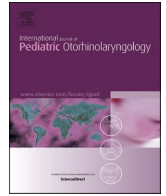




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## Annual hearing screening in children with osteogenesis imperfecta: Results from the first five years in glasgow

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## ABSTRACT

**Background:** Hearing loss is common in people with osteogenesis imperfecta (OI), although exactly how common is unknown. The prevalence of hearing loss in children with OI has been reported to be anything from 0 to 77 %. Brittle Bone Society guidelines suggest that, unless there are ear symptoms, children with OI should have their hearing tested every three years starting at age three. There is limited evidence to support this recommendation. We postulate that annual hearing screening would be easier to manage and would have a worthwhile pick-up rate.

**Methods:** In March 2019 we began a programme of annual hearing screening for all children (ages 0–16) with OI. We collected data on age, genotype, otoscopy findings, tympanometry findings, audiometric test results and subsequent outcomes for the first five years of our programme (2019–2024).

**Results:** Nineteen children with OI participated in the screening programme. Only one abnormality was found: a unilateral mild hearing impairment with a type B tympanogram, suggesting middle ear effusion. This was present in year 2 of the programme but resolved by year 3.

**Conclusion:** The screening programme has a low pickup rate (5 %) for new otological problems in the paediatric population. However, we believe that the low cost and small workload associated with the screening programme justifies continuing it until further conclusions can be drawn.

## 1. Introduction

Osteogenesis imperfecta (OI) is an inherited Mendelian disorder of bone and connective tissue which affects around 1 in 20,000 newborns [1,2]. The disease is characterised by defects in type I collagen, the main protein found in the extracellular matrix of bone, skin and tendons. It can result in low bone mass, joint deformities and hearing loss [2,3]. The Sillence classification defines 16 different types of OI [2–4]. Types I–IV are autosomal dominant and account for up to 90 % of the total: the remaining types are autosomal recessive [2,4]. Hearing loss most commonly presents in type I, but is also documented in types II and III. The reported prevalence of hearing loss in children with OI is very variable, ranging from 0 to 77 % [1,5–10]. The prevalence of hearing loss increases with age, with only around 5 % of patients experiencing hearing loss in the first decade of life [3,6,9].

Hearing loss in OI typically presents as bilateral conductive hearing loss and evolves to a mixed hearing loss due to progressive inner-ear involvement [3,11]. Hearing loss is heterogenous in terms of onset, type, severity and progression and is unrelated to other clinical features of OI [12]. Conductive hearing loss in OI can be caused by microfractures in various places, most commonly the crura of the stapes and the bony labyrinth [13,14]. OI can also cause narrowing of the middle ear cavity resulting in partial or complete enclosure of the stapes footplate, and obstruction of the oval and round windows [15].

Children with OI may also present with conductive hearing loss due to otitis media with effusion (OME) [16,17]. It is thought that these children may be more susceptible to OME because of craniofacial dysmorphism associated with OI [17]. It has been reported that up to 43 % of children with OI present with tympanometric abnormalities consistent with OME [17]. This compares to an incidence to be between 8.6 % and

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13.5 % in unaffected school age children [18,19]. A small proportion of adults with OI will present with sensorineural hearing loss due to ossification of the cochlea secondary to microfractures [16]. This form of hearing loss may be less severe with a slower overall progression than conductive/mixed hearing loss. Sensorineural hearing loss in children is typically restricted to children with type I OI [17].

Bisphosphonates are the most frequently used class of drug in the management of OI and have been routinely used since the 1990s [20, 21]. By inactivating osteoclasts, they increase bone mineral density, resulting in a reduction in bone pain and risk of fractures [21]. The treatment effect of bisphosphonates has been shown to be greater in children than in adults with OI and it has therefore been suggested that bisphosphonate treatment early in life will alter the time course of hearing loss [21].

Specific management of hearing loss in OI includes hearing aids, middle-ear surgery and cochlear implants [22,23], all of which have a role in minimising the psychosocial, learning and developmental difficulties associated with hearing loss. Cochlear implantation has been shown to be an effective treatment for sensorineural hearing loss in OI [22,23]. However, surgical outcomes are worse in patients with OI as the bones of the middle ear are weaker and less stable, making both middle ear surgery and cochlear implantation more challenging [16].

Brittle Bone Society guidelines suggest that children with OI who have no otological symptoms should be screened every three years starting between the ages of three and four, with those who demonstrate borderline hearing being assessed every year [24]. Screening is reasonable because hearing loss is common and treatable, but there is no evidence to support its effectiveness. We decided on annual screening because it is easier to manage from an administrative point of view, parents are less likely to lose contact with the service and it avoids a potential three-year delay in managing hearing loss at such a critical time in a child's development. The aim of this study is to assess whether our hearing screening programme for children with OI is an effective use of resources, with a worthwhile rate of detection of new otological problems and without an excessive additional workload for the audiology department.

## 2. Methods

### 2.1. Ethical considerations

As this is an anonymised, retrospective evaluation of an existing clinical service, no specific ethics committee review or approval is required in our institution.

### 2.2. Study population

In March 2019 we began a programme of annual hearing screening for all children (age 0–16 years) with OI within the NHS Greater Glasgow & Clyde. The department of paediatric endocrinology have a complete list of all children with OI in our health board area, and this is updated annually and shared with the audiology department. Invitations are sent out to families to attend hearing screening at a time which suits them. Those who fail to attend receive phone calls and follow up letters. Age-appropriate hearing testing (sound field visual reinforcement audiometry, play audiometry and pure tone audiometry using headphones) is carried out by experienced paediatric audiologists in sound dampened rooms according to British Society of Audiology guidelines. The 4-frequency average (mean air conduction thresholds for 0.5, 1, 2, 4 kHz) was used to define hearing loss, based on the World Health Organisation classification. Tympanometry was performed to assess middle ear pressure.

### 2.3. Data collection

NHS electronic records were accessed to retrieve data on age,

genotype, otoscopy findings, tympanometry findings, audiometric test results and subsequent outcomes for the first five years of our programme.

## 3. Results

Twenty-nine children with OI and no ongoing hearing issues were identified and offered hearing screening during the study period. None were already known to have hearing loss. Nineteen (66 %) of these attended hearing screening at any point during the programme and defined the study group. The remaining 10 children chose not to participate or did not respond to appointment letters.

The characteristics of our study cohort are summarised in Table 1. The children in the study group were aged between 3 and 16 years at the start of the programme (median 8.6 years, mean 9.3 years). There were 8 boys and 11 girls. OI genotypes were as follows: 8 children were type I (40 %); 2 were type IV (10 %); 1 was type V (5 %); and 8 had not had their type identified (40 %). Sixteen out of 19 children (84 %) were on bisphosphonate treatment. Eight children transitioned to adult services at various points during the study period but attended at least one appointment as part of the screening programme. No child attended all five appointments. Four children attended four times; four attended three times; eight attended twice; and three attended once (Fig. 1).

Only one new hearing problem was detected by the screening programme. The remaining 18 children had no hearing issues or ear abnormalities at any point during the study period. Child 4 (Table 1) has type I OI and receives zoledronate. He had a mild left-sided conductive hearing loss detected during year 2 of the screening programme, aged 8 years. He had a type B tympanogram in the left ear suggesting middle ear effusion (Fig. 2). At the time of screening there were parental concerns regarding hearing. The hearing impairment had resolved by year 3 of the study (Fig. 3).

## 4. Discussion

### 4.1. Strengths of the study

Our study is the first to evaluate the effectiveness of an annual hearing screening programme in children with OI. Previous studies have reported cross-sectional prevalence data but ours is the only one with sequential follow up tests [1,7]. Although the size of our cohort is relatively small, this is quite a large series of children in the context of a rare condition such as OI, and it is a comprehensive series based on an entire birth cohort from a specific geographical region.

**Table 1**  
Characteristics of our study cohort.

No.	Sex	Age (Start of Programme)	OI Type	Bisphosphonate	Appointments Attended
1	F	13	V	Zoledronate	2
2	F	13	I	None	2
3	F	4	Unknown	Zoledronate	4
4	M	6	I	Zoledronate	3
5	M	9	I	None	3
6	M	8	I	Pamidronate	3
7	M	13	Unknown	Zoledronate	1
8	M	16	I	None	2
9	F	5	I	Zoledronate	2
10	M	16	I	Zoledronate	2
11	F	6	Unknown	Zoledronate	2
12	F	6	Unknown	Pamidronate	2
13	M	12	I	Zoledronate	4
14	F	8	IV	Zoledronate	1
15	F	14	IV	Zoledronate	1
16	M	3	Unknown	Zoledronate	4
17	F	3	Unknown	Zoledronate	3
18	F	15	Unknown	Risedronate	2
19	F	4	Unknown	Zoledronate	4

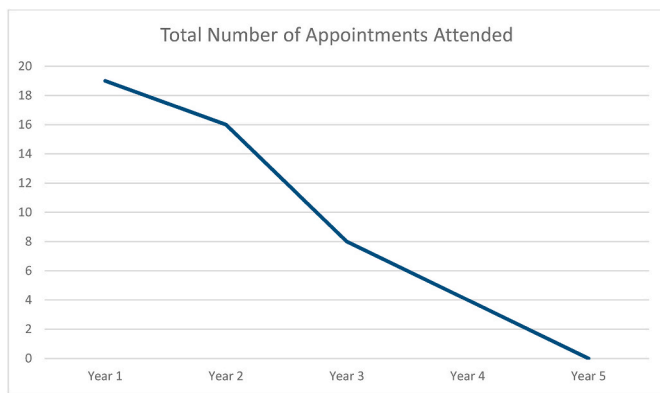


Fig. 1. Total number of appointments attended throughout the five-year screening period.

4.2. Limitations of the study

Only two-thirds of the children attended for hearing screening, and none attended every year. This is often the case for screening programmes: people may not attend appointments if they do not perceive there is a problem. The COVID-19 pandemic was also a factor in the poor rate of attendance. Our numbers are too small to draw meaningful conclusions with regards to genotype and risk of hearing loss.

4.3. Effectiveness of screening

We were surprised at the low pick up rate (5 % of children overall) for new otological problems. We believe that bisphosphonate treatment has reduced the prevalence of hearing loss in children, giving us a much lower prevalence than expected from some of the older published literature. As bisphosphonates only became routine treatment in the 1990s, many studies prior to 2010 would not have had a large number

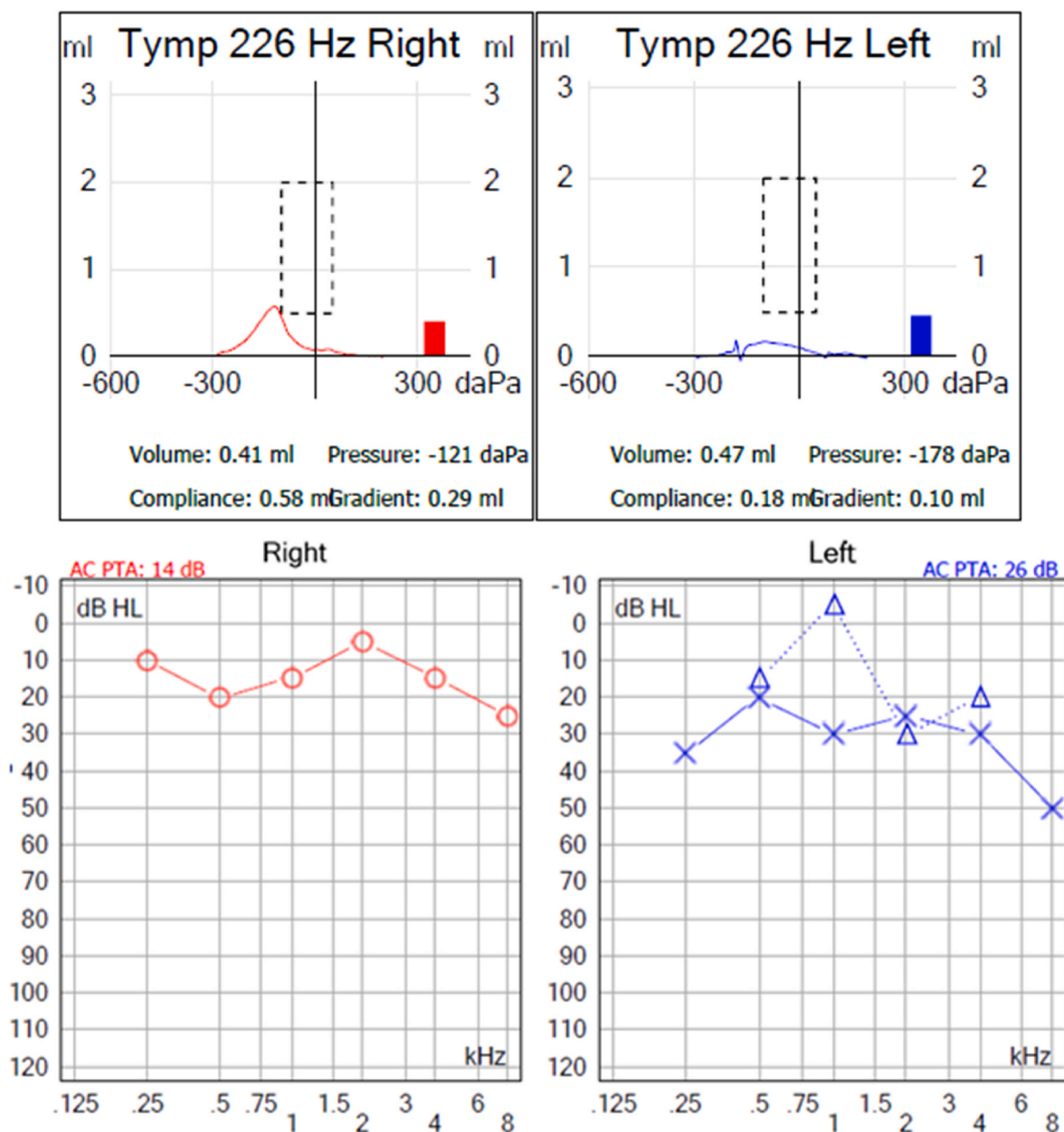


Fig. 2. Tympanogram and pure tone audiogram of Child 4 in Year 2 of the study, showing a mild left-sided conductive hearing loss and a type B tympanogram. This was the only abnormality detected during the 5 years of the study.

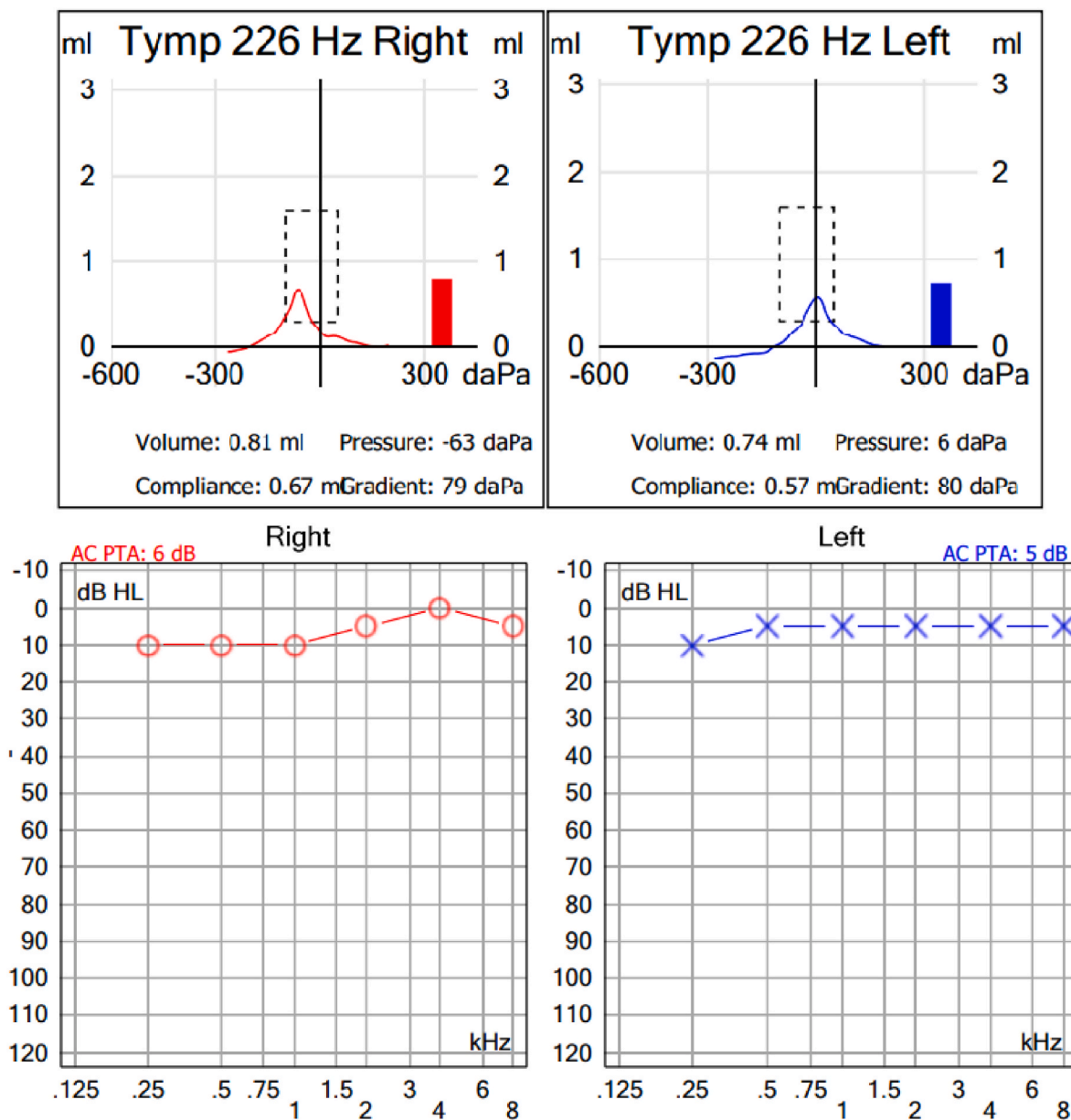


Fig. 3. Tympanogram and pure tone audiogram of Child 4 in Year 3 of the study. The previously identified hearing loss has resolved.

that had received lifelong bisphosphonates, and hence would have reported a higher prevalence of hearing loss. The prevalence of hearing loss in published studies is variable but has been reported to be as high as 77 % [5–10]. More recent studies, such as the one by Joseph and Maharaj [1], report cross-sectional data in bisphosphonate-treated children with no hearing loss identified.

The only hearing problem we encountered was a unilateral middle ear effusion with mild hearing loss which occurred during the COVID pandemic and which had resolved a year later. It is unclear whether this child’s middle ear effusion was related to the OI diagnosis in any way or simply coincidental. Clearly, this was not of huge clinical significance and no treatment was required.

The Brittle Bone Society recommends hearing screening every 3 years from age 3 or 4, with additional testing annually for those with borderline hearing [24]. This is a recommendation based on perfectly reasonable opinion, but not on any evidence. As far as we know, nobody has published data on the effectiveness of any specific hearing screening interval in osteogenesis imperfecta until now. Our audiology department prefer annual screening as they find it much easier to organise.

They have a series of annual recall lists for hearing tests of children with conditions such as trisomy 21, achondroplasia and cystic fibrosis. When we introduced the idea of regular hearing screening for children with OI, they insisted it should be done annually in line with other programmes, regardless of Brittle Bone Society recommendations. Their view was that recall intervals longer than a year led to more missed appointments, often because families have moved address or changed telephone numbers in that time. They are also more comfortable with annual testing because 3 years is a long time to have an undiagnosed hearing loss.

#### 4.4. Department workload and costing

Some audiology departments may be concerned that an annual hearing screening programme for children with OI will result in a substantial increase in workload, especially at a time where resources are already stretched. We believe that thirty additional hearing assessments per year is a small workload which any audiology department should be able to cope with. For context, there are around 201 children with

trisomy 21 and 67 children with cystic fibrosis who have an annual hearing assessment in our hospital. Hence, the additional workload created is relatively small. The cost for a hearing assessment is very affordable - £208 for children under 4 and £143 for children over 4 [25]. In our cohort, assessing 29 children would have cost £4,277 for year 1 of the programme. For a health board as large as ours, this is not a significant additional cost.

## 5. Conclusion

The prevalence of hearing impairment in children with OI undergoing annual hearing screening is lower than previously published data would suggest, possibly because of the widespread use of bisphosphonates. We believe that the low cost and small workload associated with the screening programme justifies its continuation locally until more data can be collected and further conclusions can be drawn. Other departments may wish to continue 3-yearly screening in line with Brittle Bone Society recommendations until then.

## Funding

No external funding was used for this study.

## Data availability

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

## CRediT authorship contribution statement

**Emmett Lui:** Writing – original draft, Formal analysis, Data curation. **Owen Conlan:** Writing – review & editing. **Karen Hunter:** Writing – review & editing, Data curation, Conceptualization. **Avril Mason:** Writing – review & editing, Formal analysis, Conceptualization. **Haytham Kubba:** Writing – review & editing, Supervision, Formal analysis, Conceptualization.

## Declaration of competing interest

None of the authors has any conflict of interest to declare.

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