Am J Transl Res 2025;17(9):6999-7009
www.ajtr.org /ISSN:1943-8141/AJTR0164513

Original Article

IgM mediated cefotaxime resistance of *Streptococcus pneumoniae* is linked to hearing loss in adult acute otitis media

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Received March 13, 2025; Accepted August 17, 2025; Epub September 15, 2025; Published September 30, 2025

Abstract: Objective: To investigate cefotaxime resistance in *Streptococcus pneumoniae* among adult acute otitis media (AOM) patients, its association with hearing loss, and the mediating role of immunoglobulin M (IgM). Methods: A retrospective cohort study was conducted, enrolling 188 adult AOM patients treated between January 2018 and December 2023. *Streptococcus pneumoniae* infection was confirmed via bacterial culture of ear secretions, and cefotaxime susceptibility was tested using the disc diffusion method. Hearing loss was diagnosed based on World Health Organization (WHO) criteria using tympanometry and pure tone audiometry. Univariate and multivariate logistic regression analyses were performed to assess the correlation between cefotaxime resistance and hearing loss. Spearman correlation analysis evaluated their association, and mediation analysis using Bootstrap method (5,000 resamples) was applied to examine the mediating effect of IgM. Results: Cefotaxime resistance was significantly positively correlated with hearing loss ($r = 0.25$, $P < 0.001$). The hearing loss group exhibited higher prevalence of diabetes history, tympanic effusion, chronic ear disease history, and cefotaxime resistance ($P < 0.05$). IgM levels were significantly lower in the hearing loss group ($P < 0.001$) and partially mediated the association between cefotaxime resistance and hearing loss ($P = 0.033$), accounting for 26.9% of the total effect. Multivariate analysis identified time from symptom onset to admission, tympanic effusion, chronic ear disease history, cefotaxime resistance, and IgM levels as independent predictors of hearing loss (all $P < 0.05$). Conclusion: Cefotaxime resistance is associated with an increased risk of hearing loss in adult AOM patients, with IgM partially mediating this relationship. Early identification of resistant strains and IgM monitoring may improve outcomes.

Keywords: Acute purulent otitis media, *Streptococcus pneumoniae*, cefotaxime resistance, hearing loss, immunoglobulins, mediation effect

Introduction

Acute suppurative otitis media (AOM) is a prevalent infectious worldwide disease, with a notably high incidence in pediatric populations [1]. In recent years, the clinical significance of adult AOM has gained increasing attention. Epidemiological data indicate an annual incidence rate of 0.25%-0.5% in adults, which, although lower than in children, is associated with significantly higher rates of complications, such as hearing loss, mastoiditis, and intracranial infections. These complications may be linked to comorbid conditions, including diabetes mellitus and immune dysfunction [2]. *Streptococcus pneumoniae* remains the predominant pathogenin AOM, accounting for 30%-50% of bacterial cases [3]. Moreover, the global rise in β-lactam antibiotic resistance among *S. pneumoniae* strains presents a critical challenge [4]. Surveillance reports indicate that resistance to third-generation cephalosporins, such as cefotaxime, exceeds 20% in some regions, complicating clinical management [5].

https://doi.org/10.62347/NVPW7379

Antimicrobial resistance not only increases the risk of treatment failure but also exacerbates middle ear inflammation through multiple mechanisms [6]. For example, resistant strains exhibit enhanced biofilm formation, which promotes persistent mucosal colonization and the sustained release of toxins and inflammatory mediators, ultimately damaging the ossicular chain and cochlear function [7, 8]. Hearing loss affects 15%-30% of adult AOM patients, with severe cases progressing to permanent sensorineural deafness [9].

Current research on antibiotic resistance and hearing loss primarily focuses on pediatric populations [10, 11]. However, adult AOM presents distinct epidemiological and pathophysiological characteristics, including age-related declines in mucociliary clearance and a higher prevalence of comorbidities (e.g., diabetes, hypertension), which may influence disease progression and outcomes [12]. Systematic investigations into antimicrobial resistance patterns in adult AOM, particularly their association with auditory impairment, remain limited. Furthermore, the role of host immune factors in the development of complications is poorly understood [13]. Immunoglobulins, such as IgM and IgA, are critical mediators of mucosal immunity and play essential roles in local antimicrobial defense within the middle ear [14]. This study aims to elucidate the patterns of cefotaxime resistance in adult AOM patients and explore their correlation with hearing loss, addressing critical knowledge gaps in adult antimicrobial resistance research while investigating potential immunological mechanisms.

Methods and materials

Case selection

This retrospective cohort study included 188 adult patients diagnosed with acute suppurative otitis media (AOM) and treated at Xi'an People's Hospital between January 2018 and December 2023. The study protocol was approved by the Xi'an People's Hospital Ethics Committee.

Definition of hearing loss

All patients underwent tympanometry and pure-tone audiometry. Hearing loss was diagnosed based on the World Health Organization (WHO) classification. Speech-frequency hearing loss: Average air conduction threshold at 0.5, 1, and 2 kHz > 25 dB. High-frequency hearing loss: Average air conduction threshold at 4-8 kHz > 40 dB [15].

Inclusion criteria: (1) Age ≥ 18 years. (2) Confirmed diagnosis of acute suppurative otitis media (AOM) with *Streptococcus pneumoniae* infection verified by ear secretion bacterial culture. (3) Complete clinical and laboratory data. (4) Unilateral disease (bilateral otitis media cases were excluded to minimize the influence of disease severity on hearing loss analysis). (5) No prior tympanocentesis or tympanostomy tube placement before hearing loss evaluation to avoid confounding effects of medical interventions. (6) No history of ear surgery (e.g., tympanic membrane repair or ossicular chain reconstruction) to ensure that hearing loss was primarily attributable to AOM.

Exclusion criteria: (1) Pregnant or breastfeeding women. (2) Severe underlying conditions (e.g., end-stage liver or renal disease). (3) Long-term antibiotic use prior to the admission. (4) Incomplete clinical or laboratory data. (5) Presence of other ear infections or complications (e.g., otitis externa or labyrinthitis). (6) Recent use of immunosuppressive or immunomodulatory medications.

Clinical data collection

Clinical data were retrieved from the hospital's electronic medical records and follow-up visits. Demographic characteristics included age, sex, body mass index (BMI), smoking history, and medical history (e.g., diabetes, hypertension). Disease characteristics encompassed time from symptom onset to hospitalization, affected ear, presence of tympanic effusion, and history of chronic ear disease. Laboratory indicators included immunoglobulin levels (IgM, IgA, IgG) measured at admission.

Laboratory tests

Ear secretion samples were collected for bacterial culture, primarily *Streptococcus pneumoniae* infection, and antibiotic susceptibility testing. Cultures were performed on BD BBL™ Blood Agar plates and incubated at 37°C for

Table 1. Clinical characteristics and biochemical indicators of the study population

Parameters	Total
Age	
≤ 45 years	95 (50.53%)
46-55 years	50 (26.6%)
≥ 56 years	43 (22.87%)
Sex	
Male	83 (44.15%)
Female	105 (55.85%)
BMI	
18-22.9	53 (28.19%)
23-24.9	107 (56.91%)
≥ 25	28 (14.89%)
Time from Onset to Admission	
≥ 24 hours	58 (30.85%)
< 24 hours	130 (69.15%)
Affected Ear	
Left	98 (52.13%)
Right	90 (47.87%)
Smoking History	
Yes	73 (38.83%)
No	115 (61.17%)
Diabetes History	
Yes	29 (15.43%)
No	159 (84.57%)
Hypertension History	
Yes	29 (15.43%)
No	159 (84.57%)
Tympanic Empyema	
Yes	40 (21.28%)
No	148 (78.72%)
Chronic Ear Disease History	
Yes	34 (18.09%)
No	154 (81.91%)
Cefotaxime Resistance	
Yes	50 (26.6%)
No	138 (73.4%)
IgM (mg/L)	0.37 (0.27, 0.58)
IgA (mg/L)	0.44 (0.36, 0.64)
IgG (mg/L)	6.74 ± 1.68

Note: BMI, body mass index; IgM, immunoglobulin M; IgA, immunoglobulin A; IgG, immunoglobulin G.

24-48 hours. Cefotaxime susceptibility was assessed using the Kirby-Bauer disc diffusion method, with results interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines [16].

Immunoglobulin levels, including IgM, IgA, and IgG, were measured by immunoturbidimetry using a Beckman Coulter AU5800 automated biochemical analyzer.

Definition of drug resistance

Cefotaxime susceptibility was determined using the Kirby-Bauer disc diffusion method. Resistance was classified according to CLSI guidelines as follows: (1) Sensitive (S): Inhibition zone diameter ≥ 27 mm. (2) Intermediate (I): Inhibition zone diameter 23-26 mm. (3) Resistant (R): Inhibition zone diameter ≤ 22 mm.

Follow-up

As a retrospective study, follow-up data were obtained from hospitalization records and subsequent outpatient visits over a 2-week period. Follow-up data included changes in hearing loss status, resolution of ear symptoms, and occurrence of complications or recurrence.

Outcome measures

Primary outcomes: (1) Correlation between cefotaxime resistance and hearing loss. (2) Association between hearing loss risk in patients with drug-resistant infections and clinical variables (e.g., age, diabetes history).

Secondary outcomes: (1) Impact of clinical variables (e.g., time from onset to admission, tympanic effusion) on hearing loss. (2) Potential mediating role of immunoglobulin levels in drug-resistant infections.

Statistical analysis

Data were analyzed using SPSS 25.0 and R 4.3.3. The Kolmogorov-Smirnov test was used to assess data normality. Continuous variables with a normal distribution were expressed as mean ± standard deviation (SD), while non-normally distributed variables were presented as median (interquartile range, IQR). Group differences were evaluated using independent t-tests for normally distributed data, Mann-Whitney U tests for non-normally distributed data, and chi-square tests for categorical variables. Spearman correlation analysis was performed for non-normally distributed data. To assess the impact of cefotaxime resistance and other clinical variables on hearing loss, uni-

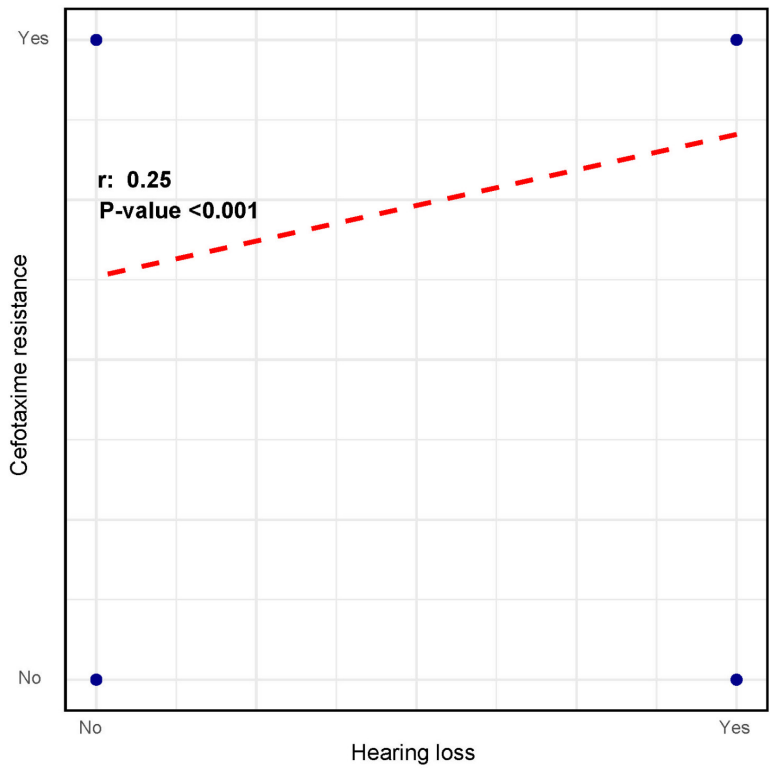

Figure 1. Correlation analysis between cefotaxime resistance and the degree of hearing loss.

variate and multivariate logistic regression analyses were performed. Variables identified in univariate analysis were included in multivariate models to evaluate their independent effects.

Interaction analyses were conducted using R packages (rms, cowplot, ggplot2, visreg) to examine interactions between cefotaxime resistance and clinical variables (e.g., age, diabetes history, immunoglobulin levels). Mediation analysis was performed using the R mediation package with 5,000 bootstrap resamples to evaluate whether IgM mediated the relationship between drug resistance and hearing loss, with direct (ADE) and indirect (ACME) effects calculated. All statistical tests were two-tailed, with a significance level of $P < 0.05$.

Results

Demographic and clinical characteristics

Among the 188 adult AOM patients, 50.5% (n = 95) were aged ≤ 45 years, 26.6% (n = 50) were 46-55 years, and 22.9% (n = 43) were ≥ 56 years. There were 83 males (44.2%) and 105 females (55.8%). BMI ranged from 23 to 24.9 in 56.9% (n = 107) of the patients. Most patients (69.2%, n = 130) were admitted within 24 hours of symptom onset. The affected ear was the left ear in 52.1% of the patients (n = 98) and the right ear in 47.9% (n = 90). Smoking history was reported in 38.8% of the patients (n = 73), diabetes in 15.4% (n = 29), tympanic effusion in 21.3% (n = 40), and chronic ear disease in 18.1% (n = 34). Cefotaxime resistance occurred in 26.6% of the patients (n = 50). Median IgM was 0.37 (IQR 0.27-0.58), IgA was 0.44 (IQR 0.36-0.64), and mean IgG was 6.74 ± 1.68 (**Table 1**).

Correlation between cefotaxime resistance and hearing loss

Spearman analysis revealed a significant positive correlation between cefotaxime resistance and hearing loss ($r = 0.25$, $P < 0.001$), suggesting higher resistance increases hearing loss risk (**Figure 1**).

Baseline differences between hearing and non-hearing groups

The hearing loss group had a higher proportion of patients aged ≥ 56 years ($P = 0.006$), admitted > 24 hours after onset ($P = 0.004$), with diabetes ($P = 0.008$), tympanic effusion ($P = 0.006$), chronic ear disease ($P = 0.009$), and cefotaxime resistance ($P < 0.001$). Additionally, IgM and IgA levels were significantly lower in the hearing loss group ($P < 0.001$). No significant differences were observed in gender, BMI, smoking history, hypertension, affected ear, or IgG (**Table 2**). These parameters showing statistical difference between hearing loss and non-hearing loss groups were assigned with values for subsequent regression analysis (**Table 3**).

Logistic regression analysis

Univariate analysis revealed that age ≥ 56 years ($P = 0.009$), delayed admission (> 24

Table 2. Comparison of baseline characteristics between patients with and without hearing loss

Factor	Hearing Loss (n = 100)	Non-Hearing Loss (n = 88)	X^2/t/Z Value	*P* Value
Age				
≤ 45 years	45 (45.00%)	50 (56.82%)	10.114	0.006
46-55 years	23 (23.00%)	27 (30.68%)		
≥ 56 years	32 (32.00%)	11 (12.5%)		
Sex				
Male	43 (43.00%)	40 (45.45%)	0.114	0.735
Female	57 (57.00%)	48 (54.55%)		
BMI				
18-22.9	27 (27.00%)	26 (29.55%)	2.845	0.241
23-24.9	54 (54.00%)	53 (60.23%)		
≥ 25	19 (19.00%)	9 (10.23%)		
Time from Onset to Admission				
≥ 24 hours	40 (40.00%)	18 (20.45%)	8.382	0.004
< 24 hours	60 (60.00%)	70 (79.55%)		
Affected Ear				
Left	54 (54.00%)	44 (50%)	0.300	0.584
Right	46 (46.00%)	44 (50%)		
Smoking History				
Yes	37 (37.00%)	36 (40.91%)	0.301	0.583
No	63 (63.00%)	52 (59.09%)		
Diabetes History				
Yes	22 (22.00%)	7 (7.95%)	7.078	0.008
No	78 (78.00%)	81 (92.05%)		
Hypertension History				
Yes	18 (18.00%)	11 (12.5%)	1.085	0.298
No	82 (82.00%)	77 (87.5%)		
Tympanic Empyema				
Yes	29 (29.00%)	11 (12.5%)	7.608	0.006
No	71 (71.00%)	77 (87.5%)		
Chronic Ear Disease History				
Yes	25 (25.00%)	9 (10.23%)	6.895	0.009
No	75 (75.00%)	79 (89.77%)		
Cefotaxime Resistance				
Yes	37 (37.00%)	13 (14.77%)	11.846	< 0.001
No	63 (63.00%)	75 (85.23%)		
IgM (mg/L)	0.34 (0.26, 0.40)	0.68 (0.29, 1.13)	4.824	< 0.001
IgA (mg/L)	0.42 (0.36, 0.50)	0.67 (0.29, 1.06)	3.397	< 0.001
IgG (mg/L)	6.83 ± 1.42	6.63 ± 1.94	-0.830	0.408

Note: BMI, body mass index; IgM, immunoglobulin M; IgA, immunoglobulin A; IgG, immunoglobulin G.

hours, P = 0.004), diabetes history (P = 0.010), tympanic effusion (P = 0.007), chronic ear disease history (P = 0.011), and cefotaxime resistance (P = 0.001) were significant risk factors for hearing loss. Lower IgM (P < 0.001) and IgA (P < 0.001) levels were also risk factors, increasing hearing loss likelihood (**Table 4**). Multivariate analysis confirmed delayed admission (P = 0.018), tympanic effusion (P = 0.039), chronic ear disease (P = 0.019), cefotaxime resistance (P = 0.009), and lower IgM (P < 0.001) and IgA (P = 0.001) levels as independent risk factors for hearing loss in AOM patients (**Table 5**).

Table 3. Variable assignment table

Variable	Type	Assignment Rule
Age	Ordinal	≤ 45 = 1, 46-55 = 2, ≥ 56 = 3
Time from Onset to Admission	Binary	≥ 24 h = 1, < 24 h = 0
Diabetes History	Binary	Yes = 1, No = 2
Tympanic Empyema	Binary	Yes = 1, No = 2
Chronic Ear Disease History	Binary	Yes = 1, No = 2
Cefotaxime Resistance	Binary	Yes = 1, No = 2
IgM (mg/L)	Binary	< 0.475 = 1, ≥ 0.475 = 2
IgA (mg/L)	Binary	< 0.50 = 1, ≥ 0.50 = 2

Note: IgM, immunoglobulin M; IgA, immunoglobulin A.

Interaction analysis

Several clinical variables were also significantly associated with the outcome. A negative correlation was observed between hearing loss with the time from symptom onset to admission (estimate = -1.125, P = 0.018), pyomatosis tympanum (estimate = -1.130, P = 0.039), and history of chronic ear disease (estimate = -1.417, P = 0.019). Additionally, higher levels of IgM (estimate = 3.116, P < 0.001) and IgA (estimate = 1.418, P = 0.001) were strongly associated with hearing loss. Age (estimate = 0.292, P = 0.254) and history of diabetes (estimate = -0.965, P = 0.097) did not reach the threshold for statistical significance (P > 0.05; **Table 6** and **Figure 2**).

Mediation analysis

Mediation analysis indicated that IgM significantly mediated the relationship between cefotaxime resistance and hearing loss (P = 0.033), accounting for 26.9% of the total effect. Other variables, including age, diabetes history, IgA levels, and tympanic effusion, did not exhibit significant mediation effects (P > 0.05). The direct effect of cefotaxime resistance on hearing loss remained significant (P < 0.001) (**Figure 3**).

Discussion

This study investigated cefotaxime resistance in *Streptococcus pneumoniae* among adult patients with acute suppurative otitis media (AOM) and its association with hearing loss, as well as the potential mediating role of immunoglobulins (IgM, IgA). Our findings revealed a significant positive correlation between cefotaxime resistance and hearing loss, offering new insights into the clinical management and prognosis of AOM. Notably, IgM was the only significant mediator in the relationship between drug resistance and hearing loss, accounting for 26.9% of the total effect. In contrast, other factors, such as IgA, age, and diabetes history, showed no significant mediating effects. These results underscore the critical roles of antibiotic resistance and host immune responses in the development of hearing loss in AOM [17].

Patients with cefotaxime-resistant infections exhibited poorer treatment outcomes and prolonged disease duration, which likely intensified local inflammation through mechanisms such as enhanced bacterial biofilm formation, ultimately impairing hearing function [18]. Drug-resistant *S. pneumoniae* strains can persistently colonize the middle ear, releasing inflammatory mediators that damage the ossicular chain and cochlear function, thereby contributing to hearing loss. These findings align with studies suggesting that resistant bacteria exacerbate tissue damage by enhancing virulence or evading host immune clearance [19]. Moreover, the resistance of these strains to conventional antibiotics complicates treatment, further elevating the risk of hearing loss.

However, Cushen et al. [20] argued that resistance alone does not necessarily correlate with increased bacterial virulence, emphasizing that hearing loss is more closely tied to delayed treatment or host immune status. Our mediation analysis supports this perspective, demonstrating that IgM significantly mediates the relationship between drug resistance and hearing loss, highlighting the importance of immune responses in this process. Conversely, clinical variables such as age, diabetes history, and tympanic effusion showed no significant mediating effects, consistent with literature suggesting that delayed treatment or immune status plays a more dominant role [21].

A key finding of this study is the mediating role of IgM in the relationship between cefotaxime resistance and hearing loss. As a critical component of the primary immune response, IgM

Table 4. Univariate logistics regression

Variable	Estimate	Std. Error	*P* Value	OR	Lower	Upper
Age	0.490	0.188	0.009	1.633	1.137	2.379
Time from Onset to Admission	-0.953	0.334	0.004	0.386	0.197	0.733
Diabetes History	-1.183	0.462	0.010	0.306	0.116	0.725
Tympanic Empyema	-1.051	0.390	0.007	0.350	0.157	0.734
Chronic Ear Disease History	-1.074	0.421	0.011	0.342	0.143	0.756
Cefotaxime Resistance	-1.220	0.365	0.001	0.295	0.140	0.591
IgM (mg/L)	2.953	0.429	< 0.001	19.167	8.672	47.472
IgA (mg/L)	1.216	0.309	< 0.001	3.375	1.858	6.242

Note: IgM, Immunoglobulin M; IgA, Immunoglobulin A.

Table 5. Multivariate logistics regression

Variable	Estimate	Std. Error	*P* Value	OR	Lower	Upper
Age	0.292	0.256	0.254	1.339	0.814	2.233
Time from Onset to Admission	-1.125	0.474	0.018	0.325	0.123	0.801
Diabetes History	-0.965	0.581	0.097	0.381	0.115	1.144
Tympanic Empyema	-1.130	0.546	0.039	0.323	0.104	0.904
Chronic Ear Disease History	-1.417	0.605	0.019	0.242	0.069	0.752
Cefotaxime Resistance	-1.318	0.504	0.009	0.268	0.095	0.695
IgM (mg/L)	3.116	0.520	< 0.001	22.555	8.698	68.045
IgA (mg/L)	1.418	0.427	0.001	4.127	1.825	9.833

Note: IgM, Immunoglobulin M; IgA, Immunoglobulin A.

Table 6. Interaction analysis between cefotaxime resistance and clinical variables

Variable	Estimate	Std. Error	z value	*p*-value
(Intercept)	2.760	2.316	1.192	0.233
Cefotaxime Resistance	-1.318	0.504	-2.615	0.009
Age	0.292	0.256	1.140	0.254
Time from onset to admission	-1.125	0.474	-2.375	0.018
History of diabetes	-0.965	0.581	-1.660	0.097
Pyomatosis tympanum	-1.130	0.546	-2.069	0.039
History of chronic ear disease	-1.417	0.605	-2.342	0.019
IgM	3.116	0.520	5.994	0.000
IgA	1.418	0.427	3.319	0.001

Note: IgM, Immunoglobulin M; IgA, Immunoglobulin A.

activates the complement system and neutralizes pathogens. In patients with cefotaxime-resistant infections, lower IgM levels were associated with higher resistance, suggesting that IgM mitigates persistent inflammation by inhibiting pathogen colonization and biofilm formation [22]. The 26.9% mediating effect of IgM indicates its potential as an immunological marker for assessing hearing loss risk in drug-resistant AOM [23]. Although IgA levels differed significantly between patients with and without hearing loss, IgA did not mediate this relationship, reflecting the distinct immunological roles of IgM and IgA. IgM likely plays a more direct role in acute-phase responses in AOM, whereas IgA is more involved in long-term mucosal defense [23]. These findings suggest that immune interventions targeting IgM could enhance AOM treatment outcomes.

Beyond drug resistance, several clinical factors were also associated with hearing loss, including age, diabetes history, tympanic effusion, and chronic ear disease. Older patients were more susceptible to hearing loss, possibly due to age-related declines in cochlear function, reduced cochlear blood supply, and impaired immune responses [24]. Diabetic patients had a higher risk of hearing loss, likely due to microvascular damage, neurodegeneration, and impaired immune function caused by chronic hyperglycemia, which may exacerbate drug-resistant in-

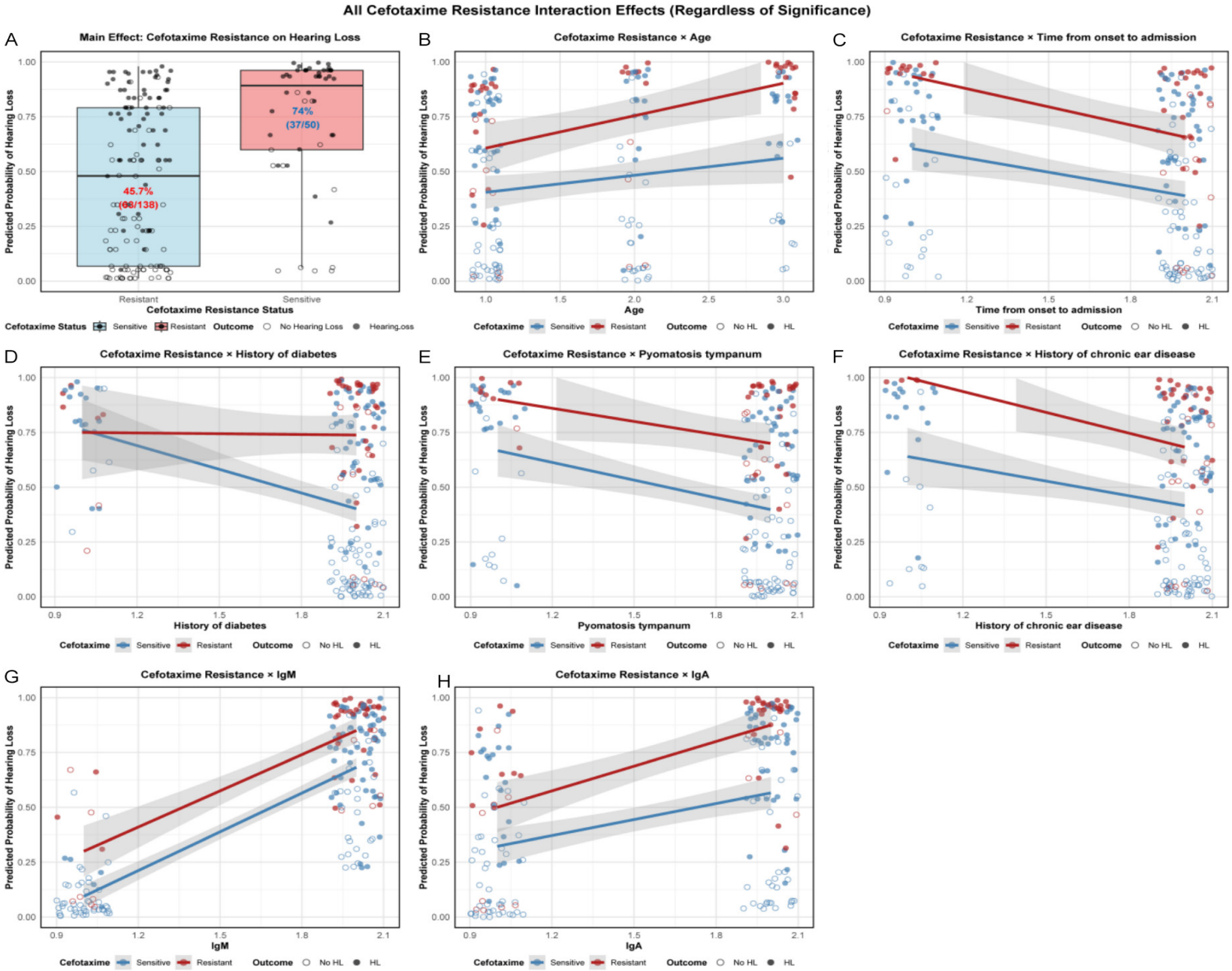
All Cefotaxime Resistance Interaction Effects (Regardless of Significance)
A
Main Effect: Cefotaxime Resistance on Hearing Loss
Predicted Probability of Hearing Loss
45.7%
(66/138)
74%
(37/50)
Resistant
Sensitive
Cefotaxime Resistance Status
Cefotaxime Status Sensitive Resistant Outcome No Hearing Loss Hearing.oss
B
Cefotaxime Resistance × Age
Age
Cefotaxime Sensitive Resistant Outcome No HL HL
C
Cefotaxime Resistance × Time from onset to admission
Time from onset to admission
Cefotaxime Sensitive Resistant Outcome No HL HL
D
Cefotaxime Resistance × History of diabetes
History of diabetes
Cefotaxime Sensitive Resistant Outcome No HL HL
E
Cefotaxime Resistance × Pyomatosis tympanum
Pyomatosis tympanum
Cefotaxime Sensitive Resistant Outcome No HL HL
F
Cefotaxime Resistance × History of chronic ear disease
History of chronic ear disease
Cefotaxime Sensitive Resistant Outcome No HL HL
G
Cefotaxime Resistance × IgM
IgM
Cefotaxime Sensitive Resistant Outcome No HL HL
H
Cefotaxime Resistance × IgA
IgA
Cefotaxime Sensitive Resistant Outcome No HL HL

Figure 2. Interaction between clinical variables and hearing loss stratified by cefotaxime resistance. A. Main effect of cefotaxime resistance on hearing loss. B. Predicted probability of hearing loss by cefotaxime resistance and age. C. Predicted probability of hearing loss by cefotaxime resistance and time from symptom onset to admission. D. Predicted probability of hearing loss by cefotaxime resistance and history of diabetes. E. Predicted probability of hearing loss by cefotaxime resistance and tympanic empyema. F. Predicted probability of hearing loss by cefotaxime resistance and history of chronic ear disease. G. Predicted probability of hearing loss by cefotaxime resistance and with IgM levels. H. Predicted probability of hearing loss by cefotaxime resistance and with IgA levels. Note: IgM, immunoglobulin M; IgA, immunoglobulin A.

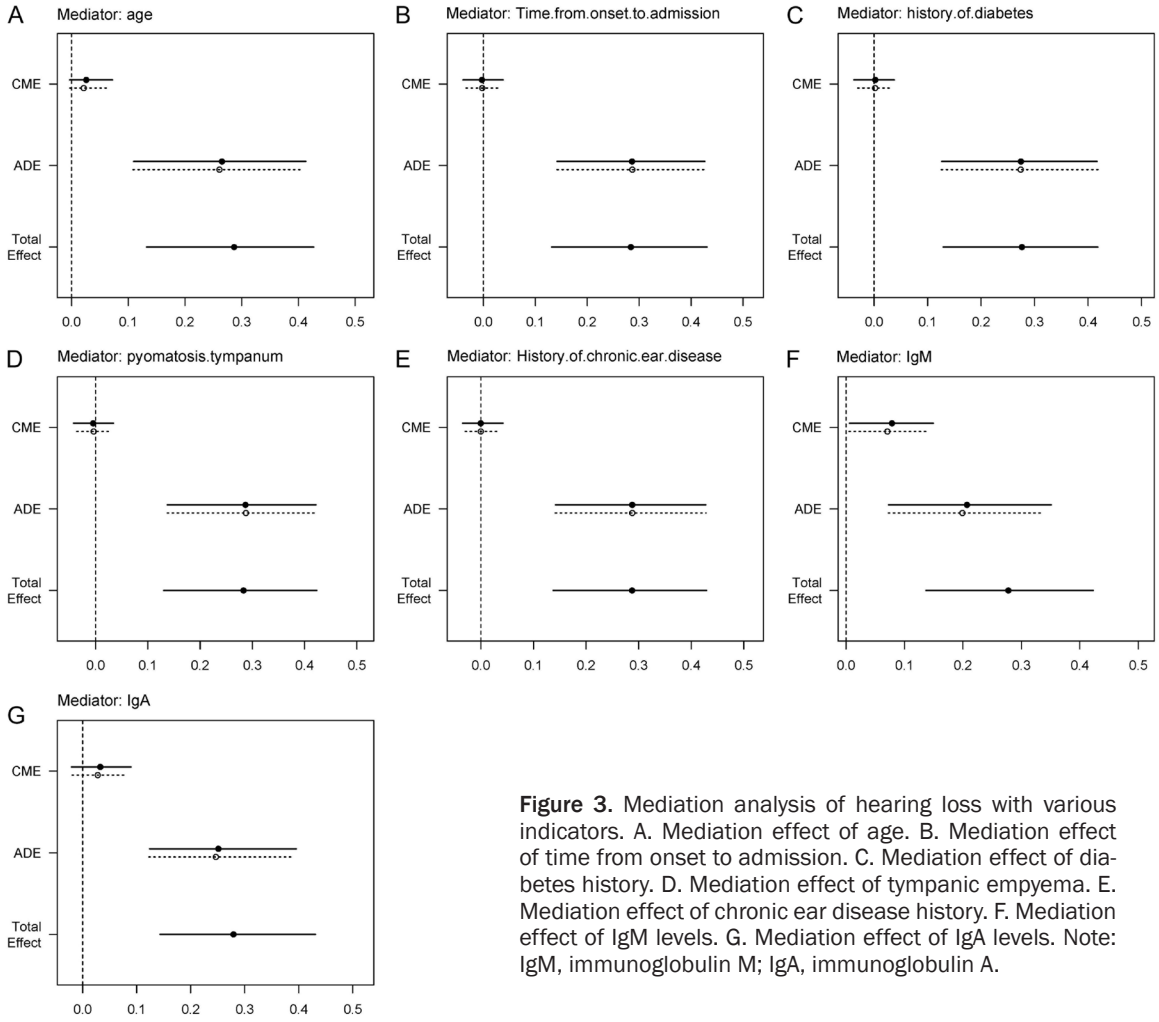

Figure 3. Mediation analysis of hearing loss with various indicators. A. Mediation effect of age. B. Mediation effect of time from onset to admission. C. Mediation effect of diabetes history. D. Mediation effect of tympanic empyema. E. Mediation effect of chronic ear disease history. F. Mediation effect of IgM levels. G. Mediation effect of IgA levels. Note: IgM, immunoglobulin M; IgA, immunoglobulin A.

fections [25]. Tympanic effusion and chronic ear disease were also significantly associated with hearing loss; Tympanic effusion reflects more severe AOM symptoms and middle ear structural damage, while chronic ear disease causes cumulative auditory damage over time [26]. These findings advocate for aggressive treatment and close monitoring in high-risk groups, such as older adults, diabetic patients, and those with chronic ear disease, to reduce the incidence of hearing loss in AOM.

This study highlights the pivotal role of IgM in hearing loss associated with drug-resistant AOM. The increasing prevalence of antibiotic-resistant bacteria has reduced the efficacy of conventional treatments, emphasizing the need for early identification of resistance and immune monitoring to improve outcomes. Future research should explore immune interventions, particularly IgM modulation, to inhibit drug-resistant bacterial colonization and minimize hearing damage.

Several limitations of this research should be noted. Its retrospective design relies on medical records, which may introduce information bias. The inclusion of only unilateral AOM cases

limits the generalizability of the findings to all AOM patients. Additionally, the short 2-week follow-up period precludes assessment of long-term IgM effects on hearing prognosis. Additionally, the specific immunoregulatory mechanisms of IgM in AOM pathogenesis remain unclear and warrant further investigation. Future prospective studies are needed to validate the role of immunoglobulins in drug-resistant AOM and to evaluate the therapeutic potential of immune-based therapies.

Conclusion

This study elucidates the relationship between *Streptococcus pneumoniae* cefotaxime resistance and hearing loss in adult AOM patients, identifying IgM as a significant mediator. Our findings suggest that immune response mechanisms, particularly IgM, modulate the impact of drug resistance on hearing loss, highlighting its potential as a therapeutic target.

Disclosure of conflict of interest

None.

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