstrates that CHL is a multifactorial condition influenced by a combination of genetic, infectious, perinatal, environmental, and other clinical and demographic risk factors. Genetic contributions were reported in seven studies, with common findings including syndromic and chromosomal abnormalities as well as non-syndromic mutations such as those in the *GJB2* gene. Family history and consanguineous marriage were also significant predictors of CHL. Infectious etiologies were highlighted in eight studies, with cCMV being the most frequently reported cause, followed by other TORCH infections such as toxoplasmosis, rubella, syphilis, and herpes.

Perinatal risk factors were consistently highlighted across nine studies and included conditions such as prematurity, low birth weight, NICU admission, use of mechanical ventilation, and hyperbilirubinemia, all of which were significantly associated with a higher likelihood of developing hearing loss. Environmental exposures were explored in five studies, with ototoxic agents like aminoglycosides frequently identified as key contributors, often acting in combination with infections or inherited susceptibilities. Additional determinants reported in six studies included craniofacial abnormalities, syndromic features, advanced maternal age, multiple births, and socioeconomic or cultural factors. Sensorineural hearing loss emerged as the predominant type, typically bilateral, although some studies also documented mixed or conductive variants. These findings emphasize the critical importance of early risk identification and reinforce the need for universal newborn hearing screening programs coupled with targeted follow-up for infants with known risk factors.

Our findings align closely with recent meta-analyses and systematic reviews, including those by Sökmen et al. (31), Han et al. (32) and Fernández-Rueda et al. (33) which revealed

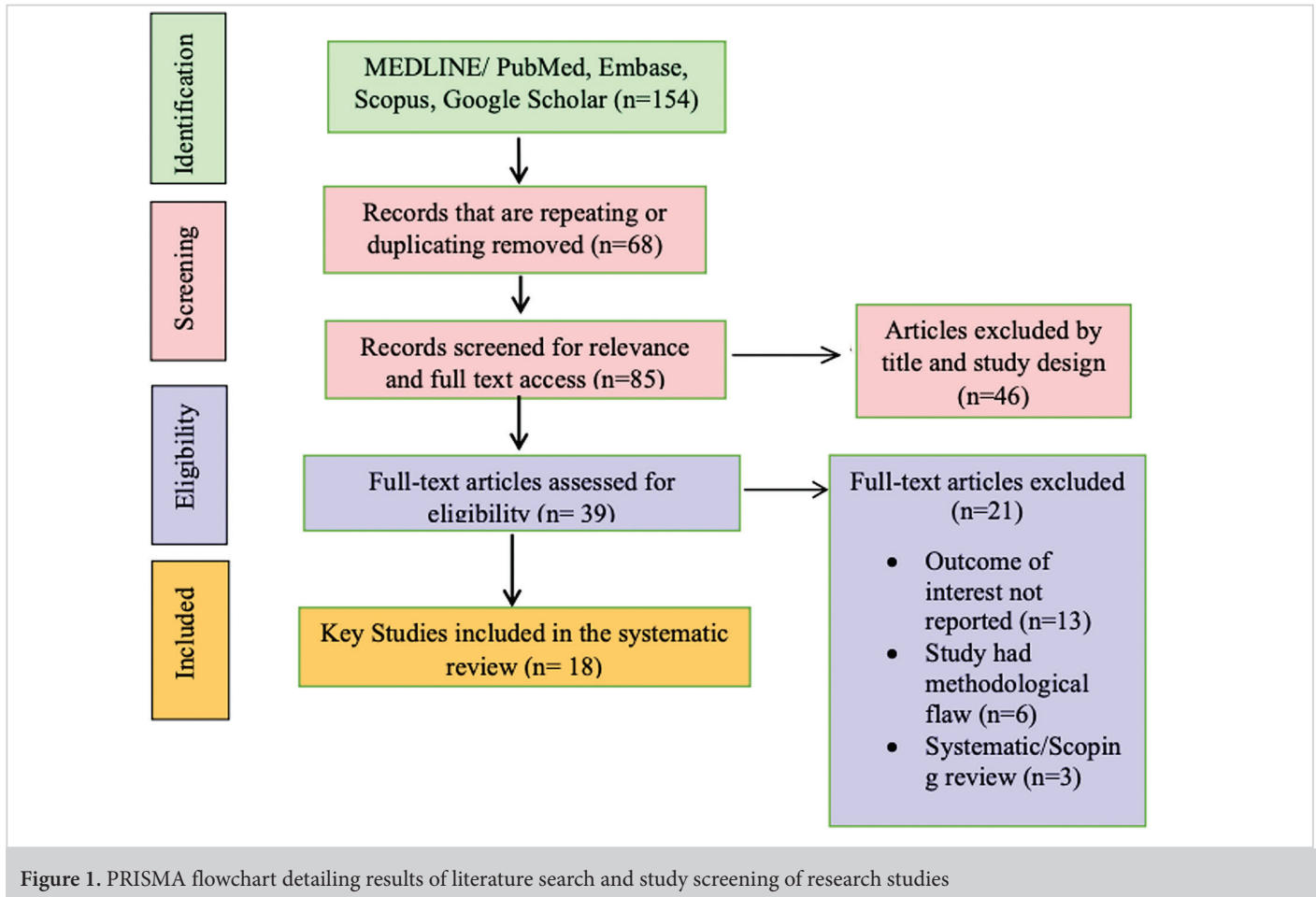


Figure 1. PRISMA flowchart detailing results of literature search and study screening of research studies

NICU stay, ototoxic exposure, and hyperbilirubinemia as consistent determinants of hearing loss in infants. The most frequent genetic contributors were *GJB2* and syndromic mutations, particularly among consanguineous populations (e.g., Iran, India, and Türkiye). Infectious causes, notably cCMV, accounted for up to 32% of the cases, emphasizing the importance of CMV screening within neonatal protocols. Perinatal and environmental factors, such as prematurity, prolonged ventilation, and aminoglycoside use, acted both independently and synergistically with genetic susceptibilities. This convergence supports the concept of gene-environment interaction in CHL pathogenesis (34,35).

Compared to earlier systematic reviews, our review incorporated more recent global datasets (2023-2025) that broaden the contextual understanding of CHL determinants (36-38). For instance, Sökmen et al. (31) highlighted NICU admission, mechanical ventilation >5 days, hyperbilirubinemia requiring exchange transfusion, consanguinity, and family history as the most prevalent risk factors—findings echoed in our analysis. Han et al. (32) provided pooled estimates supporting similar risk magnitudes, strengthening the external validity of these associations.

Verma et al. (6) included 29 studies in their systematic review spanning 1980 to 2020, examining prevalence patterns of hearing loss in neonates, children, and adults. The review identified syndromes and craniofacial anomalies as major genetic contributors, while CMV and other TORCH infections were prominent infectious causes. Perinatal factors frequently cited were NICU stay, low birth weight, mechanical ventilation, and hyperbilirubinemia. Although environmental and consanguinity factors were not extensively detailed, the study highlighted other contributors such as rural residence, advanced age, and limited awareness. The types of hearing loss varied, with sensorineural hearing loss prevalent in children and conductive loss due to otitis media noted in older age groups. Diagnostic approaches included OAE, AABR, ABR, tuning fork tests, and pure tone audiometry, with comparisons made across age brackets and rural vs. urban populations.

Satterfield-Nash et al.'s (21) scoping review across multiple countries focused on children aged under two years and identified through universal newborn hearing screening cohorts. Among 1787 children evaluated for underlying causes, genetic testing was conducted in 933 cases, with attribution rates ranging from 7.7% to 83.3%. CMV testing

was performed in 1021 cases, with causation attributed in 0-32%. While perinatal and environmental factors were not systematically examined, and data on consanguinity were absent, the review offered a comparative perspective on genetic versus CMV-related etiologies. All cases involved sensorineural hearing loss, diagnosed via OAE, ABR, dried blood spot testing, or saliva polymerase chain reaction, generally before two years of age. The importance of differentiating congenital from delayed-onset cases within this age window was emphasized.

Vos et al. (9) developed a systematic review and meta-analysis protocol targeting the identification of permanent unilateral or bilateral hearing loss in individuals aged from birth to 18 years. Although sample size was not specified, inclusion required clearly defined hearing loss and its associated risk factors. Temporary losses, case reports, and gray literature were excluded. The protocol accounted for genetic syndromes, infections like cCMV, meningitis, and toxoplasmosis, and

perinatal risks such as NICU stay, hyperbilirubinemia, and ototoxic drug exposure. Environmental exposures were included only if they led to permanent auditory damage. Factors like consanguinity and family history were incorporated when available, along with other contributors like pediatric malignancies. Types of hearing loss included sensorineural, auditory neuropathy, mixed, and permanent conductive loss. Audiologist-confirmed diagnosis was mandatory, excluding cases detected solely by automated tools. Timing of diagnosis was categorized as early-onset (<3 months) or late-onset (>3 months), with comparisons between children with and without specific risk exposures.

Future investigations on CHL should adopt a standardized, multidisciplinary framework to better understand the complex interplay of genetic, infectious, perinatal, environmental, and sociodemographic factors. There is a critical need for large-scale, multicenter prospective cohort studies utilizing consistent CHL definitions and clearly

Table 1. Risk of bias analysis for the included studies using the NOS or JBI tool as required

First author (year, country)	Study design	Tool used	Selection	Comparability	Outcome/exposure assessment	Total score	Risk level
Khan and Joseph, (2024, South Africa) (17)	Retrospective descriptive cohort	NOS	3/4	1/2	2/3	6/9	Moderate
De Cuyper et al., (2023, Belgium) (22)	Multicenter longitudinal cohort	NOS	4/4	2/2	3/3	9/9	Low
Faistauer et al., (2022, Brazil) (27)	Cross-sectional study nested in retrospective cohort	NOS	3/4	1/2	2/3	6/9	Moderate
Afshar et al., (2022, Sweden) (34)	Multicenter case-control study (400 cases, 200 controls)	NOS	4/4	2/2	2/3	8/9	Low
Zizlavsky et al., (2022, Indonesia) (37)	Cross-sectional multicenter study	NOS	4/4	2/2	2/3	8/9	Low
Fitzgibbons et al., (2021, Australia) (23)	Population-based retrospective cohort (UNHS database, Queensland)	NOS	4/4	2/2	2/3	8/9	Low
Sabbagh et al., (2021, Iran) (25)	Analytical case-control, population-based neonatal screening	NOS	4/4	2/2	2/3	8/9	Low
Anastasio et al., (2021, Brazil) (19)	Prospective cohort study	NOS	4/4	2/2	2/3	8/9	Low
Niu et al., (2020, Sweden & China) (18)	Retrospective cohort review	NOS	4/4	2/2	2/3	8/9	Low
Umehara et al., (2019, Japan) (26)	Retrospective observational cohort	NOS	3/4	2/2	2/3	7/9	Moderate
Chakrabarti and Ghosh, (2019, India) (28)	Stratified cross-sectional school-based study	NOS	4/4	2/2	2/3	8/9	Low
Foulon et al., (2019, Belgium) (20)	Prospective cohort	NOS	4/4	2/2	2/3	8/9	Low
Palma et al., (2025, Italy) (35)	Retrospective cohort	NOS	3/4	2/2	2/3	7/9	Moderate
Parab et al., (2018, India) (38)	Prospective non-randomized clinical study	NOS	4/4	2/2	2/3	8/9	Low
Barbi et al., (2006, Italy) (7)	Retrospective observational cohort	NOS	3/4	2/2	2/3	7/9	Moderate

NOS: Newcastle-Ottawa scale, JBI: Joanna Briggs Institute, UNHS: Universal newborn hearing screening

specifying onset, severity, and classification of hearing loss to improve data comparability across different populations. Incorporating genetic testing into diagnostic protocols, particularly in regions with high consanguinity rates, is essential to identify prevalent mutations, syndromic conditions, and guide genetic counseling and prevention efforts.

Research should also delve into gene-environment interactions to explore how genetic susceptibility may influence the impact of perinatal insults or infections such as CMV or ototoxic drug exposure. Additionally, long-term studies are needed to evaluate neurodevelopmental and quality-of-life outcomes in children diagnosed with CHL in early infancy, especially in resource-limited contexts. Comparative studies should assess the cost-effectiveness and outcomes of universal versus targeted newborn hearing screening programs, particularly in countries where implementation remains incomplete. Moreover, research should actively include diverse and underrepresented populations such as rural, low-income, or Indigenous groups who often face limited access to screening and early interventions. Finally, longitudinal follow-up studies evaluating the timing, type, and outcomes of early interventions—including hearing aids, cochlear implants, and speech therapy—are crucial to shaping health policy and optimizing developmental outcomes in children with CHL.

Critical Appraisal

This systematic review is methodologically robust and comprehensive in scope, synthesizing data from 18 observational studies across multiple continents to identify the determinants of CHL. It adheres to the PRISMA 2020 and PRISMA-S guidelines, includes a registered PROSPERO protocol, and employs standardized tools (NOS and JBI checklist) for quality appraisal—enhancing transparency and reproducibility. The clear PICO framework and detailed inclusion criteria lend methodological rigor. By encompassing diverse risk domains, genetic, infectious, perinatal, environmental, and sociodemographic, the review captures the multifactorial nature of CHL and situates its findings within the evolving global landscape of neonatal auditory health.

A major strength of this review lies in its attempt to examine a temporal shift in CHL etiology, exploring whether improved infection control and neonatal care have shifted the burden from infectious to genetic causes. However, this objective was constrained by a lack of high-quality genetic studies, particularly from low- and middle-income countries where access to molecular diagnostics remains limited. The reliance on heterogeneous observational designs precluded meta-analysis, and variability in diagnostic criteria, sample sizes, and reporting standards across included studies introduced

Table 2. Detailed review of studies included in the systematic review

First author (year, country)	Sample size	Age of participants	Genetic factors	Infectious causes	Perinatal factors	Environmental factors	Other risk factors
Khan and Joseph, (2024, South Africa) (17)	1,433 children	Infants and children <12 years	Syndromic: Down's, Usher, Waardenburg, CHARGE	CMV (54%), rubella, syphilis, toxoplasmosis, herpes	Ototoxic medication exposure, recurrent otitis media	All ethnic/language groups represented	Retrospective data gaps; large multisite cohort
De Cuyper et al., (2023, Belgium) (22)	387 (774 ears)	Newborns to ≥4 years	Not assessed	100% congenital CMV	Prematurity, symptomatic infection predictors	Not discussed	Exclusion of treated cases limits generalizability
Faistauer et al., (2022, Brazil) (27)	140	Up to 12 years (mean 2.0±2.3 yrs)	<i>GJB2</i> mutations (22.1%)	CMV 2.9%, syphilis, toxoplasmosis, herpes	Ototoxic exposure	Single-center	Incomplete CMV data, limited representativeness
Afshar et al., (2022, Sweden) (34)	600 (400 cases, 200 controls)	Mean age 8.9 yrs (cases)	Family history (OR=11.47), consanguinity (OR=12.48)	TORCH (OR=5.48), meningitis (OR=4.66)	Ototoxic drugs, hypoxia, seizures	Not specified	Multicenter, robust design
Zizlavsky et al., (2022, Indonesia) (37)	535	Neonates to adolescence (mean 5.5 yrs)	Family history 2-3%	TORCH (17.8%): rubella, toxoplasmosis, herpes	Ototoxic drugs (11.2%), herbal medicine (37.4%)	Herbal exposure during pregnancy	Lower maternal education → delayed diagnosis
Fitzgibbons et al., (2021, Australia) (23)	6,735 infants (from 613,027 screened)	Newborns to early infancy (screened at birth)	Family history of PCHL; syndromic associations with PCHL	Not reported	Craniofacial anomalies	None reported	Female gender; non-Indigenous status; bilateral refer result on newborn hearing screening

Table 2. Continued

First author (year, country)	Sample size	Age of participants	Genetic factors	Infectious causes	Perinatal factors	Environmental factors	Other risk factors
Sabbagh et al., (2021, Iran) (25)	5,500 newborns	3-14 days	Consanguineous marriage of parents	Not reported	Low gestational age (<35 weeks); low birth weight; hyperbilirubinemia; NICU stay; craniofacial anomalies; exposure to ototoxic drugs	None reported	Gestational diabetes; convulsions
Anastasio et al., (2021, Brazil) (19)	11,900 neonates	Newborns (1-215 days)	Craniofacial anomalies/syndromes (RR=24.47)	Congenital CMV (RR=9.54)	Ototoxic exposure synergistic with infection	Public hospitals	Strong infection-screening link
Niu et al., (2020, Sweden & China) (18)	296 children (221 BHL, 75 UHL)	Mean 13.2±14.3 months	Family history (59 cases); syndromic and chromosomal abnormalities (37.2% and 21.3% of BHL cases)	Congenital CMV and other perinatal infections (minor proportion)	Low birth weight; neonatal complications; NICU admission	Environmental causes (19.1% of BHL; 14.3% of UHL)	Craniofacial anomalies (30.7% of UHL); oxygen therapy; ear malformations (74.3% of UHL)
Umehara et al., (2019, Japan) (26)	1,071 high-risk infants in NICU; 148 had ABR ≥40 dB	Before NICU discharge (1-33 weeks post-delivery)	Oxygen administration; chromosomal aberrations	Perinatal hypoxia	NICU-related complications	Not reported	Among 148 with abnormal ABR, 102 improved, 5 deteriorated, rest unchanged
Chakrabarti and Ghosh, (2019, India) (28)	10,763	6-14 years (school-aged children)	Not detailed	Not analyzed	Not specified	Not discussed	Higher prevalence in Muslim children—suggesting influence of consanguinity and socioeconomic disparities
Foulon et al., (2019, Belgium) (20)	Not specified	Newborns to 4 years	Not assessed	Congenital CMV (symptomatic vs. asymptomatic)	First-trimester maternal infection, prematurity	Not reported	Symptomatic vs. asymptomatic subgroups; maternal infection timing
Palma et al., (2019, Italy) (35)	45 infants (6 HL cases =13.3%)	Neonatal to 8 years	Not assessed	Congenital vs. acquired CMV	Not discussed	Not reported	Before vs. after neonatal hearing screening
Manotas et al., (2019, Colombia) (30)	Not specified	At birth	Not discussed	Not detailed	Not specified	Not reported	Cases with hearing/visual defects vs. controls
Parab et al., (2018, India) (38)	5,500 newborns	3-14 days	Not discussed	Not specified	Low birth weight, prematurity, hyperbilirubinemia	Not reported	Failed vs. passed newborn screening
Townsend et al., (2013, United Kingdom) (24)	176 CMV, 214 controls	Newborns-5 years	Not studied	Congenital CMV	Not discussed	Not reported	Symptomatic vs. asymptomatic CMV; maternal infection types

HL: Hearing loss, BHL: Bilateral HL, UHL: Unilateral HL, NICU: Neonatal intensive care unit, ABR: Auditory brainstem response, CMV: Cytomegalovirus, OR: Odds ratio, PCHL: Permanent childhood hearing loss, RR: Relative risks

Table 3. Detailed review of studies included in the systematic review (extended)

First author (year, country)	Type of hearing loss	Assessment method for hearing loss	Timing of diagnosis/age at diagnosis	Comparison groups
Khan and Joseph, (2024, South Africa) (17)	CHL (28.5%), SNHL (20.1%), MHL (7.1%)	ABR, OAE, audiometry, tympanometry, case history	Retrospective; age range not precisely detailed in diagnosis	Hearing loss types vs. risk factors; odds ratios used
De Cuyper et al., (2023, Belgium) (22)	SNHL	ABR, audiometry; hearing tracked until ≥ 4 years	At birth and reassessed at ≥ 4 years	Improved vs. stable/deteriorated; with vs. without late-onset HL
Faistauer et al., (2022, Brazil) (27)	Sensorineural or mixed; bilateral	OAE, ABR, audiometry	At first visit, mean age 2 yrs	Etiological categories (e.g., genetic vs. CMV)
Afshar et al., (2022, Sweden) (34)	Severe/profound sensorineural HL	Audiological assessment and medical records (unspecified)	Diagnosed before cochlear implantation (not age-specified)	Cases (HL) vs. Controls (no HL)
Zizlavsky et al., (2022, Indonesia) (37)	Sensorineural, conductive, and mixed types across neonates to adolescents	Audiometry, tympanometry, otoscopic and clinical evaluation; TORCH serology	Neonates to adolescence (mean age 5.5 years)	Children with vs. without identifiable risk factors (family history, TORCH infections, ototoxic drugs, herbal exposure, low maternal education)
Fitzgibbons et al., (2021, Australia) (23)	Sensorineural, conductive, mixed, ANSD	OAE, ABR, tympanometry, ASSR	Within first few weeks after referral	With vs. without risk factors; bilateral vs. unilateral refer; by risk factor
Sabbagh et al., (2021, Iran) (25)	62.5% bilateral, 37.5% unilateral; mostly right-sided	TEOAE, AABR, diagnostic ABR, ASSR, tympanometry	Post-screening at 3-14 days, confirmed via ABR	Cases (refer group) vs. controls (pass group)
Anastasio et al., (2021, Brazil) (19)	Sensorineural (75%), auditory neuropathy (20.8%), 1 conductive	OAE, AABR, diagnostic ABR, immittance, tone-ABR	Confirmed at median age of 115 days (range 22-361)	Low vs. high-risk; isolated vs combined risk factors
Niu et al., (2020, Sweden & China) (18)	SNHL, CHL, Mixed (BHL and UHL analyzed separately)	ABR, ASSR, audiometry, OAE, tympanometry, imaging	Mean 13.2 ± 14.3 months	BHL vs. UHL risk factors and etiologies
Umehara et al., (2019, Japan) (26)	Sensorineural HL (uni- or bilateral)	Auditory Brainstem Response (ABR)	Before NICU discharge (1-33 weeks after delivery)	Improved vs. deteriorated vs. unchanged ABR threshold
Chakrabarti and Ghosh, (2019, India) (28)	Sensorineural hearing loss (severe/profound); higher prevalence in Muslim children	Pure tone audiometry, otoscopy, impedance testing	Diagnosed during school assessment (age 6-14)	None specified
Foulon et al., (2019, Belgium) (20)	Sensorineural hearing loss (unilateral and bilateral)	OAE, ABR, tympanometry, follow-up tests up to 4 years	Within 2 weeks of birth; follow-up until age 4	Symptomatic vs. asymptomatic; maternal infection timings
Palma et al., (2019, Italy) (35)	Sensorineural HL; 6/45 had HL (13%) bilateral & unilateral	TEOAE, ABR, audiological surveillance	Within first weeks; follow-up to 8 years	cCMV vs. aCMV; before vs after neonatal hearing screening
Manotas et al., (2019, Colombia) (30)	Sensorineural or conductive (e.g., microtia); detailed breakdown not provided	Clinical diagnosis and coding via national birth defects registry	At birth	Cases with visual/hearing defects vs. birth defect-free controls
Parab et al., (2018, India) (38)	Bilateral (62.5%), unilateral (37.5%), mostly right ear	TEOAE, AABR, diagnostic ABR, ASSR, tympanometry	Initial screen at 3-14 days; ABR confirmed HL	Case (failed screening) vs. control (passed)
Townsend et al., (2013, United Kingdom) (24)	Sensorineural hearing loss (bilateral/unilateral)	OAE, pure-tone audiometry, ABR, Griffiths developmental scale	All moderate/severe outcomes identified by 1 year of age	Symptomatic vs. asymptomatic CMV; maternal infection types

HL: Hearing loss, BHL: Bilateral HL, UHL: Unilateral HL, NICU: Neonatal intensive care unit, ABR: Auditory brainstem response, CMV: Cytomegalovirus, SNHL: Sensorineural hearing loss, OAE: Otoacoustic emissions, CHL: Congenital HL, cCMV: Congenital CMV, AABR: Automated ABR, ASSR: Auditory steady-state response, MHL: Mixed HL, ANSD: Auditory neuropathy spectrum disorder, TEOAE: Transient evoked otoacoustic emissions, aCMV: Congenital cytomegalovirus infection

potential bias. Despite these limitations, the review effectively highlights ongoing dominance of infectious and perinatal factors while emphasizing the emerging importance of hereditary causes. Overall, it offers a valuable, up-to-date synthesis that not only consolidates global evidence but also identifies critical research gaps especially the need for longitudinal, genotype-phenotype, and gene-environment interaction studies to better define the evolving etiology of CHL.

Conclusion

This systematic review synthesized the current observational evidence on the risk factors associated with CHL, with a focus on genetic, infectious, perinatal, environmental, and sociodemographic determinants. Unlike previous reviews that primarily emphasized congenital infections such as CMV or perinatal complications, our study aimed to explore whether there has been a temporal shift in the etiological spectrum, from infectious causes toward a predominance of genetic and hereditary factors, as universal newborn hearing screening and perinatal infection control have expanded globally. However, the analysis revealed a persistent paucity of high-quality genetic studies, particularly from low- and middle-income countries, where diagnostic access to molecular testing remains limited. Consequently, infectious, and perinatal factors continue to dominate the reported risk landscape, highlighting both regional disparities and research gaps. This broader, integrative review therefore not only consolidates global data up to 2025 but also underscores the urgent need for genotype-phenotype correlation studies to better delineate the evolving causes of CHL in different populations.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: T.L., A.C.A., Concept: S.T., Design: A.C.A., Data Collection and/or Processing: T.L., S.T., Analysis or Interpretation: S.T., Literature Search: T.L., S.T., Writing: T.L., A.C.A., S.T.

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Main Points

- **Multifactorial Risk Factors:** Congenital hearing loss (CHL) is associated with multiple risk domains, including genetic (e.g., *GJB2* mutations, consanguinity), infectious (especially congenital CMV and TORCH infections), perinatal (NICU admission, low birth weight, hyperbilirubinemia), and environmental (ototoxic drug exposure) factors.
- **Predominance of Sensorineural Hearing Loss:** The most commonly reported type of CHL across studies was bilateral sensorineural hearing loss, highlighting the need for early audiological screening and intervention.
- **Emphasis on Early Screening and Prevention:** The findings support the implementation of targeted screening programs and preventive strategies focusing on high-risk populations to enable early diagnosis and timely management of CHL.

References

1. Dhadwal S, Kumari S. Evaluation of hearing loss in children. *Azerbaijan Pharm Pharmacother J.* 2024; 23: 61-6. [Crossref]
2. Masava B, Nyoni CN, Botma Y. Scaffolding in health sciences education programmes: an integrative review. *Med Sci Educ.* 2022; 33: 255-73. [Crossref]
3. Renauld JM, Basch ML. Congenital deafness and recent advances towards restoring hearing loss. *Curr Protoc.* 2021; 1: e76. [Crossref]
4. Porcar-Gozalbo N, López-Zamora M, Valles-González B, Cano-Villagrana A. Impact of hearing loss type on linguistic development in children: a cross-sectional study. *Audiol Res.* 2024; 14: 1014-27. [Crossref]
5. Terlektsi E, Kreppner J, Mahon M, Worsfold S, Kennedy CR. Peer relationship experiences of deaf and hard-of-hearing adolescents. *J Deaf Stud Deaf Educ.* 2020; 25: 153-66. [Crossref]
6. Verma RR, Konkimalla A, Thakar A, Sikka K, Singh AC, Khanna T. Prevalence of hearing loss in India. *Natl Med J India.* 2021; 34: 216-22. [Crossref]
7. Barbi M, Binda S, Caroppo S, Calvario A, Germinario C, Bozzi A, et al. Multicity Italian study of congenital cytomegalovirus infection. *Pediatr Infect Dis J.* 2006; 25: 156-9. [Crossref]
8. Takesian AE, Kotak VC, Sanes DH. Developmental hearing loss disrupts synaptic inhibition: implications for auditory processing. *Future Neurol.* 2009; 4: 331-49. [Crossref]
9. Vos B, Noll D, Pigeon M, Bagatto M, Fitzpatrick EM. Risk factors for hearing loss in children: a systematic literature review and meta-analysis protocol. *Syst Rev.* 2019; 8: 1-7. [Crossref]
10. Olusanya BO, Davis AC, Hoffman HJ. Hearing loss: rising prevalence and impact. *Bull World Health Organ.* 2019; 97:

- 646-646A. Erratum in: *Bull World Health Organ.* 2020; 98: 148. [Crossref]
11. Korver AM, Smith RJ, Van Camp G, Schleiss MR, Bitner-Glindzicz MA, Lustig LR, et al. Congenital hearing loss. *Nat Rev Dis Primers.* 2017; 3: 16094. [Crossref]
 12. Choe G, Park SK, Kim BJ. Hearing loss in neonates and infants. *Clin Exp Pediatr.* 2023; 66: 369-76. [Crossref]
 13. Jensen ES, Cayé-Thomasen P, Bodilsen J, Nielsen H, Friis-Hansen L, Christensen T, et al. Hearing Loss in bacterial meningitis revisited-evolution and recovery. *Open Forum Infect Dis.* 2023; 10: ofad056. [Crossref]
 14. Pourarian S, Khademi B, Pishva N, Jamali A. Prevalence of hearing loss in newborns admitted to neonatal intensive care unit. *Iran J Otorhinolaryngol.* 2012; 24: 129-34. [Crossref]
 15. Tsao PC, Lin HC, Shen SP, Chang YC. Exploring predisposing factors of hearing loss in prematurely born children: a nationwide case-control study. *Pediatr Neonatol.* 2025; 66: 37-43. [Crossref]
 16. Jung J, Lee JS, Cho KJ, Yu S, Yoon JH, Yung Gee H, et al. Genetic predisposition to sporadic congenital hearing loss in a pediatric population. *Sci Rep.* 2017; 7: 45973. [Crossref]
 17. Khan NB, Joseph L. Risk factors and hearing outcomes in infants and young children in KwaZulu-Natal, South Africa. *S Afr J Commun Disord.* 2024; 71: e1-11. [Crossref]
 18. Niu K, Brandström A, Skenbäck S, Duan M, Uhlén I. Risk factors and etiology of childhood hearing loss: a cohort review of 296 subjects. *Acta Otolaryngol.* 2020; 140: 668-74. [Crossref]
 19. Anastasio ART, Yamamoto AY, Massuda ET, Manfredi AKS, Cavalcante JM, Lopes BCP, et al. Comprehensive evaluation of risk factors for neonatal hearing loss in a large Brazilian cohort. *J Perinatol.* 2021; 41: 315-23. [Crossref]
 20. Foulon I, De Brucker Y, Buyl R, Lichtert E, Verbruggen K, Piérard D, et al. Hearing loss with congenital cytomegalovirus infection. *Pediatrics.* 2019; 144: e20183095. [Crossref]
 21. Satterfield-Nash A, Umrigar A, Lanzieri TM. Etiology of prelingual hearing loss in the universal newborn hearing screening era: a scoping review. *Otolaryngol Head Neck Surg.* 2020; 163: 662-70. [Crossref]
 22. De Cuyper E, Acke F, Keymeulen A, De Leenheer EMR, Van Hoecke H, Padalko E, et al. Risk factors for hearing loss at birth in newborns with congenital cytomegalovirus infection. *JAMA Otolaryngol Head Neck Surg.* 2023; 149: 122-30. [Crossref]
 23. Fitzgibbons EJ, Driscoll C, Myers J, Nicholls K, Beswick R. Predicting hearing loss from 10 years of universal newborn hearing screening results and risk factors. *Int J Audiol.* 2021; 60: 1030-8. [Crossref]
 24. Townsend CL, Forsgren M, Ahlfors K, Ivarsson SA, Tookey PA, Peckham CS. Long-term outcomes of congenital cytomegalovirus infection in Sweden and the United Kingdom. *Clin Infect Dis.* 2013; 56: 1232-9. [Crossref]
 25. Sabbagh S, Amiri M, Khorramizadeh M, Iranpourmobarake Z, Nickbakht M. Neonatal hearing screening: prevalence of unilateral and bilateral hearing loss and associated risk factors. *Cureus.* 2021; 13: e15947. [Crossref]
 26. Umehara T, Hosokawa S, Kita JY, Takahashi G, Okamura J, Nakanishi H, et al. Risk factors and prognostic factors of hearing impairment in neonatal intensive care unit-treated infants. *Audiol Neurootol.* 2019; 24: 84-9. [Crossref]
 27. Faistauer M, Lang Silva A, Félix TM, Todeschini de Souza L, Bohn R, Selaimen da Costa S, et al. Etiology of early hearing loss in Brazilian children. *Braz J Otorhinolaryngol.* 2022; 88 (Suppl 1): S33-41. [Crossref]
 28. Chakrabarti S, Ghosh N. Prevalence of severe and profound sensorineural hearing loss in school children in West Bengal, India. *Indian J Otolaryngol Head Neck Surg.* 2019; 71(Suppl 2): 1099-106. [Crossref]
 29. Judge PD, Jorgensen E, Lopez-Vazquez M, Roush P, Page TA, Moeller MP, et al. Medical referral patterns and etiologies for children with mild-to-severe hearing loss. *Ear Hear.* 2019; 40: 1001-8. [Crossref]
 30. Manotas M, Sarmiento K, Ibañez-Morantes A, Suárez-Obando F, Gelvez N, López G, et al. Risk factors associated with congenital defects that alter hearing or vision in children born in the city of Bogotá between 2002 and 2016. *Int J Pediatr Otorhinolaryngol.* 2019; 126: 109594. [Crossref]
 31. Sökmen Y, Kaya Odabaş R, Taşpinar A. Prevalence and risk factors of congenital hearing loss in Turkey: a systematic review. *Neonatal Netw.* 2025; 44: 197-209. [Crossref]
 32. Han Y, Li S, Song Y, Sun J, Yan W, Wang J, et al. Risk factors for infant hearing loss: a meta-analysis. *Eur J Pediatr.* 2024; 183: 2401-9. [Crossref]
 33. Fernández-Rueda M, Calvo-Henriquez C, Fernández-Liesa R, García-Fernández A, Pedrero-Tome R, Blázquez-Gamero D, et al. Risk factors associated with late-onset hearing loss in children with congenital cytomegalovirus: a systematic review. *Eur Arch Otorhinolaryngol.* 2025; 282: 1659-76. [Crossref]
 34. Afshar PJ, Afsharmanesh J, Eslahi M, Sheikhbardsiri H, Moghadam MN. Determination risk factors for severe and profound hearing loss in child candidates for cochlear implantation in southeast of Iran during 2014-2020. *BMC Pediatr.* 2022; 22: 62. [Crossref]
 35. Palma S, Roversi MF, Bettini M, Mazzoni S, Pietrosemoli P, Lucaccioni L, et al. Hearing loss in children with congenital cytomegalovirus infection: an 11-year retrospective study based on laboratory database of a tertiary paediatric hospital. *Acta Otorhinolaryngol Ital.* 2019; 39: 40-45. [Crossref]
 36. Alhazmi W. Risk factors associated with hearing impairment in infants and children: a systematic review. *Cureus.* 2023; 15: e40464. [Crossref]

37. Zizlavsky S, Supartono N, Zachreini I, Bashiruddin J, Hajar Haryuna TS, Savitri E, et al. Factors associated with time of diagnosis and habilitation of congenital hearing loss in Indonesia: a multicenter study. *Int J Pediatr Otorhinolaryngol.* 2022; 163: 111369. [Crossref]
38. Parab SR, Khan MM, Kulkarni S, Ghaisas V, Kulkarni P. Neonatal screening for prevalence of hearing impairment in rural areas. *Indian J Otolaryngol Head Neck Surg.* 2018; 70: 380-6. [Crossref]