Journal of Otology 20 (2025) 5 – 11

Journal of Otology

journal homepage: www.sciopen.com/journal/1672-2930

Observational study to preliminarily characterize the audiological profile of chinese children with williams syndrome

Jiao Zhang[1,2,3], Minghui Zhao[1], Wei Shi[1], Haina Ding[1], Lan Lan[1,2], Dayong Wang[1,2,3] and Qiuju Wang[1,2,3,4] ✉

[1] *College of Otolaryngology Head and Neck Surgery, Chinese PLA Institute of Otolaryngology, Chinese PLA General Hospital, Chinese PLA Medical School, Beijing, China*

[2] *National Clinical Research Center for Otolaryngologic Diseases, Beijing, China*

[3] *Key Lab of Hearing Science, Ministry of Education, Beijing, China*

[4] *Beijing Key Lab of Hearing Impairment for Prevention and Treatment, Beijing, China*

ABSTRACT

Purpose: It is essential to investigate the audiological profiles of Williams syndrome in a multicultural context. This study aims to examine the characteristics and management of hearing loss in Chinese children with Williams syndrome and provide references for future clinical management. Method: Between January 2007 and March 2022, families with at least 1 WS patient was recruited from the Newborn Cohort Study of Hearing Loss. Audiological tests were performed, and then appropriate medical management was offered. Furthermore, an overview of the hearing loss phenotype in Williams syndrome in different locations was reviewed. Results: A total of two families with at least 1 Williams syndrome patient were recruited from the Newborn Cohort Study of Hearing Loss (ChiCTR2100049765). We identified moderately severe sensorineural or conductive hearing loss that emerged as early as the infancy period in Williams syndrome subjects in Chinese children. Our results extended the reported onset ages of hearing loss in WS from late childhood or early adulthood to the infancy period. We also found that with early diagnosis, proper management, and regular monitoring, children with Williams syndrome could return to a normal or near-normal school life. Conclusions: Our study demonstrated the distinct hearing profile in Chinese children with Williams syndrome for the first time. This cohort of WS subjects extends the reported onset ages of hearing loss in WS from late childhood or early adulthood to the infancy period, indicating the importance of clinicians screening and monitoring the hearing status of individuals with WS as early as possible. These data provide references for otolaryngologists and paediatricians to inform the clinical understanding and management of hearing loss in Williams syndrome.

KEYWORDS

williams syndrome, hearing loss, audiological profile, children, clinical management.

1 Introduction

Williams syndrome, also known as Williams-Beuren syndrome (WS/WBS, OMIM 194050), is a genetic disorder caused by a deletion of part of chromosome 7 (7q11.23) with an autosomal dominant mode of inheritance 2. (Beuren, Apitz and Harmjanz, 1962; Kozel et al., 2021; Williams, Barratt-Boyes and Lowe, 1961). It is a relatively rare neurodevelopmental condition with an estimated prevalence of one in 7500–20000 births and affects males and females equally (National Organization for Rare Disorders, 2006; Strømme, Bjørnstad and Ramstad, 2002). Children with WS usually show dysmorphic facies, cardiovascular disease, intellectual disability, visuospatial deficits, and hearing loss (Kruszka et al., 2018; Pinelli et al., 2020; Somerville et al., 2005; Tebbenkamp et al., 2018; Willfors et al., 2021). Hearing loss can have a profound impact on the health and education of this population. The effects begin gradually and progress as hearing loss worsens. Children with WS have visuospatial disorders requiring them to depend upon more auditory information in educational and social environments (Brodie et al., 2022; Game, Panicker and Fowler, 2010; İkiz and Yücel, 2022; Paglialonga et al., 2014).

It is essential to investigate the audiological profiles of Williams syndrome in a multicultural context. The hearing loss phenotype of WS has been well-described in the United States, Brazilians, Italians, and Israelis (Barozzi et al., 2013; Marler et al., 2010; Silva et al., 2021; Zarchi et al., 2011). However, there have been no reports regarding audiological profiles of Williams Syndrome in Asian populations. An important question is whether hearing loss is unique or nonspecific in Chinese subjects with WS. To address this question, we comprehensively investigated auditory impairments in 2 Chinese families affected with Williams syndrome and compared them with other populations in the previous literature

Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.

* Corresponding author Qiuju Wang, Email: wqjavm301@sina.com or wqcr301@vip.sina.com

https://doi.org/10.26599/JOTO.2025.9540002

Received 23 October 2024; Revised 30 December 2024; Accepted 7 January 2025

studies. We performed newborn hearing screening, diagnostic auditory testing, interventions, and follow-ups. We described the distinct auditory characteristics in Chinese WS children. To our knowledge, this is the first hearing loss report in WS cases in the Chinese population, and it preliminarily characterized the audiological profile of Chinese children with Williams syndrome to provide references for future clinical management.

2 Methods

2.1 Study design, ethics, setting, and participants

This cohort study was registered in the Chinese Clinical Trial Registry (ChiCTR2100049765). Families with at least 1 WS patient was recruited from the Newborn Cohort Study of Hearing Loss. From a total of 2082 families in the cohort, 2 families were selected. The diagnosis of WS had been clinically established and genetically confirmed previously in these patients. All patients included in the study exhibited the typical microdeletion (7q11.23). They were recruited by the Chinese PLA General Hospital, Beijing, China, between 2007 and 2022 (Fig. 1). The study was approved by the Committee of Medical Ethics of the Chinese PLA General Hospital (S2022-590-01). Written informed consent was obtained from the parents of the children.

2.2 Otologic examinations and clinical management

Otologic examinations included physical examination, otoscopic examination, imaging examination, and audiological evaluation. Certified and experienced audiologists performed the audiological assessment at the Clinical Audiology Center of the Chinese PLA General Hospital. A battery of audiological tests was performed, including visual reinforcement audiometry (VRA), conditioned play audiometry (CPA), immittance test, distortion product otoacoustic emission (DPOAE), auditory brainstem response (ABR), auditory steady-state response (ASSR), and 40 Hz auditory event-related potential (40 Hz AERP). In addition, the medical records of the individuals with WS were also reviewed. Moreover, an appropriate management strategy was offered, including hearing aids and surgery according to clinical manifestations and audiological phenotypes. Patients were monitored for at least three years.

Visual reinforcement audiometry (VRA) and conditioned play audiometry (CPA) were performed using a MEDSEN Astera audiometer (Natus, Denmark). Air and bone conduction thresholds were measured. The hearing thresholds were assessed at 0.125, 0.25, 0.5, 1, 2, 4 and 8 kHz. We analyzed the average hearing threshold calculated by averaging thresholds per ear obtained at 0.5, 1, 2, and 4 kHz. The degree and type of hearing loss were assessed based on the WHO 2021 criteria (World Health Organization, 2021). "Normal hearing" was defined by hearing thresholds of 20 dB or better in both ears, and "hearing loss" was defined by hearing thresholds above 20 dB HL in one or both ears. The degree of hearing loss was classified as "mild" when the average hearing threshold was between 20 and 35 dB HL, 'moderate' between 35 and 50 dB HL, "moderately severe" between 50 and 65 dB HL, 'severe' between 65 and 80 dB HL, 'profound' between 80 and 95 dB HL, and "total hearing loss" at more than 95 dB HL. According to the peak admittance measure, the tympanometric curve was characterized following Jerger's criteria (Jerger, 1970). Tympanometry was classified as normal (type A), flat curve (type B), negative pressure (type C), low peak curve (type As), or high peak curve (type Ad).

2.3 Statistical analysis

Data were analyzed using R (R 4.2.0) (R Core Team, 2022). Descriptive and statistical analyses were performed. Counts and percentages were calculated for categorical variables. Mean values and standard deviations (SDs) were calculated for quantitative variables. $P<0.05$ in two-tailed tests was regarded as statistically significant.

2.4 Overview of hearing loss phenotype in Williams syndrome

The EMBASE and PUBMED databases were searched for a literature review. The clinical audiological characteristics of these WS cases were summarized. Then, comparisons of the audiological phenotypes and associated management in different studies from different countries were analyzed.

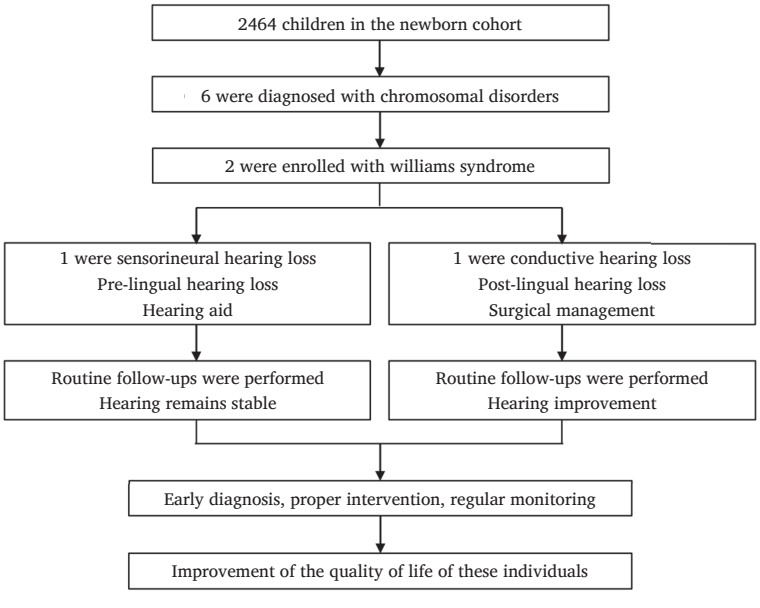


Figure 1 Enrollment and outcomes of the children with Williams syndrome participating in the clinical study. The participants were enrolled in the Newborn Cohort Study of Hearing Loss.

3 Results

3.1 Otologic tests and clinical management

Finally, 2 families were enrolled in the Newborn Cohort Study of Hearing Loss (Fig. 1). Children with Williams syndrome all received a battery of audiological tests to assess their hearing level. Then, appropriate management was offered, including hearing aids and surgery, according to clinical manifestations and audiological phenotypes. Regular monitoring was also conducted. During recent follow-ups, these WS subjects attended ordinary kindergartens in Beijing and could communicate well.

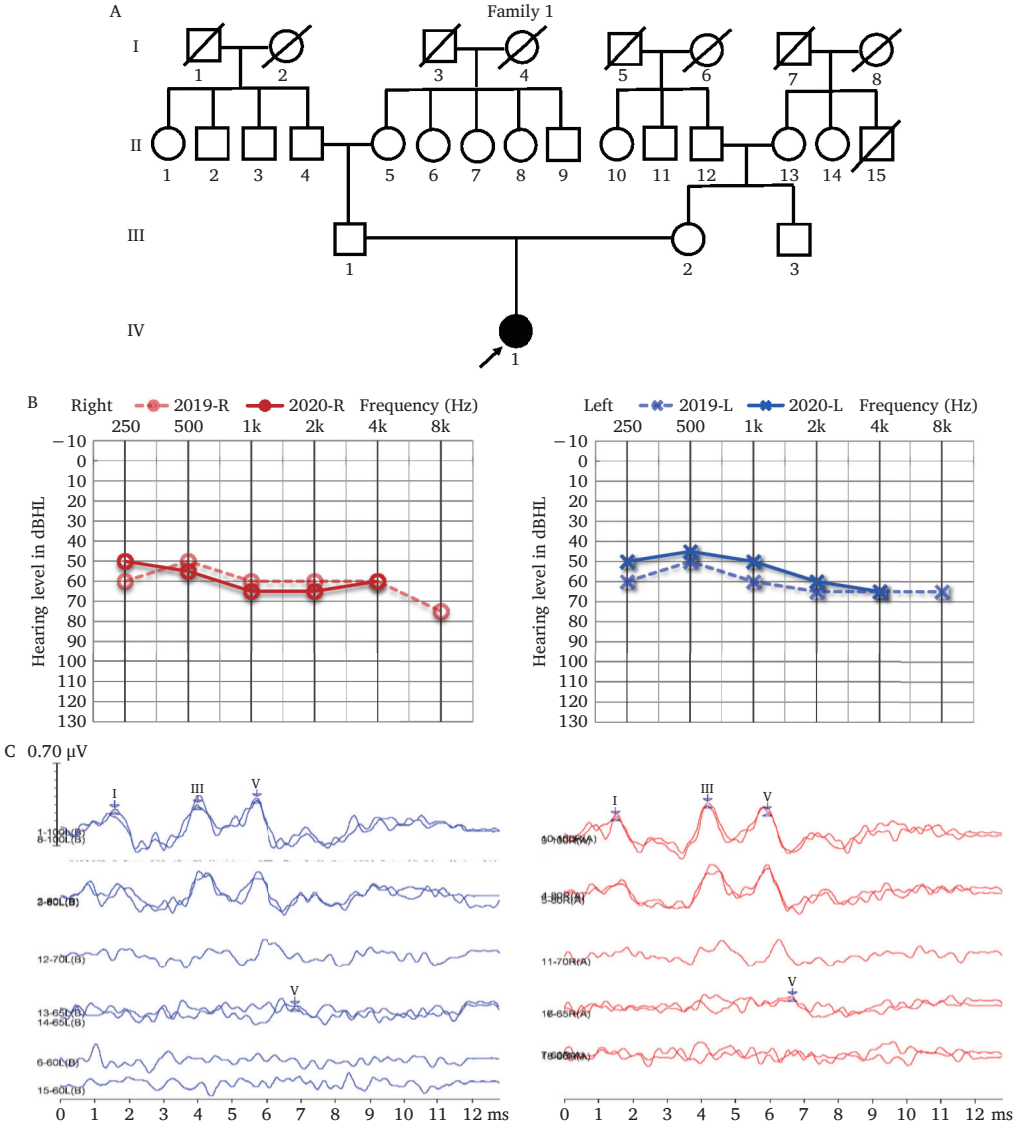
Family 1

Proband III-1 of Family 1 (Fig. 2) was a 1-year-old girl who suffered from prelingual, approximately symmetrical, and bilateral sensorineural hearing loss (Fig. 2A). She failed the newborn hearing screening initially and was diagnosed with bilateral sensorineural hearingloss at 3 months of age. Visual reinforcement audiometry (VRA) was conducted at audiometric frequencies. The results indicated a moderately severe bilateral sensorineural hearing loss (Fig. 2B). VRA audiograms of the proband showed all-frequency affected hearing impairment. The tympanogram indicated normal function of the middle ear. The thresholds of ABR were 65 dBnHL on both sides (Fig. 2C), and the ABR testing showed prolonged latencies of ABR waves I, III, and V (Table 1). The 40 Hz AERP test illustrated a threshold of 65 dBnHL on both sides (Fig. 2D). Bilateral DPOAE for the proband was absent. The ASSR audiogram showed moderately severe hearing loss, and the ASSR thresholds for the left and right sides were 51.5±12.01 and 52.75±6.75, respectively. The CT of the temporal bone in the proband of Family 1 (III:1) showed standard inner ear structure.

She was appropriately fit with hearing aids at 10 months of age and then offered language rehabilitation training. Her mother responded that the hearing aids worked well. She could listen, communicate, and participate more fully in daily activities. Follow-ups were performed after 1 year and 3 years. No significant changes were seen in hearing level. Now, she is in a regular kindergarten in Beijing and can communicate well.

Family 2

The proband of Family 2 (Fig. 3) was a 3-year-old girl diagnosed with a bilateral conductive hearing impairment following an upper respiratory tract infection. A routine otoscopic examination showed bilateral tympanic membrane depression and bilateral intratympanic effusion, suggesting bilateral otitis media with effusion (OME). Auditory examination and conditioned play audiometry showed that the conductive hearing loss was moder-



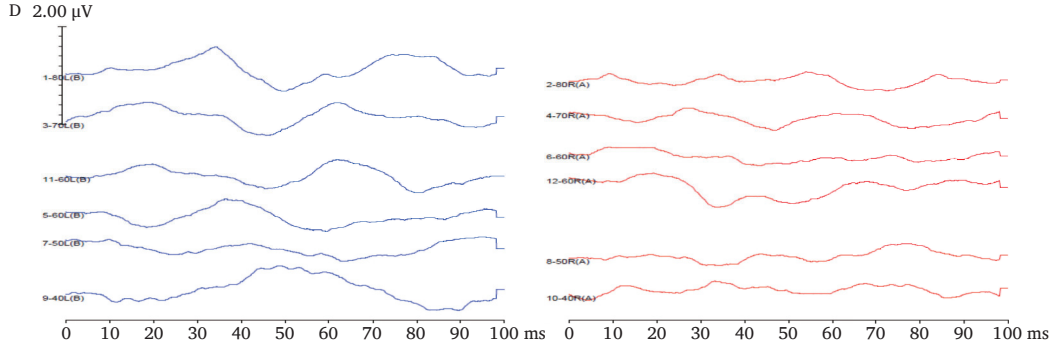


Figure 2 Pedigree and audiological phenotype of Family 1. (A) Pedigree diagrams of Family 1. Filled symbols for males (squares) and females (circles) represent affected individuals and empty, unaffected individuals. An arrow denotes the proband. (B) Audiograms of both ears from the proband in Family 1 (III:2). Symbols "o" and "x" denote air conduction thresholds at different frequencies in the right and left ear, respectively. dB HL, decibels hearing level; Hz, Hertz. (C) ABR of both ears from the proband in Family 1 (III:2). ABR, Auditory brainstem response. (D) 40 Hz-AERP of both ears from the proband in Family 1 (III:2). 40Hz-AERP, 40 Hz auditory event-related potentials. The blue line represents the left ear results (L), and the red line represents the right ear (R).

Table 1 Auditory brainstem response latencies (ms) of the proband III-1 of Family 1

	I	III	V	I-III	III-V	I-V
Left-1	1.57	4.00	5.72	2.43	1.72	4.15
Right-1	1.52	4.20	5.95	2.68	1.75	4.43
Left-2	1.55	3.95	5.70	2.40	1.75	4.15
Right-2	1.48	4.18	5.75	2.70	1.57	4.27

Data from the Newborn Cohort Study of Hearing Loss. Numbers "1" and "2" denote the Auditory brainstem response latency results of the first and second visit, respectively.

ately severe (Fig. 3). The tympanogram displayed a "Type B" curve, indicating noncompressible fluid within the middle ear space (otitis media). Bilateral DPOAE was absent. The CT of the temporal bone in the proband of Family 2 (III:1) showed bilateral otitis media, mastoiditis, and standard inner ear structure.

Since OME lasts for more than 3 months, with the chief complaint being inaudibility accompanied by frequent requests to speak more loudly, the surgical management of insertion of tympanostomy tubes was conducted to promote drainage of persistent unresolved effusions and improve hearing. During surgery, a pale yellow jelly-like discharge was suctioned and washed from the bilateral tympanums. After that, a tympanostomy tube was inserted on each side. Postoperative follow-ups were performed at 1 month and 2 months after surgery. Parents reported that the child's hearing had improved significantly, and they were no longer asked to speak at higher volumes. Currently, the patient is in a regular kindergarten in Beijing and can communicate well.

3.2 Overview of hearing loss phenotype in Williams Syndrome

The hearing loss phenotype of WS is summarized in Table 2. Worldwide, the audiological profiles of hearing loss in WS have been described previously in the United States, Brazilians, Italians, and Israelis (Barozzi et al., 2012; Bedeschi et al., 2011; Cherniske et al., 2004; Fagundes Silva et al., 2021; Marler et al., 2005; Silva et al., 2022). Hearing loss (sensorineural or conductive), which is progressive and emerges early, was frequently reported to a mild or moderate degree in subjects with WS. Sensorineural hearing loss was predominant in at least half of the cases and was positively associated with age. Conductive hearing loss has been reported in WS children, with a prevalence higher than that of the general population (Barozzi et al., 2012). In the present study, we reported the characteristics and management of hearing loss in Chinese WS subjects. We found that hearing loss could emerge as early as infancy, which was not previously reported. We also found sensorineural and conductive hearing loss in WS subjects in our cohort, but to a more severe degree of hearing loss than published literature. Furthermore, we tried to improve the quality of life of these individuals with early diagnosis, proper management, and regular monitoring.

4 Discussion

Comprehensively, we investigated the characteristics of hearing loss in Chinese WS children, extending the reported locations of the previous series on hearing loss in WS by focusing specifically on subjects from Asia. In addition, we also found that hearing loss could emerge as early as infancy in WS children in our cohort, which has not been previously reported. Furthermore, we demonstrated that young children with WS can return to a typical or near-normal school experience with early diagnosis, proper management, and regular monitoring.

In the present study, we comprehensively investigated auditory impairments in 2 families affected with Williams syndrome in the Chinese population enrolled in our Newborn Cohort Study of Hearing Loss (ChiCTR2100049765, https://www.chictr.org.cn/). In contrast to previous studies (Barozzi et al., 2012; Bedeschi et al., 2011; Cherniske et al., 2004; Fagundes Silva et al., 2021; Marler et al., 2005; Silva et al., 2022) that typically evaluated only auditory assessments, such as otoacoustic emission, tympanogram, and pure tone audiometric examination, in this study, we analyzed a battery of audiological tests, including visualreinforcement audiometry (VRA), conditioned play audiometry (CPA), immittance test, distortion product otoacoustic emission (DPOAE), auditory brainstem response (ABR), auditory steady-state

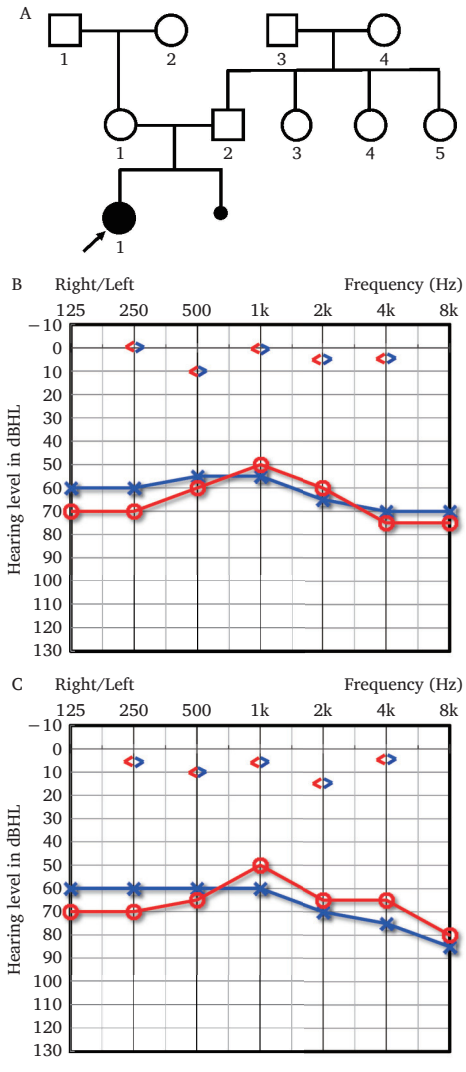


Figure 3 Pedigree and audiological phenotype of Family 2. (A) Pedigree diagrams of Family 2. Filled symbols for males (squares) and females (circles) represent affected individuals and empty, unaffected individuals. An arrow denotes the proband. (B and C) Audiograms of the first and second visit of the proband in Family 2 (III:1). Symbols "o" and "x" denote air conduction thresholds at different frequencies in the right and left ear, respectively. Symbols ">" and "<" denote bone conduction thresholds at different frequencies in the right and left ear, respectively. dB HL, decibels hearing level; Hz, Hertz. The blue line represents the left ear results (L), and the red line represents the right ear (R).

response (ASSR), and 40 Hz auditory event-related potential (40 Hz AERP).

It is essential to combine different audiological measures better to assess the hearing level of these WS subjects. Thus, the combination and cross-validation of subjective and objective inspections were performed to ensure the accuracy and reliability of the audiological results. Finally, we found moderately severe sensorineural and conductive hearing loss in the WS children in our cohort, which for the first time demonstrated the hearing loss type and degree of Chinese WS children.

Regarding the onset age of hearing loss in WS, we found that the subject with the lowest chronological age (three months) already presented sensorineural hearing loss. Several studies addressing WS have reported sensorineural hearing loss involvement that begins in late childhood or early adulthood (Barozzi et al., 2012; Bedeschi et al., 2011). Our results further confirmed the early onset of hearing loss in subjects with WS, showing that hearing loss involvement can emerge during infancy. This WS child received close medical care since she failed the newborn hearing screening and was then diagnosed with bilateral sensorineural hearing loss at 3 months of age. Such monitoring care is critical to identify hearing loss as early as possible in WS subjects, possibly before the onset of severe hearing impairment and the rise of associated speech and language development disabilities. This cohort of WS subjects extends the reported onset ages of hearing loss in WS from late childhood or early adulthood to the infancy period, indicating the importance of clinicians screening and monitoring the hearing status of individuals with WS as early as possible.

Current research indicates that with early diagnosis, proper intervention, and regular monitoring, we tried to improve the quality of life of these individuals. WS children could return to a normal or near-normal school experience. According to the clinical guidelines (Morris and Braddock, 2020; Williams Syndrome Guideline Development Group, 2017), once a diagnosis of hearing loss in WS is made, an audiologic assessment should be performed annually throughout their lives. Their families should be counseled and well-trained in their children's hearing and speech needs with WS. Based on the results of these hearing evaluations, proper interventions should be recommended, including compensation strategies, amplification systems, and even surgery. This is particularly important since children with WS have visual-spatial problems and depend on auditory information for educational and psychosocial development (Chailangkarn et al., 2016; Miezah et al., 2021). Even mild hearing loss can have a lasting effect on children's language ability, psychosocial development, academic success, and vocational development (Brodie et al., 2022; Tomblin et al., 2020; Yeshoda, Raveendran and Konadath, 2020). It is important to emphasize that WS children could return to a normal or near-normal school experience under proper medical care and regular monitoring.

This study also has limitations. First, the sample size needs to be bigger, which may not adequately capture the diversity within a certain population. Hence, further investigations involving larger-scale subjects are required to validate these findings. Besides, this study was conducted in a Chinese children cohort, and the data may not yield worldwide generalizability. Therefore, it is essential to investigate audiological profiles in a multicultural context in the future.

5 Conclusions

In conclusion, we demonstrated the distinct hearing profile in Chinese children with Williams syndrome for the first time. We found that moderately severe sensorineural or conductive hearing loss emerged as early as infancy in these subjects. Our results extended the reported onset ages of hearing loss in WS from late childhood or early adulthood to the infancy period. These data can be a reference for otolaryngologists and paediatricians to inform the clinical understanding and management of hearing loss in Williams syndrome. Early screening and management of hearing loss is particularly important since children with WS have visual spatial problems and depend on auditory information for both educational and psychosocial development. In the future, a larger prospective investigation would be necessary, in which young WS individuals are followed longitudinally to understand better if and to what extent the audiological characteristics of these

Table 2 A summary of literature showing characteristics of hearing loss in Williams syndrome

Populations	References	Age (years)	Gender	WS cases	HL cases	Affected ears	Audiologic findings (affected ear)						
							Type	Severity	Tympanograms	OAE	HL Criteria	Intervention	Follow-ups
Chinese-1	Present study	0 – 3	2F	2	2 (100%)	2L2R	2 SNHL 2 CHL	4 Moderately severe	2 As 2 B	4 Absent	PTA > 20 dB HL (WHO, 2021)	Yes (HA & surgery)	Yes
American-1	Cherniske (2004)	30 – 51	10M10F	20	12 (60%)	23 Ears	20 SNHL 1 CHL 2 NA	16 Mild to moderate 1 Mild 6 NA	/	/	/	/	/
American-2	Marler (2005)	6–48	15M12F	27	23 (85.2%)	/	/	/	/	6 Present 19 Absent 2 NA	Threshold > 20 dB HL	/	/
American-3	Marler (2010)	5–59	37M44F	81	57 (70.4%)	99 Ears	/	/	/	/	Response > 20 dB HL	/	/
Brazilian-1	Silva (2021)	7 – 17	10M7F	17	6 (35.3%)	4L5R	9 SNHL	8 Mild 1 Moderate	/	/	Response > 20 dB HL	/	/
Brazilian-2	Silva (2021)	7 – 17	10M7F	17	0	0	/	/	/	/	PTA > 25 dB HL	/	/
Brazilian-3	Silva (2022)	7 – 17	15M7F	22	11 (50%)	9L10R	15 SNHL 4 MHL	12 Mild 5 Moderate 2 Severe	14 A 3 Ad or B 2 C	16 Present 9 Absent 19 NA	Thresholds > 20 dB HL	/	/
Israel-1	Zarchi (2011)	/	/	44	25 (56.8%)	50 Ears	23 SNHL 19 MHL 8 CHL	40 Mild 10 Moderate to profound	61 A 20 B 7 C	/	Thresholds > 25 dB HL	Yes (CI)	/
Italian-1	Bedeschi (2011)	17–39	7M6F	45	8 (17.8%)	8L8R	5 SNHL 1 CHL 2 MHL	8 Mild	/	/	/	/	/
Italian-2	Barozzi (2012)	2 – 30	35M34F	69	14 (20.3%)	12L11R	7 SNHL 6 CHL 1 MHL 9 NA	16 Slight 2 Mild 4 Moderate 1 Severe	102 A 32 B or C	42 Present 46 Absent 50 NA	PTA > 15 dB HL VRA > 20 dB HL	/	/
Italian-3	Barozzi (2013)	5 – 14	14M10F	24	3 (12.5%)	4	2 SNHL 1 CHL 1 NA	4 Slight	33 A 10 C 5 As	15 Present 14 Absent 19 NA	PTA > 15 dB HL	/	Yes
Italian-4	Paglialonga (2014)	9 – 31	9M4F	13	0	0	/	/	/	/	PTA > 15 dB HL	/	/

Abbreviations: M, Male; F, Female; WS, Williams syndrome; HL, hearing loss; R, Right; L, Left; SNHL, sensorineural hearing loss; CHL, conductive hearing loss; MHL, mixed hearing loss; dB HL, decibels Hearing Level; HA, hearing aid; CI, cochlear implant; OAE, Otoacoustic Emissions; NA, not available.

subjects progressively evolve.

Acknowledgements

The authors thank the children with WS and their families for their invaluable participation.

Funding source

This work was supported by the grants of the National Key Research and Development Program of China (Grant No.2023YFC2508400) and the National Natural Science Foundation of China (Grant No.82350005).

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, 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.

References

Barozzi, S., Soi, D., Comiotto, E., et al., 2012. Audiological findings in Williams syndrome: a study of 69 patients. *Am. J. Med. Genet. Part A* 158A(4), 759–771.

Barozzi, S., Soi, D., Spreafico, E., et al., 2013. Audiological follow-up of 24 patients affected by Williams syndrome. *Eur. J. Med. Genet.* 56(9), 490–496.

Bedeschi, M.F., Bianchi, V., Colli, A.M., et al., 2011. Clinical follow-up of young adults affected by Williams syndrome: experience of 45 Italian patients. *Am. J. Med. Genet. Part A* 155A(2), 353–359.

Beuren, A.J., Apitz, J., Harmjanz, D., 1962. Supravalvular aortic stenosis in association with mental retardation and a certain facial appearance. *Circulation* 26(6), 1235–1240.

Brodie, K.D., David, A.P., Kriss, H., et al., 2022. Outcomes of an early childhood hearing screening program in a low-income setting. *JAMA Otolaryngol. Head Neck Surg.* 148(4), 326–332.

Chailangkarn, T., Trujillo, C.A., Freitas, B.C., et al., 2016. A human neurodevel-

opmental model for Williams syndrome. *Nature* 536(7616), 338–343.

Cherniske, E.M., Carpenter, T.O., Klaiman, C., et al., 2004. Multisystem study of 20 older adults with Williams syndrome. *Am. J. Med. Genet. Part A* 131A(3), 255–264.

Fagundes Silva, L.A., Honjo Kawahira, R.S., Kim, C.A., et al., 2021. Abnormal auditory event-related potentials in Williams syndrome. *Eur. J. Med. Genet.* 64(3), 104163.

Game, X., Panicker, J., Fowler, C.J., 2010. Williams-Beuren syndrome. *N. Engl. J. Med.* 362(15), 1449–1450.

İkiz, M., Yücel, E., 2022. The relationships between language, working memory and rapid naming in children with mild to moderate hearing loss. *Int. J. Pediatr. Otorhinolaryngol.* 158, 111156.

Jerger, J., 1970. Clinical experience with impedance audiometry. *Arch. Otolaryngol.* 92(4), 311–324.

Kozel, B.A., Barak, B., Kim, C.A., et al., 2021. Williams syndrome. *Nat. Rev. Dis. Primers* 7(1), 42.

Kruszka, P., Porras, A.R., de Souza, D.H., et al., 2018. Williams-Beuren syndrome in diverse populations. *Am. J. Med. Genet. Part A* 176(5), 1128–1136.

Marler, J.A., Elfenbein, J.L., Ryals, B.M., et al., 2005. Sensorineural hearing loss in children and adults with Williams syndrome. *Am. J. Med. Genet. Part A* 138A(4), 318–327.

Marler, J.A., Sitcovsky, J.L., Mervis, C.B., et al., 2010. Auditory function and hearing loss in children and adults with Williams syndrome: cochlear impairment in individuals with otherwise normal hearing. *Am. J. Med. Genet. Part C: Semin. Med. Genet.* 154C(2), 249–265.

Miezah, D., Porter, M., Rossi, A., et al., 2021. Cognitive profile of young children with Williams syndrome. *J. Intellect. Disabil. Res.* 65(8), 784–794.

Morris, C.A., Braddock, S.R., Council on Genetics, 2020. Health care supervision for children with Williams syndrome. *Pediatrics* 145(2), e20193761.

National Organization for Rare Disorders, 2006. Williams syndrome. Available at https://rarediseases.org/rare-diseases/williams-syndrome/. Accessed 9 Jun 2022.

Paglialonga, A., Barozzi, S., Brambilla, D., et al., 2014. Analysis of subtle auditory dysfunctions in young normal-hearing subjects affected by Williams syndrome. *Int. J. Pediatr. Otorhinolaryngol.* 78(11), 1861–1865.

Pinelli, M., Terrone, G., Troglio, F., et al., 2020. A small 7q11. *23 microduplication involving GTF2I in a family with intellectual disability. Clin. Genet.* 97(6), 940–942.

R Core Team, 2022. R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Available at https://www.R-project.org/. Accessed 9 Jun 2022.

Sauna-Aho, O., Bjelogrlic-Laakso, N., Sirén, A., et al., 2019. Cognition in adults with Williams syndrome-A 20-year follow-up study. *Mol. Genet. Genomic Med.* 7(6), e695.

Silva, L.A.F., Kawahira, R.S.H., Kim, C.A., et al., 2021. Auditory hypersensitivity in Williams syndrome. *Int. J. Pediatr. Otorhinolaryngol.* 146, 110740.

Silva, L.A.F., Kawahira, R.S.H., Kim, C.A., et al., 2022. Audiological profile and cochlear functionality in Williams syndrome. *Codas* 34(3), e20210041.

Somerville, M.J., Mervis, C.B., Young, E.J., et al., 2005. Severe expressive-language delay related to duplication of the Williams-Beuren locus. *N. Engl. J. Med.* 353(16), 1694–1701.

Strømme, P., Bjømstad, P.G., Ramstad, K., 2002. Prevalence estimation of Williams syndrome. *J. Child Neurol.* 17(4), 269–271.

Tebbenkamp, A.T.N., Varela, L., Choi, J., et al., 2018. The 7q11.23 protein DNAJC30 interacts with ATP synthase and links mitochondria to brain development. *Cell* 175(4), 1088–1104.e23.

Tomblin, J.B., Oleson, J., Ambrose, S.E., et al., 2020. Aided hearing moderates the academic outcomes of children with mild to severe hearing loss. *Ear Hear.* 41(4), 775–789.

Willfors, C., Riby, D.M., van der Poll, M., et al., 2021. Williams syndrome: on the role of intellectual abilities in anxiety. *Orphanet J. Rare Dis.* 16(1), 472.

Williams, J.C.P., Barratt-Boyes, B.G., Lowe, J.B., 1961. Supravalvular aortic stenosis. *Circulation* 24(6), 1311–1318.

Williams Syndrome Guideline Development Group, 2017. Management of Williams syndrome. A clinical guideline. Available at https://williams-syndrome.org.uk/wp-content/uploads/2018/07/williams_syndrome_guidelines_pdf.pdf. Accessed 9 Jun 2022.

World Health Organization, 2021. World report on hearing. Geneva: World Health Organization. Available at https://www.who.int/publications/i/item/9789240020481. Accessed 9 Jun 2022.

Yeshoda, K., Raveendran, R., Konadath, S., 2020. Perception of vocal emotional prosody in children with hearing impairment. *Int. J. Pediatr. Otorhinolaryngol.* 137, 110252.

Zarchi, O., Attias, J., Raveh, E., et al., 2011. A comparative study of hearing loss in two microdeletion syndromes: velocardiofacial (22q11.2 deletion) and Williams (7q11.23 deletion) syndromes. *J. Pediatr.* 158(2), 301–306.