Title

Comparison of Wideband Acoustic Immittance in Chinese Infants under Three Months of Age with Normal and Abnormal Middle Ear Function

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Abstract

Objectives: This study aims to compare the characteristics of Wideband Acoustic Immittance (WAI) in Chinese infants under three months of age, with either normal or abnormal middle ear function.

Methods: We recruited 98 infants with either normal or abnormal middle ear function, and subsequently divided them into four groups based on their middle ear function and chronological age. The absorbances at tympanometric peak pressure (TPP) were collected across 1/3rd octave frequencies ranging from 226 to 8000 Hz.

Results: Among infants with normal middle ear function, no significant differences were observed concerning ear laterality. However, significant differences were noted at 3364 Hz and 4000 Hz with respect to age. For infants with either normal or abnormal middle ear function, we found significant differences at the majority of frequencies. Additionally, the receiver operating characteristic (ROC) curves and maxima Youden index indicated that absorbances at 1682 Hz and 1297 Hz could be employed to evaluate the middle ear function of infants at 1 and 2 months of age.

Conclusion: This study demonstrates that WAI holds promise as a valuable tool for assessing the middle ear condition of infants at 1 and 2 months of age. Infants aged 1 and 2 years, having absorbance values equal to or greater than 0.7470 at 1682 Hz and 0.6775 at 1297 Hz respectively, may indicate normal middle ear function. Furthermore, it underscores the necessity of establishing ethnicity- and age-specific norms for WAI in infants under 3 months of age.

[Key Words] Wideband Acoustic Immittance; Infants; Middle Ear Function

Introduction

The Year 2019 position statement of the American Joint Committee of Infant Hearing on early hearing detection and intervention programs proposed a new target timeline of '1-2-3 months' for children with hearing loss. This entails completing hearing screening by one month of age, obtaining an audiological diagnosis by two months of age, and initiating early intervention no later than three months of age. In the context of audiological diagnosis, assessing middle ear function is a crucial component of early hearing detection, as it aids in diagnosing conductive hearing loss and distinguishing it from sensory or neural hearing loss [1]. The peripheral auditory system undergoes rapid development from birth to 12 months, wherein the middle ear transitions from a mass-dominated system to a stiffness-dominated system. This transformation is characterized by a decrease in the overall mass and resistance of the middle ear due to the loss of mesenchyme and changes in bone density of the ossicles. Simultaneously, there is an increase in the overall stiffness of the middle ear, attributed to changes in the orientation and fiber content of the tympanic membrane, fusion of the tympanic ring, and tightening of the ossicular joints [2]. These developmental changes result in distinct features of the middle ear during the first year of life, making it challenging to accurately identify its specific condition using conventional tympanometry, such as with the use of a 226 Hz or 1000 Hz probe tone [3].

Wideband Acoustic Immittance (WAI) is an advanced method designed for assessing the wideband, power-based response characteristics related to acoustic impedance, admittance, and reflectance within the human ear canal [4, 5]. This technique provides insights into the acoustic response properties of the middle ear across a broad range of frequencies and has shown promise as a valuable indicator of middle ear status, particularly in neonates and young children [3, 6]. For instance, a recent study by Stuppert et al. [3] involved 150 normal hearing children aged between 11 days and 14;10 years. The results confirmed that WAI was an important additional tool for assessing middle ear problems in pediatric audiology.

However, it is essential to highlight that several studies suggest the need for developing age-specific normative WAI data for infants from birth to 12 months (e.g., Kei et al. [7], Aithal et al. [8], Hunter et al. [9]; Aithal et al. [10], Qi et al. [11], Myers et al. [12], Wali et al. [13]). Kei et al. [7] conducted a comprehensive review of multiple studies on WAI and concluded that further age-specific longitudinal and cross-sectional normative data for infants from birth to 12 months were necessary to validate and strengthen the existing findings. Aithal et al. [8] conducted a prospective cross-sectional study focusing specifically on infants under 6 months of age. Their results emphasized the importance of developing age-specific normative data for WAI using a large sample of young infants. As a result, a further recommendation by Wali et al. [13] proposed the establishment of age-specific normative data for three distinct age groups: neonates, infants aged 1 to 2 months, and infants aged 3 to 6 months.

Furthermore, the study conducted by Hunter et al. [9] revealed not only a significant influence of age on WAI within the first 6 months but also notable effects of race. The results showed that ambient absorbance and absorbance at the positive tail of pressure between 6 and 8 kHz exhibited significant differences between races, with African Americans and individuals of other races displaying contrasting outcomes when compared to Caucasians. Moreover, there was also an interaction between age and race concerning ambient absorbance.

Therefore, it is crucial to establish the Wideband Acoustic Immittance (WAI) norms for Chinese infants under 3 months of age to enable early audiological diagnosis. Previous studies have demonstrated that the normal value of WAI shows a distinctive pattern with double peaks for neonates and infants aged 1 and 2 months [14-17]. For instance, Xiong et al. [14] observed two peaks at 1498 Hz and 6727 Hz, along with two valleys around 667 Hz and 3776 Hz, in typically developing Chinese infants aged 1 and 2 months. Similarly, Hao et al. [15] found double peaks at 1296 Hz and 5339 Hz, and double valleys at 667 Hz and 3363 Hz in neonates aged 48 to 72 hours at peak pressure. These studies showed a similar pattern with different peak frequencies and notches in Chinese infants within the specified age ranges. However, a recent study by Peng et al. [18] reported a single peak at around 2000 Hz, which differed from previous findings in the WAI of Chinese infants with typical development at 1 and 2 months of age. This discrepancy might be attributed to differences in frequency resolution used in data collection and the age range of the recruited children.

To the best of our knowledge, while there have been some WAI studies referring to Chinese normal infants under 3 months of age, none of the previous studies have compared the WAI of Chinese infants between those with normal and abnormal middle ear function. Therefore, the current cross-sectional study aimed to investigate the differences in WAI frequency characteristics in Chinese infants at 1 month and 2 months of age with normal and abnormal middle ear function. The first hypothesis posits that the most distinctive frequencies in WAI measures would be identified in infants between normal and abnormal middle ear function in each age group. Consequently, the cut-off value of absorbance for detecting normal middle ear function at individual frequencies would be determined using Receiver Operating Characteristic (ROC) curves and the Youden index, which represents the maximum vertical distance between the ROC curve and the diagonal or chance line [19]. The second hypothesis suggests that the absorbances of infants with normal middle ear function at 1 month and 2 months of age would exhibit significant differences at some frequencies. Hypothesis 3 states that the absorbances of infants with normal middle ear function would not show significant differences between the left and right ears.

Materials and Methods

1.1 Participants

A total of 98 infants with either normal or abnormal middle ear function were recruited in this study. They were divided into two age groups based on their chronological age at the time of receiving WAI testing: the 1-2 months of age group and the 2-3 months of age group.

Diagnostic and inclusion criteria were as follows:

1) Infants with normal middle ear function:

    a) Chronological age at the time of the test: between 1 and 3 months.

b) Normal middle ear function: They passed the Distortion Product Otoacoustic Emission (DPOAE) or Transient Evoked Otoacoustic Emission (TEOAE) screening test and exhibited a single positively peaked tympanogram at 1000 Hz tympanometry [8].

2) Infants with abnormal middle ear function:

a) Chronological age at the time of the test: between 1 and 3 months.

b) Abnormal middle ear function: They displayed abnormality in the Distortion Product Otoacoustic Emission (DPOAE) or Transient Evoked Otoacoustic Emission (TEOAE) screening test and the absence of a peak in the 1000 Hz tympanogram.

Table 1 presents a summary of the demographic information of the participants in the two groups. There were no significant differences in the chronological ages of infants with normal or abnormal middle ear function in each age group, as determined by independent-samples t-tests ($p = 0.540$; $p = 0.896$). Furthermore, there were no significant differences in gender distribution between the 1-2 months of age group and the 2-3 months of age group among infants with normal middle ear function, as confirmed by the Chi-square test ($x^2 = 0.800$, df = 1; $p = 0.371$). The same result was observed for infants with abnormal middle ear function ($x^2 = 1.434$, df = 1; $p = 0.231$). Additionally, there were no significant gender differences between infants with normal and abnormal middle ear function in both the 1-2 months of age group ($x^2 = 0.244$, df = 1; $p = 0.621$) and the 2-3 months of age group ($x^2 = 0.156$, df = 1; $p = 0.693$).

Table 1. Summary of demographic information of infants included in this study

	Infants with normal middle ear function					Infants with abnormal middle ear function				
	Male/ Female	Total number of infants	Age range (Mean ± SD) (Months;Days)	Number of Ears Left/Right	Total number of Ears	Male/ Female	Total number of infants	Age range (Mean ± SD) (Months;Days)	Number of Ears Left/Right	Total number of Ears
1-2 months of age	25/9	34	1;0.6~1;28.2 (1;13.7±0;8.3)	22/30	52	19/5	24	1;2.5~1;29.2 (1;15.0±0;8.6)	19/15	34
2-3 months of age	15/9	24	2;0.2~2;29.8 (2;15.0±0;8.6)	20/18	38	9/7	16	2;1.2~2;28.8 (2;14.7±0;8.8)	14/13	27

1.2 Hearing Screening tests

The DPOAE or TEOAE screening test was conducted using the Otometrics AccuScreen PRO device. DPOAEs were measured in response to pairs of primary tones with f2 set at 2000, 2500, 3200, and 4000 Hz. To achieve an overall Pass result, three out of four frequencies needed to pass with phase statistics as the evaluation method. The f2/f1 ratio was 1.24 for each primary tone pair, and the stimulus level of f1 was 59 dB sound pressure level (SPL), while that of f2 was 50 dB SPL. TEOAEs were measured in response to a non-linear click sequence with a sound pressure level of 70-84 dB SPL. The AccuScreen binomial statistics were used to determine a Pass or Refer result.

1000 Hz tympanometry was conducted using the Interacoustics Titan device with a stimulus level of 69 dB HL AGC (automated gain control) for the 1000 Hz pure tone, and the air pressure range was from -600 to +300 daPa. As specified in the inclusion criteria, normal middle ear function was defined as passing the OAE test and displaying a single positively peaked tympanogram in 1000 Hz tympanometry.

1.3 WAI measurement

WAI measurementwas performed using the Interacoustics Titan device with an intensity level of 96 dB peSPL for the 226 Hz – 8000 Hz broadband stimulus. The absorbances at TPP were measured at 1/24th octave frequencies from 226 to 8000 Hz. For statistical analysis in this study, data at 1/3rd octave frequencies (including 226, 324, 408, 500, 667, 841, 1000, 1297, 1682, 2000, 2670, 3364, 4000, 5339, 6727, and 8000 Hz) were collected. The WAI at TPP provides an optimal representation of the sound transmission properties of the middle ear by compensating for the difference in air pressure between the middle ear and the atmosphere, and it offers better test-retest reliability [15, 20].

1.4 Data analysis

Several statistical analyses were conducted in the present study. Chronological age comparisons of infants with normal or abnormal middle ear function in each age group were analyzed using independent-samples t-tests for normally distributed variables. As all data were non-normally distributed, all hypotheses were tested using the Mann-Whitney *U* test. If appropriate, the *p*-values were corrected using the Bonferroni method [21]. Additionally, the area under the ROC curve (AUC) plot was calculated to identify the most important frequencies for diagnosing abnormality in WAI absorbance between normal and abnormal middle ear function in each age group. The maximum Youden index was also calculated to indicate the threshold of absorbance at individual frequencies for distinguishing normal or abnormal middle ear function in each age group. The maximum Youden index represents the point on the ROC curve farthest from the diagonal or chance line, indicating the best discriminative ability.

Results

1.1 Comparisons of Absorbances between left and right ears in the infants with normal middle ear function

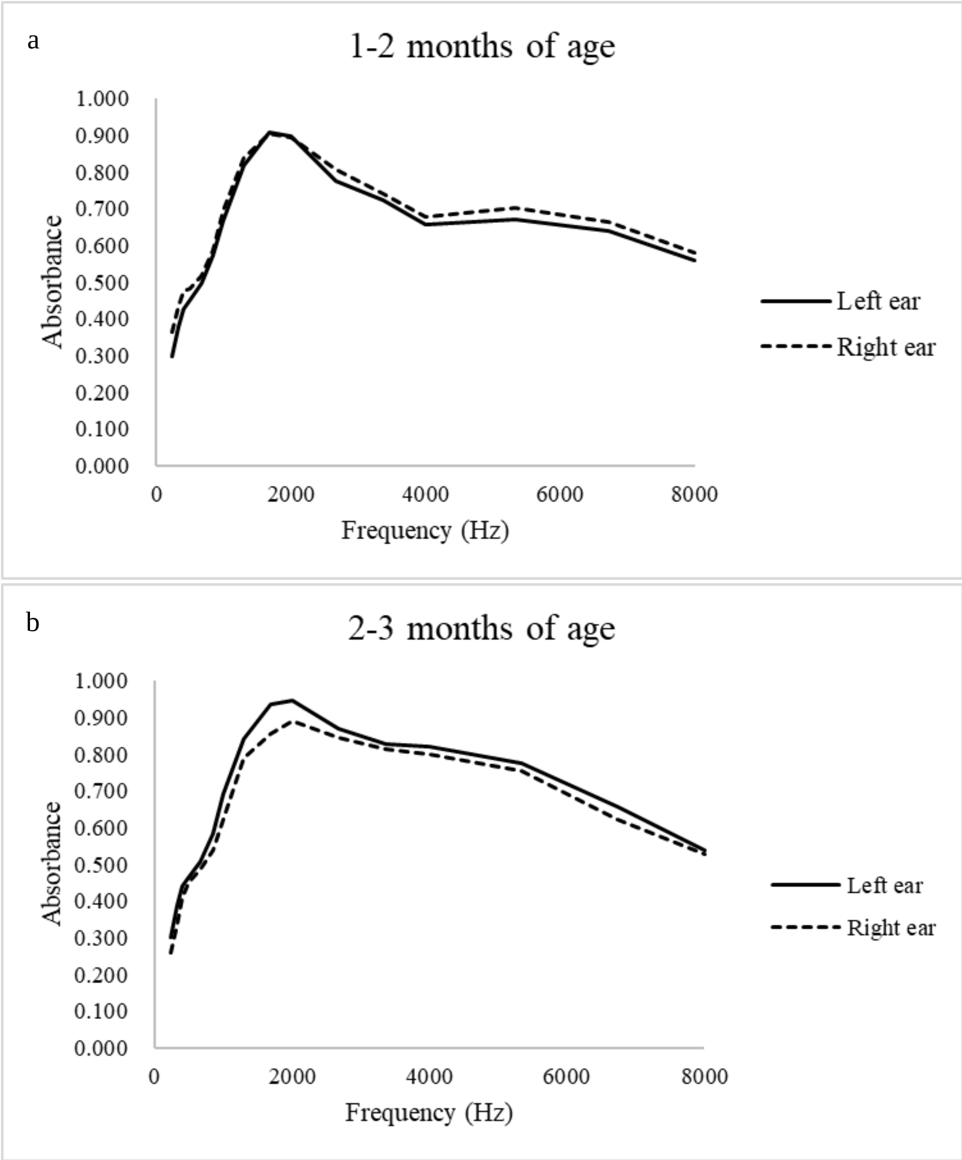


Figure 1 The mean absorbances of left and right ears in each age group. a. Absorbances of infants in 1-2 months of age group; b. Absorbances of infants in 2-3 months of age group.

In Figure 1a and 1b, the mean absorbances of the left and right ears in each age group were displayed, and the results revealed single peaks at around 2000 Hz, irrespective of the ear side. Furthermore, the Mann-Whitney U tests indicated that there were no significant differences between the left and right ears within each age group ($p > 0.05$). Consequently, to increase the sample size for subsequent analyses, the absorbance values of both the left and right ears in each age group were combined.

1.2 Comparisons of the Absorbances of the infants with normal middle ear function in two age groups

In Figure 2, the mean absorbances and 90% confidence intervals (CIs) of infants in both age groups were depicted, revealing single peaks at around 2000 Hz, similar to Figure 1. However, there were notable differences between the two age groups at specific frequencies. The absorbances at 3364 Hz and 4000 Hz in the 2-3 months of age group were found to be significantly higher than those at the same frequencies in the 1-2 months of age group. These differences were determined to be statistically significant using the Mann-Whitney *U* tests, and the *p*-values were corrected by the Bonferroni method ($p_{3364Hz} = 0.0025$; $p_{4000Hz} = 0.0001$).

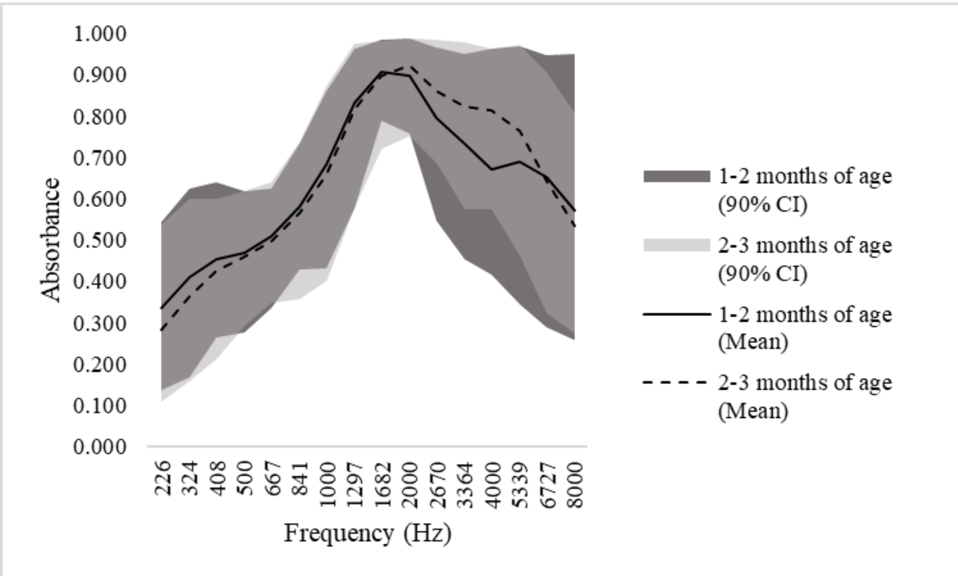
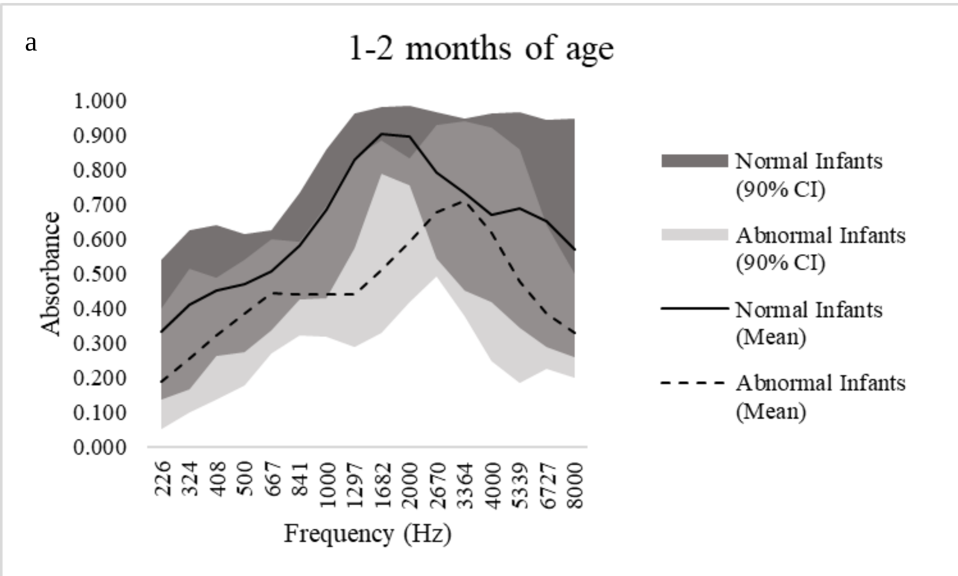


Figure 2 The mean absorbances and 90% confidence intervals (CIs) of infants in both of age groups

1.3 Comparisons of absorbances in infants between normal and abnormal middle ear function

Based on the absence of significant differences in absorbances between the left and right ears of infants with normal middle ear function, the absorbances of both ears in infants with abnormal middle ear function were combined to increase the sample size in each age group for subsequent comparisons. These comparisons revealed double peaks, and both maximal peaks were observed at 3364 Hz.

Figure 3 displayed the mean absorbances and 90% confidence intervals of infants with normal or abnormal middle ear function in each age group. The results indicated significant differences between normal and abnormal infants at each frequency in both the 1-2 months and 2-3 months age groups. These differences were established using the Mann-Whitney U tests ($p < 0.0031$) with the exception of frequencies at 3364 Hz and 4000 Hz in the 1-2 months age group ($p_{3364Hz} = 0.5393$; $p_{4000Hz} = 0.3469$) and 667 Hz in the 2-3 months age group ($p_{667Hz} = 0.0050$). All p-values were corrected using the Bonferroni method.



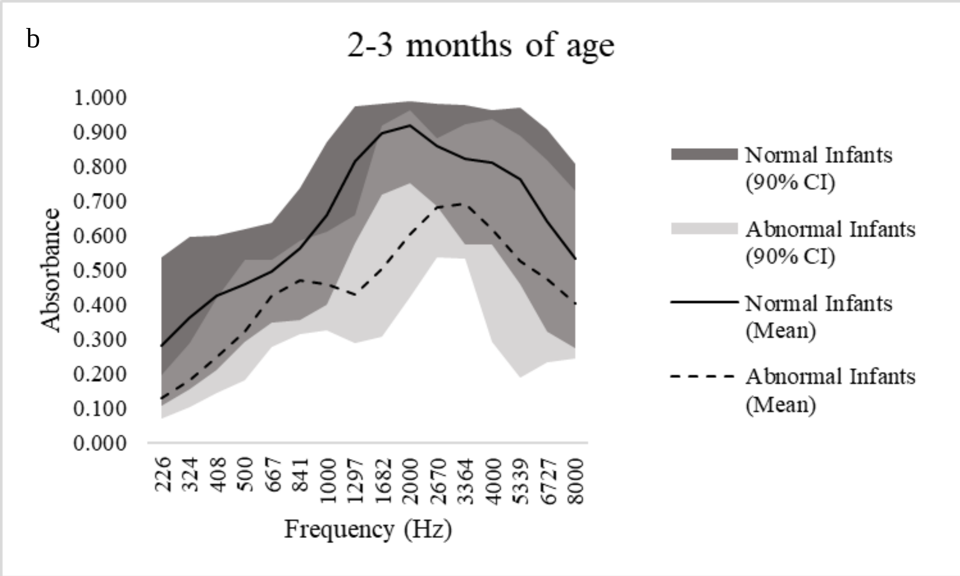
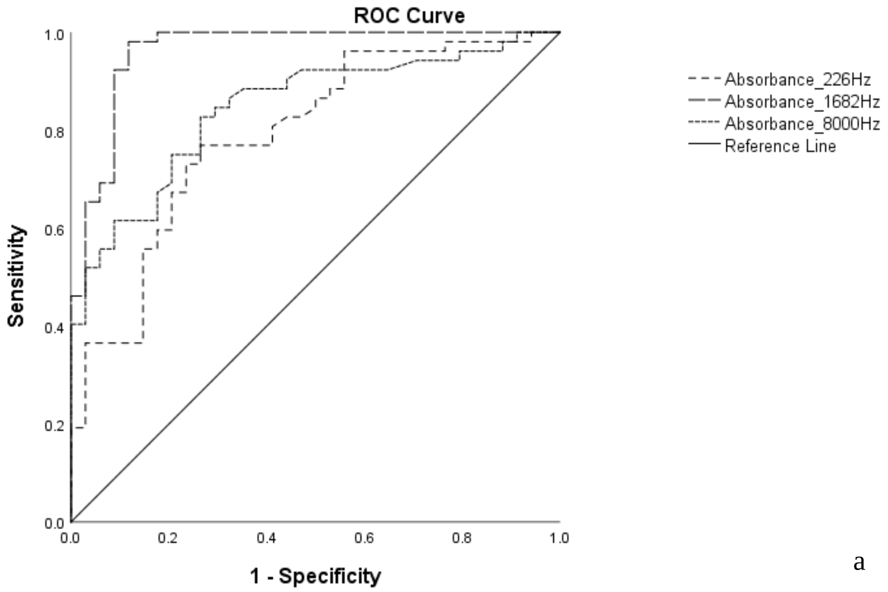
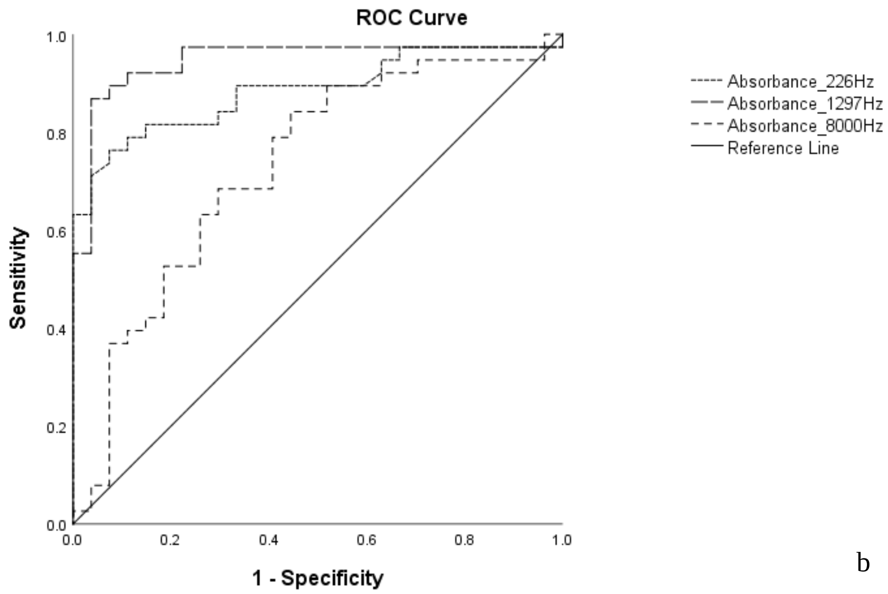


Figure 3 The mean absorbances and 90% confidence intervals of infants with normal or abnormal middle ear function in each age group. a. Absorbances of infants in 1-2 months of age group; b. Absorbances of infants in 2-3 months of age group.

Based on the results, ROC curves were plotted for both age groups in Figure 4. Additionally, the AUC (area under the curve) values were calculated to identify the most valuable frequency for distinguishing absorbances between normal and abnormal middle ear function in each age group. The analysis indicated that the largest AUC was observed at 1682 Hz in the 1-2 months of age group and at 1297 Hz in the 2-3 months of age group (Table 2).



a



b

Figure 4 ROC curves at part of frequencies in each age group. a. 1-2 months of age group. b. 2-3 months of age group

Table 2 Summary of the AUROC plots and 95% CIs in each age group

	1-2 months of age				2-3 months of age			
	AUROC	SE	95% CI		AUROC	SE	95% CI	
Absorbance_226Hz	0.791	0.050	0.694	0.888	0.885	0.042	0.803	0.967
Absorbance_324Hz	0.789	0.051	0.689	0.889	0.883	0.042	0.800	0.965

Absorbance_408Hz	0.773	0.051	0.673	0.873	0.880	0.042	0.797	0.962
Absorbance_500Hz	0.710	0.057	0.600	0.821	0.822	0.055	0.714	0.930
Absorbance_667Hz	0.714	0.057	0.601	0.826	0.706	0.064	0.580	0.832
Absorbance_841Hz	0.867	0.044	0.781	0.952	0.759	0.059	0.644	0.875
Absorbance_1000Hz	0.908	0.034	0.841	0.975	0.874	0.045	0.787	0.962
Absorbance_1297Hz	0.946	0.027	0.893	0.999	**0.945**	**0.031**	**0.884**	**1.000**
Absorbance_1682Hz	**0.962**	**0.021**	**0.920**	**1.000**	0.922	0.038	0.847	0.996
Absorbance_2000Hz	0.954	0.020	0.916	0.993	0.882	0.051	0.782	0.982
Absorbance_2670Hz	0.735	0.058	0.621	0.848	0.859	0.046	0.769	0.950
Absorbance_3364Hz	0.539	0.064	0.413	0.665	0.773	0.060	0.656	0.891
Absorbance_4000Hz	0.560	0.064	0.436	0.685	0.768	0.063	0.644	0.892
Absorbance_5339Hz	0.749	0.053	0.644	0.854	0.767	0.060	0.650	0.884
Absorbance_6727Hz	0.856	0.039	0.780	0.932	0.723	0.065	0.595	0.851
Absorbance_8000Hz	0.845	0.042	0.763	0.926	0.728	0.065	0.600	0.856

Table 3 presents the maximum Youden index and the corresponding absorbance threshold at each frequency for infants in each age group. This implies that infants would be classified as having normal middle ear function if their absorbance values were greater than or equal to the specified thresholds.

Table 3 Maximum Youden index and corresponding threshold of absorbance in each age group

Frequency	1-2 months of age group	Frequency	2-3 months of age group

	Threshold of absorbance	Youden Index		Threshold of absorbance	Youden Index
1682 Hz	0.7470	0.863	1297 Hz	0.6775	0.831

Discussion

1.1 The effect of ear laterality on the WAI in infants under 3 years old

In this study, no significant differences were observed in the absorbances between the left and right ears in each age group. These findings align with previous research results. For instance, a cross-sectional study by Aithal et al. [8] included 50 newborns, 36 infants at 1 month of age, 30 infants at 2 months of age, 33 infants at 4 months of age, and 28 infants at 6 months of age, which also found no significant difference in WAI at ambient environment between left and right ears. Similarly, Peng et al. [17] conducted a study involving 12 infants at 1 month of age and 11 infants at 2 months of age and found no significant difference in the absorbances of the left and right ears at TPP. These consistent results support Hypothesis 1, suggesting that ear laterality does not impact the WAI in infants. Therefore, combining the absorbance data of both ears for analysis is appropriate, especially when dealing with smaller sample sizes.

1.2 Effect of age on the WAI in infants under 3 years old

The present study revealed that the absorbances at 3364 Hz and 4000 Hz were significantly higher in the older age group compared to the younger age group. This finding confirms Hypothesis 2, indicating that age is an influential factor for WAI in infants. Other studies have also addressed the effect of age on the WAI in infants within the first 6 months of life. For instance, Aithal et al. [8] concluded that developmental effects of WAI were evident during the first 6 months of life. Wali et al. [13] recommended establishing separate age-specific normative data for neonates, infants aged 1 to 2 months, and infants aged 3 to 6 months. Additionally, Peng et al. [17] and Peng et al. [18] suggested the necessity of establishing the normal values of WAI in infants at 1 and 2 months of age, respectively. These studies collectively support the notion that age plays a significant role in WAI characteristics in infants, and age-specific norms are crucial for accurate assessment and diagnosis during early audiological evaluations.

However, certain results in the present study differed from those of previous research [8, 13, 17, 18]. For instance, the mean WAI results in our study showed differences in absorbances at 3364 Hz and 4000 Hz. In contrast, Aithal et al. [8] reported a significant difference only at 800 Hz between the 1-2 months of age group and the 2-3 months of age group. Similarly, Wali et al. [13] found differences in WAI at 400 Hz and 4000 Hz between the two age groups. Peng et al. [17] indicated that absorbances of infants at 1-2 months of age were significantly higher than those of infants at 2-3 months of age between 226 Hz and 545 Hz. Additionally, Peng et al. [18] demonstrated a significant difference in absorbances only at 4000 Hz between the two age groups. These variations may be attributed to the ethnicity of participants, as Aithal et al. [8] recruited Caucasian infants, while Wali et al. [13] enrolled Malay, Indian, and Chinese infants. Moreover, differences in sample size could also play a role, with studies having varying numbers of infants in each age group (e.g., 16 and 16 infants in each age group in Aithal et al. [8]; 12 and 11 infants in Peng et al. [17];

16 and 14 infants in Peng et al. [18]).

As a result, our study highlights the importance of establishing ethnicity- and age-specific norms for WAI in infants under 3 months of age. Furthermore, the significant increase in WAI at 3364 Hz and 4000 Hz suggests that the evolution middle ear from a mass-dominated system to a stiffness-dominated system is attributed to maximising the effective transmission of speech sounds.

1.3 Differences of WAI in the infants under 3 years old with normal or abnormal middle ear function

To date, no studies have investigated the differences in WAI between infants with normal and abnormal middle ear function under 3 months of age. In light of the importance of early audiological diagnosis for infants, our study aimed to explore these differences in Chinese infants. The results revealed that the absorbances of infants with normal middle ear function were significantly higher than those of infants with abnormal middle ear function at the majority of frequencies. This finding confirms Hypothesis 3, indicating that WAI exhibits significant differences between infants with normal and abnormal middle ear function. Furthermore, our study employed ROC curves and the maxima of the Youden index, demonstrating that the normal middle ear function status for infants at 1-2 months and 2-3 months of age can be evaluated by the WAI at 1682 Hz and 1297 Hz, respectively. Specifically, the WAI thresholds for normal middle ear function in infants at 1 and 2 years old were determined to be 0.7470 at 1682 Hz and 0.6775 at 1297 Hz, respectively.

However, it is essential to note that there are certain limitations in the present study, including its cross-sectional nature and relatively small sample size. Therefore, further longitudinal studies with larger sample sizes are necessary to validate the results before implementing them in clinical practice. Longitudinal studies can provide more reliable data concerning the development of children [22], and studies with larger sample sizes yield results with smaller variances, which can be generalized to a wider population [23]. Such studies will contribute to strengthening the evidence and ensuring the robustness of the findings.

Conclusion

This present study highlights that WAI shows promise as a valuable tool for assessing the middle ear condition in infants at 1 and 2 months of age. According to the results obtained from ROC curves and the maxima of the Youden index, Infants aged 1 and 2 years, having absorbance values equal to or greater than 0.7470 at 1682 Hz and 0.6775 at 1297 Hz respectively, may indicate normal middle ear function. However, it should be noted that further confirmation is required through longitudinal studies with larger sample sizes in subsequent research. Moreover, this study emphasizes the necessity of establishing ethnicity- and age-specific norms for WAI in infants under 3 months of age. Additionally, there was no significant difference in absorbance between the left and right ears in infants with normal middle ear function. It implies that it would be acceptable to use merged absorbances of left and right ears as the WAI norms in future studies.

Human subjects

Research protocol for the current study satisfied the appropriate ethics review policies at West China Hospital of Sichuan University (Approval Number: Review in 2022 (No. 145)).

Declaration of interest: The authors report no conflicts of interest.

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