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Perinatal risk factors and preliminary prediction of conductive hearing loss in infancy

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ABSTRACT

Purpose: To investigate the perinatal risk factors for conductive hearing loss (CHL) in infancy and develop an initial prediction model to facilitate accurate diagnosis and early detection of CHL. Method: This retrospective study utilized data from the Newborn Cohort Study of Hearing Loss (ChiCTR2100049765). Infants who underwent diagnostic audiological assessments at our hospital between January 2003 and June 2024 were included. Data analysis was conducted using R (version 4.4.1) to construct an initial prediction model for CHL in infancy, applying the LASSO regression technique. Results: A total of 661 infants (1322 ears) were included, with 1253 ears in the normal hearing group and 69 ears in the CHL group. Statistically significant differences were observed between the groups in the following factors: parent-reported infant response to sound, craniofacial deformities, neonatal hemolysis, jaundice treatment, and neonatal hypoglycemia. A multivariate prediction model and nomogram for CHL in infancy were developed and validated, achieving an accuracy of 92.5% and a specificity of 91.3%. Conclusions:This study identified key risk factors for CHL in infancy and developed a preliminary predictive model, improving the diagnostic accuracy for CHL. Improved diagnostic precision can decrease misdiagnoses, reduce delays in treatment, and limit unnecessary antimicrobial prescriptions for infants.

KEYWORDS

conductive hearing loss, infant, perinatal, risk factors, prediction.

1 Introduction

Conductive hearing loss (CHL) in infancy encompasses conditions such as secretory otitis media, acute otitis media, and chronic otitis media (Lieu et al., 2020; Prasad et al., 2024; World Health Organization, 2021). The prevalence of CHL in infancy is estimated at approximately 0.22 per 1000 infants. Bamford et al. reported a prevalence of moderate or more severe CHL at 0.03 per 1,000, based on newborn hearing screenings and follow-up data in infancy (2019 Summary of Hearing Screening, 2021; 2019 Type and Severity Summary, 2021; Uus and Bamford, 2006). CHL in infancy is thus a primary cause of pediatric ENT emergency visits, antibiotic prescriptions, and surgical interventions. Complications and sequelae related to conductive otitis media also represent significant causes of hearing impairment, particularly in developing countries (Brewster et al., 2023; Daggett et al., 2022; Krueger et al., 2024; Pitaro et al., 2019; Rothman et al., 2018).

Clinical signs of CHL in infancy typically include ear scratching, irritability, and crying. Given their young age and limited language skills, infants cannot communicate symptoms effectively, often resulting in delayed diagnoses. Such delays can lead to inappropriate antibiotic use and progression of illness, including hindered speech development, reduced attention, and, in severe cases, mastoiditis, meningitis, brain abscesses, or life-threatening conditions (Merchant and Neely, 2023).

Accurate diagnosis and early identification are thus critical for effective CHL treatment in infancy. However, diagnosing CHL in infants requires substantial clinical experience, posing challenges for less experienced doctors. Despite advances in clinician training, dissemination of clinical guidelines, acoustic conductance measurements, and other technologies (Higgins Joyce et al., 2019; McCreery et al., 2023; Merchant et al., 2021; Paul et al., 2020), diagnostic accuracy among primary care and pediatric providers has remained at approximately 70% or lower (Jones and Kaleida, 2003; Pichichero and Poole, 2001; Pichichero, 2002; Rosenfeld, 2002), highlighting the need for further innovation and improvement in diagnostic approaches.

As a designated children's hearing diagnostic center in Beijing, we have gathered extensive clinical data and diagnostic experience since our establishment in 2003. Drawing on this resource, we analyzed perinatal risk factors for CHL in infancy based on a preestablished cohort of children with hearing loss. We also

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developed a preliminary prediction model for CHL in infancy using a machine learning algorithm to offer a practical reference for accurate diagnosis and early identification of CHL in clinical settings.

2 Methods

2.1 Study design, ethics, setting and participants

This study was a retrospective analysis conducted within the Newborn Cohort Study of Hearing Loss (ChiCTR2100049765) at the Chinese PLA General Hospital. The participants included infants who received diagnostic audiological evaluations at our hospital from January 2003 to June 2024. These infants aged 0–1 years, referred from various maternal and child health institutions in Beijing, underwent thorough audiological assessments. The study followed the ethical guidelines outlined in the Helsinki Declaration and received approval from the Research Ethics Committee of the Chinese PLA General Hospital. Written informed consent was obtained from the guardians of all participants.

2.2 Data collection and processing

Data collection was primarily conducted using case report forms, where comprehensive inquiries were documented. Epidata 3.1 software facilitated data entry, with verification based on clinic IDs and case numbers. Recorded data encompassed basic characteristics, perinatal factors, and audiological data.

2.3 Inclusion exclusion and diagnostic criteria

Inclusion criteria were: (1) infants who completed audiological diagnosis, and (2) infants with signed informed consent.

Exclusion criteria were: (1) infants with incomplete essential medical records, and (2) infants without signed informed consent.

Diagnostic criteria for CHL included a tympanogram with type B or C acoustic impedance, air-conducted ABR thresholds exceeding 35 dBnHL, and normal bone-conducted thresholds (Expert Group on Universal Newborns Hearing Screening, 2018; Joint Commission on Infant Hearing, 2019).

2.4 Statistical analysis

Data analysis was conducted using R (version 4.4.1). Descriptive and statistical analyses were performed, with counts and percentages calculated for categorical variables, and means with standard deviations (SDs) for quantitative variables. Comparisons between groups employed the Student's t-test, Wilcoxon rank-sum test, and Chi-square test. A $p<0.05$ in two-tailed tests was considered statistically significant.

3 Results

3.1 Baseline characteristics of the participates

From a total of 2082 children in the Newborn Cohort Study of Hearing Loss, 661 infants (1322 ears) were selected, with 1253 ears in the normal hearing group and 69 ears in the CHL group. Baseline characteristics of the participants are presented in Table 1. The age range of the study subjects was 3 to 12 months, with a median age of 3.0 (3.0, 5.0) months and an average age of 4.3 ± 2.3 months.

Table 1 Baseline characteristics of the participates.

Characteristics	Participants (No)	Percent (%)
gender		
male	771	58.32
female	551	41.68
response to sound		
good	880	66.57
average	420	31.77
bad	22	1.66
maternal abortion history		
no	824	62.33
yes	498	37.67
maternal diabetes		
no	1169	88.43
yes	153	11.57
maternal hypertension		
no	1277	96.60
yes	45	3.40
delivery		
no	690	52.19
yes	632	47.81
amniotic fluid pollution		
no	1244	94.10
yes	78	5.90
fetal distress		
no	1255	94.93
yes	67	5.41
craniofacial deformity		
no	1236	93.50
yes	86	6.51
NICU history		
no	1149	86.91
yes	173	13.09
neonatal pneumonia		
no	1215	91.91
yes	107	8.09
neonatal hemolysis		
no	1301	98.41
yes	21	1.59
jaundice treatment		
no	936	70.80
medication	185	13.99
light therapy	201	15.20
neonatal hypoglycemia		0.00
no	1293	97.67
yes	29	2.19

3.2 Comparison of risk factors of infants in the two groups

The comparative analysis of risk factors between the CHL group and the normal hearing group is shown in Table 2. Statistically significant differences were observed between the groups in factors such as parent-reported infant response to sound, cranio-

Table 2 Comparison of risk factors of infants in the two groups.

Characteristics	Normal	CHL	*x*2	*p*
gender			3.30	0.07
male	738	33		
female	515	36		
response to sound			60.49	0.00
good	854	26		
average	385	35		
bad	14	8		
maternal abortion history			0.40	0.52
no	778	46		
yes	475	23		
maternal diabetes			0.00	1.00
no	1108	61		
yes	145	8		
maternal hypertension			0.33	0.56
no	1209	68		
yes	44	1		
delivery			0.38	0.54
no	651	39		
yes	602	30		
amniotic fluid pollution			0.56	0.45
no	1181	63		
yes	72	6		
fetal distress			11.29	1.00
no	1190	65		
yes	63	4		
craniofacial deformity			42.56	0.00
no	1185	51		
yes	68	18		
NICU history			1.19	0.28
no	1092	57		
yes	161	12		
neonatal pneumonia			0.89	0.34
no	1956	206		
yes	120	18		
neonatal hemolysis			18.97	0.00
no	1238	63		
yes	15	6		
jaundice treatment			14.22	0.00
no	893	43		
medication	180	5		
light therapy	180	21		
neonatal hypoglycemia			0.00	0.00
no	1229	64		
yes	24	5		

CHL: conductive hearing loss

facial deformities, neonatal hemolysis, jaundice treatment, and neonatal hypoglycemia.

3.3 *Preliminary prediction model for CHL in infancy*

Eight clinically significant predictors were identified using LASSO regression (Figure 1), and these were incorporated into a multivariate prediction model for CHL in infancy using Logistic regression (Table 3). Validation with test group data revealed an accuracy of 92.5%, a specificity of 91.3%, and an area under the ROC curve of 0.7366.

3.4 *Nomograph of the CHL in infancy*

A nomogram for CHL in infancy was also developed based on perinatal characteristics to aid in accurate diagnosis (Figure 2).

4 Discussion

Conductive hearing loss (CHL), often manifesting as acute or chronic otitis media, is notably prevalent in infancy (Lieu et al., 2020; World Health Organization, 2021). Due to infants' young age and limited language abilities, accurately diagnosing CHL requires substantial clinical experience, presenting challenges for less experienced clinicians. This study identified key risk factors for CHL in infancy and developed a preliminary predictive model using data from a pediatric hearing loss cohort spanning over 20 years. With an identification accuracy of 92.5% and specificity of 91.3%, this model offers a valuable reference tool for clinical practice.

Infant CHL can impact both speech and personality development and, in severe cases, may lead to complications such as mastoiditis, meningitis, brain abscess, and potentially life-threatening conditions. Therefore, early identification and diagnosis, followed by timely intervention, are crucial for reversing and improving CHL prognosis in infancy. Prediction based on risk factors and the LASSO algorithm can reduce diagnostic delays. The CHL predictive model can also help lower healthcare burdens and reduce morbidity associated with misdiagnosis (Barzilay et al., 2024; Bower et al., 2023; Joint Committee on Infant Hearing, 2007; Shaikh et al., 2024).

Although hearing loss risk factors span all life stages, perinatal risk factors are particularly significant in infants. Prior research has highlighted maternal gestational diabetes, hypertension, anemia, amniotic fluid abnormalities, preterm birth, low birth weight, hyperbilirubinemia, neonatal infections, prolonged mechanical ventilation, and a history of neonatal pneumonia as high-risk factors for CHL in infants and young children (Aithal et al., 2012; American Academy of Pediatrics, 2007; Collins et al., 2022; de Lyra-Silva et al., 2015; Okada et al., 2017; Sung et al., 2019; Tang et al., 2022). In our study, a machine learning algorithm was employed to identify significant predictors of CHL in infancy, ultimately selecting eight perinatal risk factors: gender, amniotic fluid contamination, parent-reported infant response to sound, number of births, craniofacial deformities, neonatal hemolysis, jaundice treatment, and neonatal hypoglycemia.

Previous studies have noted gender differences in the prevalence of CHL, potentially linked to variations in acoustic conductance resistance and energy reflectivity between genders (Gai et al., 2023; Liu et al., 2021). In this study, we observed that CHL in infants was associated with gender, which may relate to differences in the equivalent volume of the external auditory canal between male and female infants (Jung et al., 2021; Morita et al., 2018; Morita et al., 2019; Morita et al., 2022). Additionally, a statistically signifi-

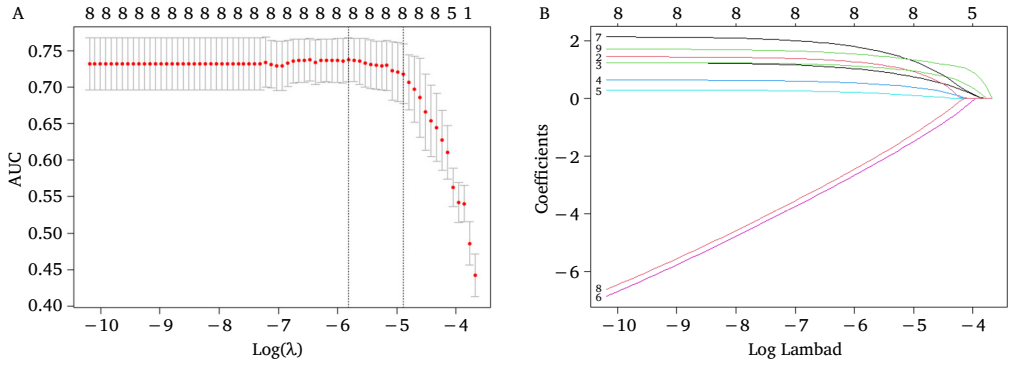

Figure 1 Variables selected for predictive models with LASSO regression. (A) Optimal parameters selected by Ten-fold Cross-Validation. (B) Coefficient distribution of the selected features by LASSO regression.

Table 3 Parameters of the prediction model of conductive hearing loss in infancy.

Characteristics	Coef	S.E.	*Wald Z*	*p*
Intercept	−4.08	0.31	−13.36	0.00
gender	0.48	0.27	1.80	0.07
response to sound	2.94	0.52	5.61	0.00
delivery	0.27	0.13	0.47	0.14
amniotic fluid pollution	0.77	0.48	1.62	0.11
craniofacial deformities	1.80	0.34	5.36	0.00
newborn hemolysis	1.93	0.62	3.12	0.00
jaundice treatment	0.50	0.33	1.54	0.12
neonatal hypoglycemia	0.74	0.60	1.24	0.12

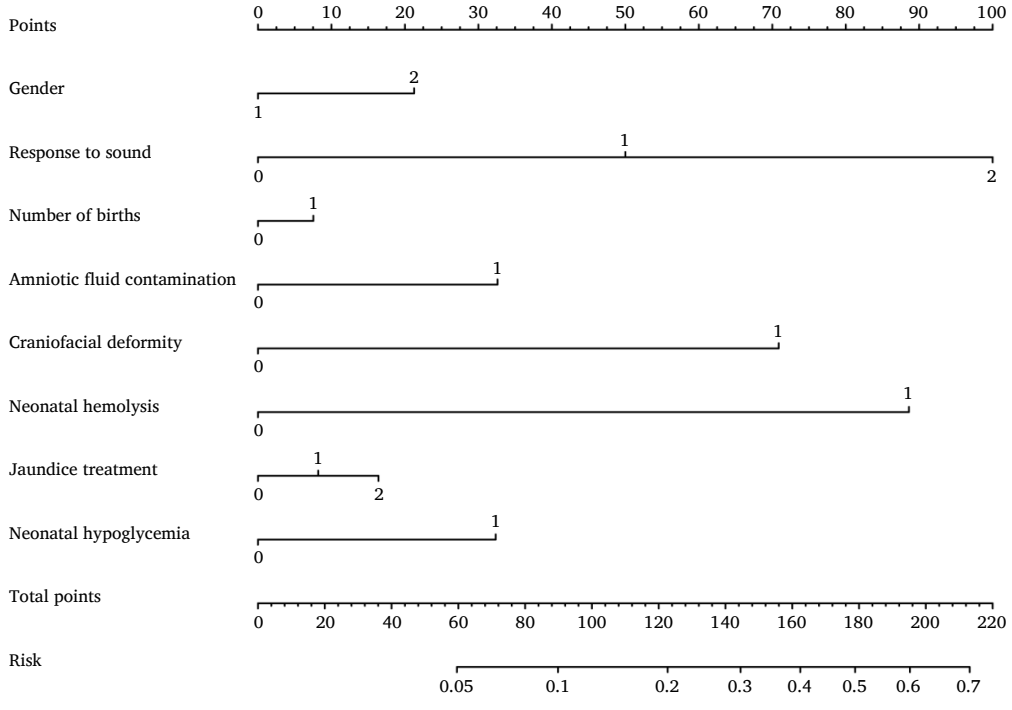

Figure 2 Nomogram prediction model for conductive hearing loss in infancy. The predictors of the nomogram include gender, amniotic fluid contamination, parent-reported infant response to sound, number of births, craniofacial deformities, neonatal hemolysis, jaundice treatment, and neonatal hypoglycemia.

cant difference was found in the average peak pressure within the tympanic cavity across genders (Coathup et al., 2020; Do et al., 2020; Kørvel-Hanquist et al., 2016; van Ingen et al., 2021).

Intrauterine amniotic fluid contamination during pregnancy has been identified as an independent risk factor for CHL in infants. Contaminated amniotic fluid can elevate inflammatory

factor levels, which, through inter-regulatory effects, influences inflammatory exudation in the middle ear and can even alter the middle ear mucosa. These changes may prolong inflammation, worsening otitis media symptoms in affected children. Other factors, including gender, parent-reported infant response to sound, number of births, craniofacial deformities, neonatal hemolysis, jaundice treatment, and neonatal hypoglycemia, can also heighten the risk of infections in infants (Adegbiji et al., 2018; Horáčková et al., 2020). Coupled with the anatomical traits of infants' short, wide, and straight eustachian tubes and their immature immune defenses, infants are more vulnerable to pathogens and, consequently, to developing CHL.

This study has certain limitations. First, it is based on data from a single large tertiary hospital, and lacks external validation from other centers; thus, multi-center validation will be crucial in future research. Second, while we developed a prediction model for CHL in infancy, further studies are needed to explore prognostic models.

5 Conclusions

In conclusion, we analysed perinatal risk factors for CHL in infancy and developed a preliminary predictive model for CHL. This model may improve the accuracy of CHL diagnosis, thereby reducing misdiagnosis, treatment delays, and unnecessary antimicrobial prescriptions in infants.

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Declaration of interest

The authors declare that they have no conflicts of interest.

Author contributions

QW, and JZ designed the study and wrote the paper. JZ, MZ, WS, HD, LL, YG and DW, were involved in data processing, and analysis. All authors read and approved the final manuscript.

Data availability statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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