Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Etiological profile of severe-to-profound sensorineural hearing loss in children undergoing cochlear implantation: the role of brain MRI in the etiological diagnosis of congenital cytomegalovirus

MARCO ALBUQUERQUE

marco.albuquerque@hc.fm.usp.br

Universidade de São Paulo

Marla Monteiro

Universidade de São Paulo

Vitor Lopes Braga

Universidade de São Paulo

Mariana Correggliano

Universidade de São Paulo

Robinson Koji

Universidade de São Paulo

Fernando Kok

Universidade de São Paulo

Research Article

Keywords: sensorineural hearing loss, congenital cytomegalovirus, magnetic resonance imaging, neurodevelopment, leukoencephalopathy, cochlear implant

Posted Date: November 10th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11135174/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Etiological profile of severe-to-profound sensorineural hearing loss in children undergoing cochlear implantation: the role of brain MRI in the etiological diagnosis of congenital cytomegalovirus

Marco Antônio Veloso de Albuquerque, MD, PhD1; Marla Rochana Braga Monteiro, MD1; Vitor Lucas Lopes Braga, MD1; Mariana Rossi Correggliano, MD3; Robinson Koji, MD, PhD2; Fernando Kok, MD, PhD1

ORCID iDs:

- Marco Antônio Veloso de Albuquerque: 0000-0002-7764-0597
- Marla Rochana Braga Monteiro: 0000-0001-8602-3999
- Vitor Lucas Lopes Braga: 0000-0001-8649-3931
- Mariana Rossi Correggliano: 0000-0002-3475-9248
- Robinson Koji: 0000-0001-5164-0786
- Fernando Kok: 0000-0002-7577-9122

Affiliations:

- 1 Department of Neurology, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HCFMUSP), São Paulo, Brazil
- 2 Cochlear Implant Program, Department of Otorhinolaryngology, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HCFMUSP), São Paulo, Brazil
- 3 Neuroradiology, Department of Radiology, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HCFMUSP), São Paulo, Brazil

Corresponding author:
Marco Antônio Veloso de Albuquerque, MD, PhD
Department of Neurology, Hospital das Clínicas, University of São Paulo (HCFMUSP)
Av. Dr. Enéas de Carvalho Aguiar, 255
São Paulo, SP 05403-000, Brazil
Email: marco.albuquerque@hc.fm.usp.br
Phone: +55 11 3069 7878

Running title: Etiology of Pediatric SNHL: Role of Brain MRI

Keywords: sensorineural hearing loss; congenital cytomegalovirus; magnetic resonance imaging; neurodevelopment; leukoencephalopathy; cochlear implant

Abstract

Background: Congenital cytomegalovirus (cCMV) is the leading non-genetic cause of pediatric sensorineural hearing loss (SNHL), but the contribution of brain magnetic resonance imaging (MRI) to its etiological diagnosis remains insufficiently explored. This study aimed to characterize the etiological profile of children with severe-to-profound SNHL undergoing cochlear implant evaluation and to investigate the clinical and neuroimaging spectrum of cCMV infection.

Methods: This retrospective study included 126 children with severe-to-profound SNHL evaluated at a tertiary cochlear implant center. Clinical, etiological, genetic, and neuroimaging data were reviewed. Brain MRI examinations were systematically reassessed by a neuroradiology team, with particular emphasis on white-matter abnormalities.

Results: An etiological diagnosis was established in 76% of cases. Acquired and congenital non-genetic causes accounted for 56 cases (44%), followed by genetic etiologies in 29 (24%). Congenital cytomegalovirus infection was identified in 25 patients (20%), representing the most frequent non-genetic etiology. Brain white-matter abnormalities, a hallmark of cCMV, were diffuse in 17/25 patients (68%), temporal in 4 (16%), periventricular in 2 (8%), and focal in 2 (8%). Three descriptive clinical-radiological groups were outlined: apparently isolated SNHL (n=7), SNHL with neurological involvement (n=14), and classical multisystem cCMV (n=4). Diffuse white-matter abnormalities predominated among patients with neurological manifestations but were also observed in children with apparently isolated hearing loss. Additional structural abnormalities, including ventriculomegaly, intracranial calcifications, parenchymal cysts, and cortical malformations, were more common in the classical multisystem group.

Conclusion: Congenital cytomegalovirus was the leading non-genetic cause of severe-to-profound SNHL in this cohort. White-matter abnormalities frequently represented the primary clue to diagnosis, including in children with apparently isolated hearing loss. These findings support the concept of cCMV as a clinicoradiological spectrum and reinforce preoperative brain MRI, which may represent the final opportunity for reliable brain assessment before cochlear implantation.

1. Background

Congenital sensorineural hearing loss (SNHL) is one of the most common sensory deficits in childhood, affecting approximately 1–3 per 1,000 live births [1]. Severe-to-profound hearing loss has a profound impact on language acquisition, cognitive development, and social integration, and remains one of the principal indications for cochlear implantation [1,2].

The etiological spectrum of pediatric SNHL is highly heterogeneous, encompassing both genetic and acquired disorders [3,4]. Although genetic conditions account for a substantial proportion of congenital hearing loss, congenital infections remain important potentially identifiable causes, particularly in children with early-onset severe disease. Among these, congenital cytomegalovirus (cCMV) infection is the most common congenital infection worldwide, affecting approximately 0.2–2.5% of live births and representing the leading non-genetic cause of pediatric SNHL [5–7].

Congenital CMV infection exhibits a broad clinical spectrum, ranging from apparently isolated hearing loss to severe multisystemic disease. Transmission may occur following primary maternal infection or viral reactivation during pregnancy, and the severity of fetal involvement largely depends on the timing of infection [5]. Neurological manifestations include motor impairment, epilepsy, cognitive deficits, autism spectrum disorder, attention-deficit/hyperactivity disorder, and delayed-onset or progressive hearing loss [5,8,9].

Brain magnetic resonance imaging (MRI) plays an important role in the evaluation of children with congenital CMV infection and may reveal abnormalities reflecting different stages of fetal brain injury. Common neuroimaging findings include white-matter abnormalities, ventriculomegaly, cortical malformations, temporal lobe lesions, intracranial calcifications, and parenchymal cysts [10,11]. Although white-matter abnormalities are among the most frequent MRI findings in cCMV, they are heterogeneous in distribution and should be interpreted within the broader neuroradiological context.

Despite growing recognition of these imaging findings, their contribution to the etiological investigation of children presenting with severe congenital hearing loss remains insufficiently explored. In routine clinical practice, diagnostic evaluation frequently prioritizes genetic testing and temporal bone imaging, whereas abnormalities of the brain parenchyma may receive less attention. Consequently, congenital CMV infection may remain unrecognized, particularly in children presenting with apparently isolated SNHL. This issue is especially relevant before cochlear implantation, as postoperative brain MRI may become substantially limited by implant-related artifacts, reducing the opportunity to recognize characteristic neuroradiological findings.

Therefore, the aim of this study was to characterize the etiological profile of children with severe-to-profound SNHL undergoing cochlear implant evaluation and to investigate the contribution of brain MRI in raising the suspicion of congenital CMV infection during the etiological work-up of these patients. We also sought to describe the clinical and neuroradiological spectrum of cCMV in this population.

2. Methods

This retrospective study included children with severe-to-profound sensorineural hearing loss (SNHL) who were evaluated as candidates for cochlear implantation at a tertiary referral center between 2022 and 2025. All patients underwent a standardized multidisciplinary evaluation including pediatric otorhinolaryngology, pediatric neurology, medical genetics, audiology, speech therapy and neuroradiology.

The study was conducted under Research Protocol No. 65111517.0.0000.0068, approved by the Research Ethics Committee of Hospital das Clínicas, Faculty of Medicine, University of São Paulo (CAPPesq approval No. 2,224,363). Clinical and neuroimaging data were retrospectively reviewed in accordance with institutional ethical standards.

Clinical data were systematically extracted from medical records and included prenatal history (maternal infections and pregnancy-related complications), perinatal factors (prematurity, neonatal intensive care unit admission, hypoxic events, and neonatal complications), developmental milestones, family history of hearing loss, and findings from otorhinolaryngological and neurological evaluations. Neurodevelopmental disorders, including autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), intellectual disability, epilepsy, and cerebral palsy, were also recorded.

As part of the institutional cochlear implant protocol, all patients underwent comprehensive audiological evaluation, temporal bone computed tomography (CT) and inner ear magnetic resonance imaging (MRI). Brain MRI examinations were reviewed whenever available and were specifically requested before cochlear implantation whenever central nervous system involvement or an acquired etiology was suspected. When previous neuroimaging was incomplete, additional brain MRI sequences were obtained or previously acquired examinations were re-evaluated to better characterize cerebral abnormalities.

The etiological investigation included genetic testing for the most common hereditary causes of congenital hearing loss, including GJB2, GJB6, and mitochondrial variant, with syndrome-directed molecular investigations performed whenever clinically indicated. Additional genetic investigations were undertaken in selected unresolved cases according to clinical availability during the study period.

Etiologies were classified into four categories: genetic (syndromic and non-syndromic), acquired/congenital non-genetic (prenatal, perinatal, and postnatal), cochlear malformations, and unknown.

All available brain MRI examinations were independently reviewed by an experienced neuroradiology team blinded to the final etiological diagnosis. White-matter abnormalities were classified according to their distribution (diffuse or focal) and predominant anatomical location (periventricular, temporal, parietal, or occipital). Additional structural abnormalities, including ventriculomegaly, intracranial calcifications, cortical malformations, parenchymal cysts, hippocampal abnormalities, and temporal lobe lesions, were systematically recorded.

Because many children were referred several years after birth, definitive virological confirmation of congenital cytomegalovirus (cCMV) infection was frequently unavailable. Consequently, brain MRI findings were not considered diagnostic in isolation but rather served as the principal clue prompting etiological suspicion. Cases showing a characteristic neuroimaging pattern suggestive of cCMV underwent multidisciplinary review by pediatric neurologists and neuroradiologists. Alternative causes of white-matter abnormalities, including prematurity-related injury, hypoxic-ischemic brain injury, inherited leukoencephalopathies, and other congenital disorders, were systematically considered during the diagnostic work-up. Whenever available, laboratory findings, including neonatal polymerase chain reaction (PCR) or serological investigations, were incorporated into the final diagnostic assessment. Cases considered incompatible with congenital CMV were referred for further etiological investigation.

To frame the clinical description of the cCMV subgroup, patients were organized into three descriptive clinical-radiological groups according to neurological involvement: (1) apparently isolated SNHL, defined as severe-to-profound hearing loss without clinically detectable neurological signs or neurodevelopmental disorders; (2) SNHL with neurological involvement, defined as hearing loss accompanied by one or more neurological or neurodevelopmental manifestations; and (3) classical multisystem cCMV, defined by the co-occurrence of hearing loss with the hallmark systemic and structural features of congenital CMV disease. Neurological status was derived from the standardized multidisciplinary evaluation performed for all patients as part of the institutional cochlear implant protocol; only the grouping itself was performed retrospectively, after data collection. These groups are intended to describe the clinical-radiological spectrum of the cohort and should be regarded as hypothesis-generating rather than as a validated classification system.

Descriptive statistics were used to summarize clinical, etiological, and neuroimaging data. Associations between neuroimaging patterns and the clinical-radiological groups were explored descriptively.

3. Results

3.1 Cohort characteristics

A total of 126 children with severe-to-profound sensorineural hearing loss (SNHL) were included in the study. The mean age at evaluation was 71 months (range, 21–116 months), and males accounted for 62% of the cohort. A positive family history of hearing loss was reported in 13% of patients. The mean age at hearing loss identification was 8 months (range, 0–72 months), indicating early recognition in a substantial proportion of children. The mean age at cochlear implantation was 36 months (range, 6–143 months).

3.2 Etiological distribution

An etiological diagnosis was established in 96 of 126 patients (76%). Non-genetic etiologies were the most frequent cause of severe-to-profound SNHL, accounting for 56 patients (44%), followed by genetic causes in 29 (24%). Ear malformations were identified in 10 patients (8%), whereas no etiology could be established in 31 children (24%). Within the genetic group, non-syndromic forms were slightly more frequent than syndromic forms, representing 15 (51.7%) and 14 (48.3%) cases, respectively.

Among acquired causes, prenatal causes predominated (31/56; 55.4%), including congenital infections and non-infectious congenital conditions, with congenital cytomegalovirus (cCMV) infection representing the single most frequent non-genetic etiology (25 cases). Perinatal causes accounted for 15 cases (26.8%), and postnatal causes for 10 cases (17.8%). The etiology was not defined in 31 cases (24%). The etiological distribution of the cohort is summarized in Table 1.

Table 1. Distribution of etiological categories in children with severe-to-profound SNHL

Cause	n (%)	Details
Genetic (total)	29 (24%)	—
Non-syndromic	15 (51.7% of genetic cases)	*GJB2*, *POU3F4*, *CARD11* and *MT-RNR1*
Syndromic	14 (48.3% of genetic cases)	Waardenburg (4), CHARGE (4), Usher (2), Mowat–Wilson (1), Goldenhar (1), Baraitser–Winter (1)
Acquired / congenital non-genetic (total)	56 (44%)	—
Prenatal infectious	29 (51.8% of acquired cases)	Congenital CMV (25), syphilis (2), toxoplasmosis (1), rubella (1)

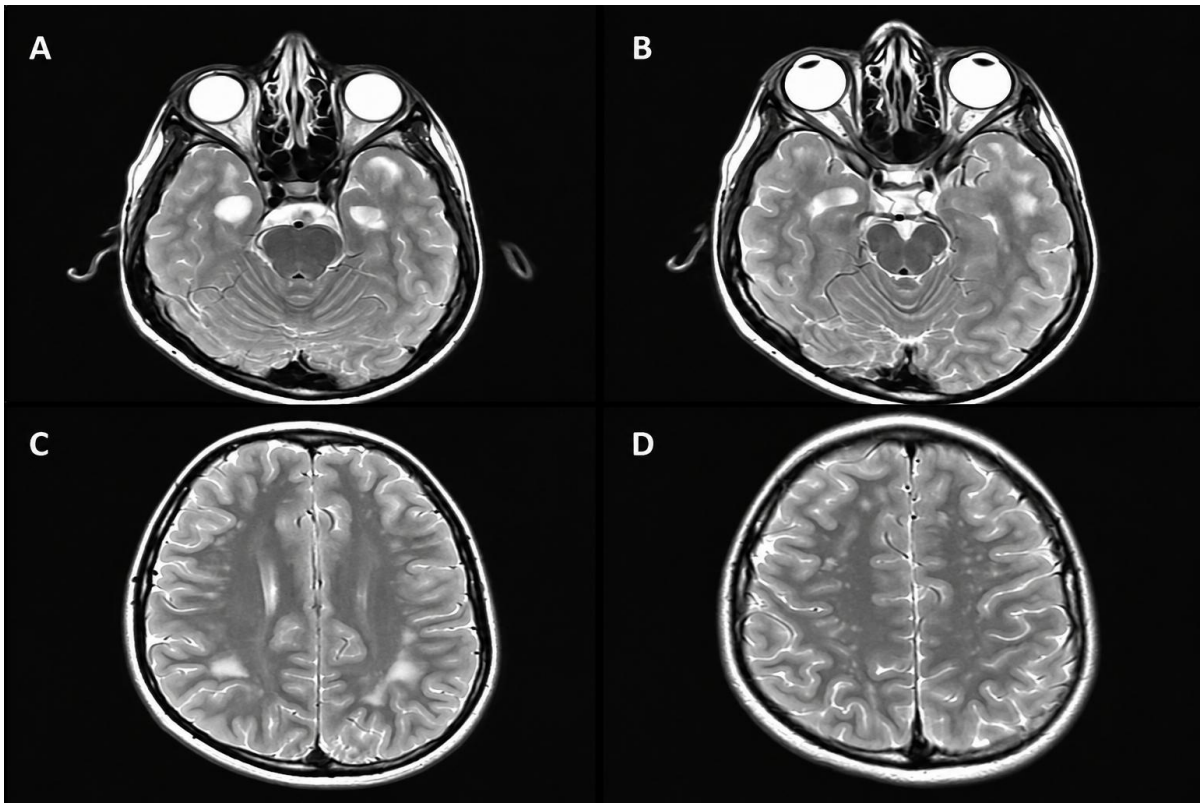
Other congenital non-infectious conditions	2 (3.6% of acquired cases)	Moebius syndrome (2)
Perinatal	15 (26.8% of acquired cases)	Prematurity/ototoxic exposure (7), kernicterus (6), hypoxia (2)
Postnatal	10 (17.8% of acquired cases)	Meningitis, trauma
Cochlear malformations	10 (8%)	—
Unknown (idiopathic)	31 (24%)	No cause identified

Abbreviation: CMV, cytomegalovirus.

3.3 Clinical and neuroimaging spectrum of the cCMV subgroup

Twenty-five patients were diagnosed with congenital cytomegalovirus (cCMV) infection, representing the most common non-genetic etiology in this cohort. Brain MRI demonstrated abnormalities in all patients and frequently represented the first clue raising the suspicion of congenital CMV during the etiological investigation.

White-matter abnormalities were identified in all patients and demonstrated a heterogeneous distribution, including diffuse involvement in 17/25 patients (68%), temporal involvement in 4/25



(16%), periventricular involvement in 2/25 (8%), and focal abnormalities in 2/25 (8%) (Figure 1).

Figure 1. Representative brain MRI findings in children with congenital cytomegalovirus infection. Axial T2- weighted images demonstrate white-matter abnormalities with different patterns: (A–B) focal hyperintensities involving the temporal lobes; (C–D) diffuse white-matter abnormalities affecting periventricular and subcortical regions.

To better characterize the clinical spectrum of cCMV, patients were organized into three descriptive clinical-radiological groups according to their neurological presentation:

- Group 1 – Apparently isolated SNHL (n = 7): severe-to-profound sensorineural hearing loss associated with white-matter abnormalities but without clinically detectable neurological signs or neurodevelopmental disorders.
- Group 2 – SNHL with neurological involvement (n = 14): severe-to-profound sensorineural hearing loss associated with white-matter abnormalities and one or more neurological or neurodevelopmental manifestations, including cerebral palsy, epilepsy, intellectual disability, attention-deficit/hyperactivity disorder, or autism spectrum disorder.
- Group 3 – Classical multisystem cCMV (n = 4): severe-to-profound sensorineural hearing loss associated with the classical manifestations of congenital CMV infection, including microcephaly, chorioretinitis, intracranial calcifications, extensive structural brain abnormalities, and severe cerebral palsy.

The proportion of patients with diffuse white-matter involvement increased monotonically across these groups, from 3/7 (43%) in apparently isolated SNHL to 10/14 (71%) in SNHL with neurological involvement and 4/4 (100%) in classical multisystem cCMV, whereas focal and periventricular patterns clustered at the milder end of the spectrum.

Although diffuse white-matter involvement tended to be associated with neurological manifestations, it was also identified in patients with apparently isolated hearing loss, indicating that the extent of white-matter abnormalities alone does not fully explain clinical severity (Table 2).

Table 2. Relationship between the distribution of white-matter abnormalities on brain MRI and the clinical-radiological groups in children with cCMV

Clinical-radiological group	Diffuse	Temporal	Periventricular	Focal	Total
Group 1 – Apparently isolated SNHL (n=7)	3 (42.9%)	1 (14.3%)	2 (28.6%)	1 (14.3%)	7 (100%)
Group 2 – SNHL with neurological involvement (n=14)	10 (71.4%)	3 (21.4%)	0	1 (7.1%)	14 (100%)
Group 3 – Classical multisystem cCMV (n=4)	4 (100%)	0	0	0	4 (100%)
Total (n=25)	**17 (68%)**	**4 (16%)**	**2 (8%)**	**2 (8%)**	**25 (100%)**

Abbreviation: cCMV, congenital cytomegalovirus.

Additional structural brain abnormalities included ventriculomegaly (16%), intracranial calcifications (12%), parenchymal cysts (12%), polymicrogyria (4%), and hippocampal malrotation (4%). These abnormalities were predominantly observed in the classical multisystem group, suggesting that increasing neurological severity may reflect the cumulative burden of cerebral injury rather than white-matter abnormalities alone.

4. Discussion

This study provides a comprehensive etiological characterization of children with severe-to-profound sensorineural hearing loss (SNHL) undergoing cochlear implant evaluation at a tertiary referral center, with particular emphasis on the contribution of brain MRI to the recognition of congenital

cytomegalovirus (cCMV) infection. An etiological diagnosis was established in 76% of patients, reflecting the value of a systematic multidisciplinary investigation integrating audiological, neurological, genetic, and neuroimaging assessments. These findings are comparable with previous reports from tertiary cochlear implant centers, in which extensive etiological investigation substantially increases diagnostic yield [15–18].

Genetic disorders accounted for approximately one-quarter of cases, confirming their major contribution to congenital SNHL. Nevertheless, non-genetic etiologies predominated in our cohort, with prenatal disorders representing the largest subgroup. Among these, congenital CMV infection emerged as the most frequent individual non-genetic cause, accounting for 20% of the entire cohort. This observation is consistent with previous epidemiological studies identifying cCMV as the leading acquired cause of childhood SNHL worldwide [6–8,19].

The principal contribution of our study is the demonstration that characteristic brain MRI abnormalities may represent the first clue raising the suspicion of congenital CMV infection during the etiological investigation of children with otherwise unexplained severe congenital hearing loss. Importantly, our intention is not to suggest that isolated white-matter abnormalities are diagnostic of cCMV. Rather, the diagnosis resulted from integration of neuroimaging findings with neurological evaluation, exclusion of alternative etiologies, and available laboratory information within a multidisciplinary setting.

White-matter abnormalities were identified in all patients with cCMV but exhibited heterogeneous imaging patterns, including diffuse, temporal, periventricular, and focal involvement. These abnormalities occurred across the entire clinical spectrum, from children with apparently isolated hearing loss to those with severe systemic neurological disease. Although diffuse white-matter abnormalities predominated among patients with neurological manifestations and were present in all patients in the classical multisystem group, they were also observed in several children with apparently isolated SNHL.

Conversely, focal and periventricular abnormalities occurred predominantly in children without significant neurological impairment. These findings indicate that the extent of white-matter abnormalities alone does not determine neurological severity and reinforce the concept that these lesions should be interpreted within the broader neuroradiological context rather than as isolated diagnostic markers [19,20].

Rather than a diagnostic classification, the three-group framework serves to order the clinical-radiological spectrum of cCMV. Congenital CMV should not be viewed simply as either symptomatic or asymptomatic: our findings suggest a clinicoradiological continuum in which apparently isolated congenital hearing loss may represent the mildest expression of fetal brain involvement, whereas progressively greater neurological impairment is associated with an increasing burden of structural

brain abnormalities. Notably, 43% of patients without any clinical neurological sign already exhibited diffuse white-matter involvement, indicating that a normal neurological examination does not exclude cerebral involvement in cCMV.

This interpretation is biologically plausible and consistent with current knowledge of the neurotropism of CMV. Experimental and imaging studies have demonstrated that fetal CMV infection disrupts neuronal proliferation, migration, and cortical organization, producing a wide range of abnormalities that vary according to the timing and severity of infection [21–23].

Accordingly, patients with apparently isolated SNHL in our cohort frequently exhibited white-matter abnormalities without additional structural lesions, whereas patients in the classical multisystem group more commonly demonstrated ventriculomegaly, intracranial calcifications, parenchymal cysts, cortical malformations, and other structural abnormalities. Together, these findings support the hypothesis that neurological severity reflects the cumulative burden of cerebral injury rather than the extent of white-matter abnormalities alone.

From a clinical perspective, our findings have direct implications for the etiological investigation of children undergoing cochlear implant evaluation. In routine practice, diagnostic work-up frequently prioritizes genetic testing and temporal bone imaging, whereas detailed evaluation of the brain parenchyma may receive less attention. In our experience, several children were referred after cochlear implantation without an established etiological diagnosis. In these patients, postoperative brain MRI was frequently limited by implant-related artifacts, preventing recognition of characteristic neuroimaging patterns that could have raised suspicion of congenital CMV before implantation.

Our results therefore suggest that, in children with severe-to-profound SNHL of undefined etiology after genetic testing, brain MRI should be obtained before cochlear implantation: not because MRI alone establishes the diagnosis of cCMV, but because recognition of a characteristic constellation of neuroradiological findings may direct appropriate etiological investigation while this diagnostic opportunity remains available. In this setting, the preoperative examination may represent the last reliable opportunity for parenchymal brain assessment.

This study has several limitations. Its retrospective design introduces potential selection and information biases, and the relatively small number of patients with cCMV precluded more robust analyses of specific neuroimaging patterns and neurological outcomes. Furthermore, the proposed clinical-radiological grouping is exploratory and should be interpreted as hypothesis-generating. Neurological evaluations were performed as part of routine clinical care rather than according to a standardized prospective protocol, and MRI examinations were obtained over an extended study period using different imaging protocols. However, all available studies were systematically reviewed by an experienced neuroradiology team, minimizing variability in image interpretation.

5. Conclusions

Congenital cytomegalovirus was the leading non-genetic cause of severe-to-profound SNHL in this cohort. White-matter abnormalities on brain MRI frequently represented the primary clue to the diagnosis, including in children with apparently isolated hearing loss, supporting the concept of cCMV as a clinicoradiological spectrum. These findings provide real-world evidence from a large tertiary cochlear implant program and reinforce the value of systematic preoperative brain MRI, which may represent the final opportunity for reliable brain assessment before cochlear implantation, thereby improving etiological diagnosis and facilitating appropriate neurological assessment and multidisciplinary follow-up.

Declarations

Abbreviations

ADHD: Attention-deficit/hyperactivity disorder; **ASD:** Autism spectrum disorder; **cCMV:** Congenital cytomegalovirus; CAPPesq: Comitê de Ética para Análise de Projetos de Pesquisa (Research Ethics Committee of the Hospital das Clínicas, FMUSP); CMV: Cytomegalovirus; CT: Computed tomography; MRI: Magnetic resonance imaging; PCR: Polymerase chain reaction; SNHL: Sensorineural hearing loss.

Ethics approval and consent to participate

This study was performed in accordance with the Declaration of Helsinki and with relevant institutional and national guidelines and regulations. It was approved by the Research Ethics Committee of the Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (CAPPesq; Research Protocol No. 65111517.0.0000.0068; approval No. 2.224.363; approved on August 17, 2017). This was a retrospective study based on review of clinical records and neuroimaging data. Written informed consent to participate was obtained from the parents or legal guardians of all participants, all of whom were younger than 16 years of age.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

The following statements apply in accordance with the CRediT (Contributor Roles Taxonomy):

- **Marco Antônio Veloso de Albuquerque (MAV):** Conceptualization, Formal analysis, Supervision, Writing – review & editing.
- **Marla Rochana Braga Monteiro (MRB)**: Data curation, Investigation.
- **Vitor Lucas Lopes Braga (VLB):** Data curation, Investigation.
- **Mariana Rossi Correggliano (MRC):** Investigation.
- **Robinson Koji (RK)**: Writing – review & editing.
- **Fernando Kok (FK):** Writing – review & editing.

All authors read and approved the final manuscript.

Acknowledgements

The authors thank the multidisciplinary team of the Cochlear Implant Program at the Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, for their support in the evaluation and management of the patients included in this study.

References

1. Smith RJH, Bale JF Jr, White KR. Sensorineural hearing loss in children. Lancet. 2005;365:879–890.
2. Morton CC, Nance WE. Newborn hearing screening: a silent revolution. N Engl J Med. 2006;354:2151–2164.
3. van Beeck Calkoen EAA, Engel MSD, van de Kamp JM, et al. The etiological evaluation of sensorineural hearing loss in children. Eur J Pediatr. 2019;178:1195–1205.
4. Robson CD, Lewis M, D'Arco F. Non-syndromic sensorineural hearing loss in children. Neuroimaging Clin N Am. 2023;33(4):531–542.
5. Leruez-Ville M, Foulon I, Pass R, Ville Y. Cytomegalovirus infection during pregnancy: state of the science. Am J Obstet Gynecol. 2020;223:330–349.
6. Lanzieri TM, Dollard SC, Bialek SR, Grosse SD. Systematic review of the birth prevalence of congenital cytomegalovirus infection. Int J Infect Dis. 2014;22:44–48.
7. Boppana SB, Ross SA, Fowler KB. Congenital cytomegalovirus infection: clinical outcome. Clin Infect Dis. 2013;57(Suppl 4):S178–S181.
8. Fowler KB, Boppana SB. Congenital cytomegalovirus infection. Semin Perinatol. 2018;42(3):149–154.

9. Chilosi AM, Comparini A, Scusa MF, et al. Neurodevelopmental disorders in children with severe-to-profound SNHL. Dev Med Child Neurol. 2010;52:856–862.
10. Manara R, Balao L, Baracchini C, et al. Brain MRI findings in symptomatic congenital cytomegalovirus infection. Pediatr Radiol. 2011;41:962–970.
11. Fink KR, Thapa MM, Ishak GE, Pruthi S. Neuroimaging of pediatric central nervous system cytomegalovirus infection. Radiographics. 2010;30:1779–1796.
12. Alarcón A, de Vries LS, Parodi A, Arnáez J, Cabañas F, Steggerda S, et al. Neuroimaging in infants with congenital cytomegalovirus infection and its correlation with outcome: emphasis on white matter abnormalities. Arch Dis Child Fetal Neonatal Ed. 2024;109(2):151–158.
13. Diogo MC, Glatter S, Binder J, Kiss H, Prayer D. The MRI spectrum of congenital cytomegalovirus infection. Prenat Diagn. 2020;40(1):110–124.
14. Xiang J, Jin Y, Song N, Chen S, et al. Comprehensive genetic testing improves the clinical diagnosis and medical management of pediatric patients with isolated hearing loss. BMC Med Genomics. 2022;15(1):142.
15. Boudewyns A, van den Ende J, Declau F, Wuyts W, Peeters N, Brandt AHD, et al. Etiological work-up in referrals from neonatal hearing screening: 20 years of experience. Otol Neurotol. 2020;41(9):1240–1248.
16. Kim YS, Kim Y, Jeon HW, Yi N, Lee SY, Kim Y, et al. Full etiologic spectrum of pediatric severe to profound hearing loss of consecutive 119 cases. Sci Rep. 2022;12(1):12335.
17. Morris JA, Gonzalez T, Blanton SH, et al. GJB2-related hearing loss: genotype-phenotype correlations, natural history, and emerging therapeutic strategies. Int J Mol Sci. 2026;27(1):491.
18. Gooch C, Rudy N, Smith RJ, Robin NH. Genetic testing hearing loss: the challenge of non-syndromic mimics. Int J Pediatr Otorhinolaryngol. 2021;150:110872.
19. Dreher AM, Arora N, Fowler KB, et al. Spectrum of disease and outcome in children with symptomatic congenital cytomegalovirus infection. J Pediatr. 2014;164(4):855–859.
20. Barkai G, Katorza E, Lassman S, Levinberg I, et al. Association between white matter T2 hyperintense signals in fetal brain magnetic resonance imaging and neurodevelopment of fetuses with cytomegalovirus infection. Diagnostics (Basel). 2024;14(8):797.
21. Vande Walle C, Keymeulen A, Schiettecatte E, Acke F, Dhooge I, Smets K, et al. Brain MRI findings in newborns with congenital cytomegalovirus infection: results from a large cohort study. Eur Radiol. 2021;31(10):8001–8010.
22. van der Knaap MS, Vermeulen G, Barkhof F, Hart AA, Loeber JG, Weel JF. Pattern of white matter abnormalities at MR imaging: use of polymerase chain reaction testing of Guthrie cards to link pattern with congenital cytomegalovirus infection. Radiology. 2004;230(2):529–536.

23. Kwak M, Yum MS, Yeh HR, Kim HJ, Ko TS. Brain magnetic resonance imaging findings of congenital cytomegalovirus infection as a prognostic factor for neurological outcome. Pediatr Neurol. 2018;83:14–18.