

# Ocular pseudoexfoliation associated with hearing loss

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## ABSTRACT

**Objective:** Ocular pseudoexfoliation (PXF) has been recently considered as a systemic disease affecting other organs as well as the eye. This prospective study is to assess the relationship between PXF and sensorineural hearing loss.

**Methods:** Patients attending a general ophthalmic clinic at King Hussein Medical Center, Amman, Jordan from (March 2002 through to March 2003) who were found to have ocular PXF on routine ophthalmic examination were referred to the Audiometric Department. Pure tone hearing threshold was measured at 1, 2, 3 kHz for each ear and was compared with International Standard (ISO 7029) median age associated hearing loss at 1, 2, 3 kHz (AAHL).

**Results:** Forty-one patients were studied of whom 24 were males (58.5%); the mean age of the male patients was 78-years while that of the female group was

72-years. All patients had PXF affecting at least one eye, 16 patients (39%) had bilateral PXF. Overall (72-years) of 36 patients (87%) had a higher hearing threshold level (HTL) at 1, 2, 3 kHz (HTL (1, 2, 3) than the ISO 7029 median AAHL 1, 2, 3 which included (44 ears) of 22 patients in the male group (87%) and (28 ears) of 14 patients in the female group 82%. Approximately 26.8% of patients had glaucoma, however; there was no correlation between glaucoma and sensorineural hearing threshold level.

**Conclusion:** The majority of patients with ocular PXF had sensorineural hearing loss compared to age-matched controls. Thus, there is increasing evidence that PXF is a systemic disease.

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The pseudoexfoliation (PXF) syndrome is relatively common but easily overlooked cause of chronic open angle glaucoma; it is unilateral in approximately 2/3 of cases; with no clear hereditary pattern but common in Scandinavians.<sup>1</sup> Grey white fibrillogranular extra cellular material is deposited in and around anterior segment of the eye (tissues affected are the anterior capsule, iris, anterior chamber angle, zonules, ciliary body, anterior vitreous face, and conjunctiva).<sup>1-4</sup> These deposits of fibrillar extra cellular material is both histo-chemically and ultra-structurally similar to amyloid.<sup>1,3</sup> Exfoliative fibrilopathy has been reported and documented pathologically in the

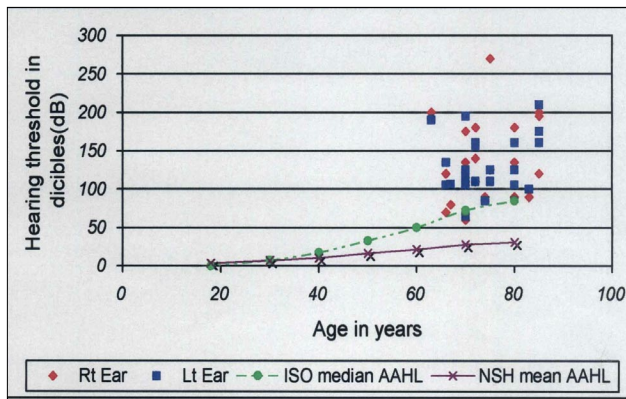
basement membrane of extra ocular orbital tissues, the skin, visceral organs, and vessel walls as well as cardiac structures, suggesting that PXF syndrome is an ocular manifestation of a systemic disease.<sup>5-10</sup> The organ of corti is a complex structure in the inner ear, it contains hair cells that sit on the basilar membrane (a collagen containing element); and are overlaid by the tectorial membrane. There are 2 types of hair cells in the cochlea; the inner hair cells and outer hair cells. One row of inner cells spirals up the cochlea near the central axis, while 3-4 rows of adjacent outer hair cells spirals up the cochlea further from the central axis.<sup>11,12</sup> The tectorial and basilar membrane are connected centrally; sound

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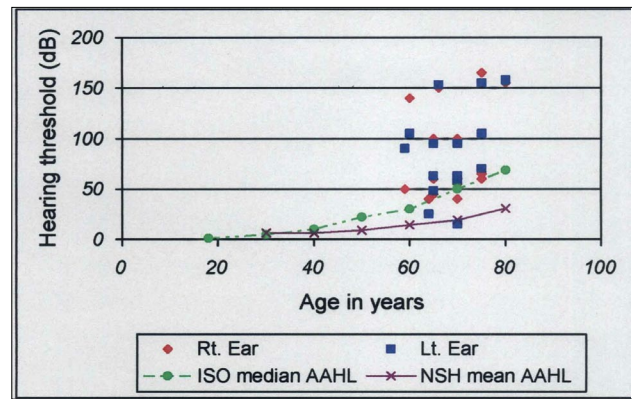
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**Figure 1** - Male right and left ear hearing threshold level<sup>1-3</sup> compared with international standardization organization 7029 median age associated hearing loss<sup>1-3</sup> and national study of hearing mean age associated hearing loss.<sup>1-3</sup>



**Figure 2** - Female right and left ear hearing threshold level<sup>1-3</sup> compared with international standardization organization 7029 median age associated hearing loss<sup>1-3</sup> and national study of hearing mean age associate hearing loss.<sup>1-3</sup>

moves these structures differentially producing a shear force that bends the stereocilia. The tectorial membrane, a soft fibrillated lamina, the structure of which is characterized by a hydrated matrix stabilized by collagen fibers, covers the stereocilia. The conversion of the mechanical energy produced by a sound wave to electrical energy resulting in hearing requires deflection of stereocilia, induced by a shearing motion between the reticular lamina and the tectorial membrane. This shearing motion is produced by the basilar membrane moving as a result of the traveling sound wave.<sup>11-13</sup> Presbycusis is loss of hearing in the elderly which is associated with natural ageing process; it is slowly progressive, and symmetric. More than one third of persons over 75-years of age are usually affected. The cause remains unclear, hearing loss is usually greatest in frequencies >2000 Hz.<sup>11-13</sup> The International standard 7029 gives values of normal age associated hearing loss as deviations relative to the median thresholds of young otologically normal subjects. The standard is derived from a meta-analysis of a number of large test populations.<sup>14,15</sup> The National Study of Hearing (NSH) was carried out on a smaller but more typical population than the ISO 7029; thus, greater hearing loss will be found in the general population than with ISO 7029<sup>16</sup>.

**Methods.** Patients attending a general ophthalmic clinic at King Hussein Medical City, Amman, Jordan, who were found to have PXF on routine ophthalmic examination from March 2002 through to March 2003 were selected. Full medical history was taken for all patients; they were also asked current or previous medical and surgical treatment for glaucoma. Exclusion criteria included history of previous ear surgery, history of tympanic membrane perforation, history of noise exposure, or working in a noisy environment, or repeated

exposure to gunfire, use of ototoxic drugs, and concurrent upper respiratory tract infection at time of examination. Each patient underwent a full ocular examination including snellen visual activity, slit lamp biomicroscopy, gonioscopy, applanation tonometry, and dilated funduscopy. Patients were referred to audiometric department. Pure tone hearing threshold was measured at 1, 2, 3 KHz using air conduction audiometry and if necessary bone-conduction audiometry, to differentiate between sensorineural and conductive hearing loss. Results for each ear were compared with ISO 7029 median AAHL 1, 2, 3 and with NSH. The Hearing threshold levels of each ear of all patients were summed over the three frequencies (HTL 1, 2, 3) to the nearest 5 decibels (dB). Testing was started approximately 60 dB above the expected threshold and continued on descending 10 dB steps below threshold. Testing was then completed using 5 dB ascending steps until 2 of 4 sounds were heard. Control data were taken from the international standard ISO 7029 which gives values of normal age associated hearing loss as deviations relative to the median thresholds of young otologically normal subjects.<sup>14,15</sup> For comparison, control data on a smaller, more typical population derived from the NSH were also used.<sup>16</sup> Each patient's HTL<sup>1-3</sup> for each ear was plotted on a graph against the ISO 7029 median age associated hearing loss, which was similarly summed over the 3 frequencies of 1, 2, and 3 kHz (AAHL);<sup>1-3,15</sup> however separate graphs were plotted for HTLs for males and females (**Figures 1 & 2**); as there was difference between their AAHL patterns. Subjects of the NSH were plotted on the same graphs. The hearing threshold for each ear was considered with regard to the ipsilateral eye findings. So a 3 way comparison was made in between ears (with HTL<sup>1-3</sup> higher than the ISO 7029 median AAHL)<sup>1-3</sup> on the same side as eyes without PXF, ears on the same side as eyes with PXF, but

without glaucoma, and similarly the proportion of ears on the same side as eyes with PXF and glaucoma. This comparison was made in both the male and female group of patients to determine the significance of any association.

**Results.** Total number of patients included in this study was 41 in whom 24 were male (58.5%). The mean age of male patients was 78-years, while it was 72 in females; demographic data are shown in (Table 1). All patients had bilateral audiometry data so that in total 82 ears were studied, all patients had PXF affecting at least one eye and overall 25 eyes had no evidence of PXF (male 18 eyes; 21.9%), 41 eyes had PXF but no glaucoma (male 26; 31.7%), and 16 eyes had glaucoma (male 4; 4.8%) (Table 2). There were some differences in the age associated hearing thresholds when the same age groupings in both the ISO 7029 and the NSH control data where compared using the 1, 2, 3 kHz audiometric descriptors; these differences are shown for comparison in both males and females in (Table 3). Overall, 70 eyes (85.3%) had a higher threshold than the ISO 7029 median AAHL<sup>1-3</sup> which included 42 of 48 ears in the male group (87.5%) and 28 of 34 ears in the female group (82.3%) **Figures 1 & 2** (scatter gram), and (Table 2). When the hearing threshold for each ear was considered with regard to the ipsilateral eye findings, there was no significant difference between the proportion of ears with thresholds higher than the ISO 7029 median AAHL on the same side as eyes without PXF, with PXF but no glaucoma and with PXF and glaucoma, in either the male or female groups. In the 25 patients with unilateral PXF the hearing thresholds and their relation to the ISO 7029 median AAHL<sup>1-3</sup> was similar in both ears.

**Discussion.** Previous studies have shown no difference in hearing threshold among patients with glaucoma and population based standards.<sup>18</sup> Up to 50% of patients with PXF will develop glaucoma.<sup>1,3,19</sup> In our study 26.8% of patients had glaucoma; however, our patients were recruited from a general ophthalmic clinic rather than a glaucoma clinic. As noted in our study as well as in previous studies that glaucoma itself is not associated with hearing loss; as ears with mean hearing thresholds greater than the population standard was the same in PXF patients, whether the eye ipsilateral to the tested ear had glaucoma or not.<sup>17</sup> The ISO 7029 was used to compare our patients with normal AAHL which is based on very large sample populations who are otologically normal. We also compared our patients with NSH because these studies were based on a more typical population but have had the disadvantages of smaller numbers of subjects. The decision to use 1,

**Table 1 -** Demographic data.

	n of patients	Average age range	Unilateral PXF (%)
Male group	24	78 years (63-80)	18 (75)
Female group	17	72 years (59-80)	7 (41)
<b>Total</b>	<b>41</b>	<b>71.9 years</b>	<b>25 (60.9)</b>
PXF - pseudoexfoliation			

**Table 2 -** Pseudoexfoliation syndrome and sensorineural hearing loss. Results of hearing tests in ipsilateral ears.

Ears tested	Eyes without PXF	Eyes with PXF without glaucoma	Eyes with PXF with glaucoma	Total
Total number of ears tested	18	26	4	<b>48</b>
N (%) above ISO 7029 medial AAHL <sup>1-3</sup>	16 (88)	23 (88)	3 (75)	-
Total number of ears tested female patients	7	15	12	<b>34</b>
N (%) above ISO 7029 median AAHL <sup>1-3</sup>	6 (85)	13 (86)	9 (75)	-
<b>Total</b>	<b>25</b>	<b>41</b>	<b>16</b>	<b>82</b>
PXF - pseudoexfoliation ISO - International Organization for Standardization AAHL - age associated hearing loss				

**Table 3 -** Control data provided by international standardization organization 7029 and by national study of hearing.

Age grouping in years	18-30	31-40	41-50	51-60	61-70	71-80
ISO 7029 median AHL <sup>1-3</sup> data* in kHz (males)	0-5	5-10	10-25	25-40	40-60	60-85
NSH data** in kHz (males)	3.6	6.7	10.3	16.3	21.4	30.8
ISO 7029 median AAHL <sup>1-3</sup> data* in kHz (females)	0	5-10	10-25	25-30	30-45	50-60
NSH data** in kHz (females)	6.2	6.4	9.1	14.3	19.1	30.8
ISO - international standardization organization NSH - national study of hearing AAHL - age associated hearing loss						

2, and 3 khz as descriptors was intended to compare our results with the previous study of hearing loss associated with PXF<sup>17</sup> who used these control data in their study.

In our study the overall patients of PXF had high hearing threshold than AAHL (85%), which is slightly higher than the (73%) reported in the study carried out at Institute of Ophthalmology, University College, Dublin, Ireland.<sup>17</sup> So we believe that in this study there is an association between PXF and sensorineural hearing loss. Pseudoexfoliation is a systemic condition and has been demonstrated in basement membrane of the extracellular matrices of extra ocular tissues, the skin, visceral organs and cardiac structures.<sup>1-5</sup> If ocular PXF is part of widespread deposition of PXF fibrils in the body; then deposition of PXF fibrils in the basement membrane of the organ of corti in the inner ear (before and independently of any manifestation of eye anterior segment structures), may explain the association between PXF and hearing loss. Structural alteration of either (or both) the tectorial and basilar membranes by deposition of PXF fibrils may change the way in which vibratory energy is conducted to the sensory hair cells and alter their surrounding chemical environment resulting in sensorineural hearing loss.<sup>20,21</sup> A significant association has been found in this study between PXF and sensorineural hearing loss. The majority of patients with ocular PXF had sensorineural hearing loss compared to age matched controls. Thus, there is increasing evidence that PXF is a systemic disease.

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