

Prevalence of Pseudoexfoliation Syndrome in Patients with Sensorineural Hearing Loss

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ABSTRACT

Background: Pseudoexfoliation syndrome (PEX) is a complex systemic disorder of the extracellular matrix primarily affecting the eye and visceral organs. In this age-related disease fibrillar extracellular material is produced and accumulates in many ocular and extraocular tissues.

Objective: To study the prevalence of pseudoexfoliation syndrome among patients with sensorineural hearing loss. **Patients and Methods:** A cross-sectional study, conducted on 50 patients with sensorineural hearing loss at the departments of Ophthalmology and Otolaryngology of Aswan University Hospital, was performed among patients aged 50 years and older and both sexes were included while patients with a history of acute ear disease, head trauma, long term exposure to heavy noise, intake of ototoxic drugs and chronic suppurative otitis media (cholesteatoma) were excluded.

Results: The prevalence of PEX among SNHL patients was estimated in the current study as 36%. The mean age was 61 (± 7.1) years and ranged from 50 to 77 years old. The majority of participants (35 patients, 70%) were female. Thirty-three patients (66%) of participants had chronic co-morbidities. Unilateral PEX was represented by 10 patients (55.6%), while bilateral PEX was represented by 8 patients (44.4%).

Conclusion: This study establishes the reciprocal association between pseudoexfoliation and sensorineural hearing loss. The main reason for this association remains unclear although the infiltrative nature of PEX can still explain this concurrence.

Keywords: Pseudoexfoliation Syndrome, Sensorineural hearing loss.

INTRODUCTION

Pseudoexfoliation (PEX) is defined as an age-related disease, in which abnormal fibrillar extracellular material is formed and progressively accumulates in many ocular and extraocular tissues⁽¹⁾. Recent reports showed that an identical fibrilopathy to that seen in PEX and was documented pathologically in the basement membranes and extracellular matrices of extraocular orbital tissues, the skin and visceral organs such as heart, lung, liver, gall bladder, kidney, and cerebral meninges; which suggest that PEX is a systemic disease⁽²⁾.

The incidence and prevalence of PEX vary even in different sites of the same population. The prevalence of PEX is reported to be 5% to 20% regardless of geographical features. The other important result of the studies is that the prevalence of PEX is higher over the age of 50⁽³⁾.

Sensorineural hearing loss (SNHL) is related to pathologies affecting the inner ear, cochlear nerve, and auditory cortex. Congenital autoimmune and metabolic syndromes, infections, drugs, vascular disorders, exposure to noise or chemical substances, acoustic neuroma, cochlear otosclerosis, Meniere's disease, are among common⁽⁴⁾. Some studies, using pure-tone audiometry, have reported that sensorineural hearing loss is significantly more common in patients with PEX⁽⁵⁾. Moreover, PEX material has been found on the tectorial and basilar membrane of the organ of Corti of the inner ear.

Aggregations of pseudoexfoliative material on these structures interfere with normal hearing threshold levels due to dysfunction of the mechanoreceptors of the ear by alterations in fine vibrations induced by sound waves and thereby inhibiting the conversion of the vibration energy to bioelectric, resulting in hearing loss⁽⁶⁾.

As there is increasing evidence that pseudoexfoliation not only affects ocular anterior segment structures but may also be a systemic disease, this study was done to assess the relationship between PEX and sensorineural hearing loss⁽⁵⁾.

So this work aimed to study the prevalence of pseudoexfoliation syndrome among patients with sensorineural hearing loss.

PATIENTS AND METHODS

This cross-sectional study was conducted at the Departments of Ophthalmology and Otolaryngology of Aswan University Hospital. The study population included 50 patients with evident sensorineural hearing loss and the sampling was sequential till completing the sample size.

Patients with sensorineural hearing loss aged 50 years or older of both sexes were included. On the other hand, patients with a history of acute ear disease or head trauma, those with long-term exposure to heavy noise, patients with a history of intake of ototoxic drugs such as aminoglycosides as well as



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those with chronic suppurative otitis media (cholesteatoma) were excluded.

Following obtaining informed consents from all included patients, they were subjected to pure tone audiometry (air and bone conduction) using diagnostic audiometer R 27 A (Resonance, Italy) where both ears were tested for air conduction firstly at 250Hz, 500Hz, 1000Hz, and then at 2000Hz, 4000Hz and 8000Hz. After testing the air conduction thresholds, the examiner proceeded in the same way to test bone conduction, applying a bone vibrator over the mastoid process of the patient. SNHL was diagnosed when there is no gap between the air and bone conduction curve on audiometry and the loss was more than 20 dB.

Patients who were diagnosed with sensorineural hearing loss were subjected to detailed history taking including baseline information as age, gender, race, medical history, underlying ocular disease as well as previous ocular surgeries. Refraction and best-corrected Snellen visual acuity was determined. Slit-lamp examination of the anterior segment, gonioscopy using Goldman 3-mirror lens, Goldman applanation tonometry as well as fundus examination using slit-lamp biomicroscopy were done. Pseudoexfoliation was diagnosed on slit-lamp biomicroscopy by the presence of white dandruff-like material at the pupillary margin, on the anterior lens capsule, trabecular meshwork, or corneal endothelium, in one or both eyes.

The study protocols were revised and approved by the Institutional Review Board of Aswan Faculty of Medicine and followed the Declarations of Helsinki.

Ethical approval and written informed consent :
An approval of the study was obtained from Aswan University academic and ethical

committee. Every patient signed an informed written consent for acceptance of the operation.

Statistical analysis

Data was entered, manipulated, and analyzed using the Statistical Package for Social Sciences (SPSS version 25, Chicago, IL, USA). Quantitative data were summarized as mean ± standard deviation and range, while categorical data were summarized as frequencies and percentages. A 95% confidence interval was calculated for the estimated prevalence of PEX among study participants. Associations between categorical variables were tested for statistical significance by the Chi-square test and Fisher’s exact test when appropriate. Comparing the quantitative variables within the categories of categorical variables were tested for statistical significance by the independent-samples T-test. P-values less than 0.05 were considered statistically significant at a 95% level of confidence.

RESULTS

The present study included 50 patients with sensorineural hearing loss (SNHL). Their mean age was 61 (±7.1) years and ranged from 50 to 77 years old. The majority of participants (35 patients, 70%) were female. Thirty-three patients (66%) of participants had chronic co-morbidities. Chronic heart diseases (CHD), diabetes mellitus (DM), and hypertension (HTN) are represented by 12 (24%), 12 (24%), and 18 (36%) patients, respectively. Chronic hepatitis C virus was reported by four patients (8%). On audiometry, two ears (2% out of 100 ears) had normal audiometry. Mild SNHL constituted the largest proportion (42% of all ears) followed by severe SNHL (38%) and moderate hearing loss (18%) (Table 1).

Table (1): Distribution of participants’ ears according to audiometry findings (N=100 ears)

| | | No. | % |
|---------------|-----------------|-----|------|
| Normal | | 2 | 2.0 |
| SNHL | Mild | 42 | 42.0 |
| | Moderate | 18 | 18.0 |
| | Severe | 38 | 38.0 |

There was no statistically significant difference in the SNHL distribution between male and female patients (Table 2).

Table (2): Distribution of participants’ ears according to audiometry findings and patients’ sex (N=100 ears)

| | Sex | | | | p-value |
|----------------------|-------------|-------|---------------|-------|---------------------|
| | Male | | Female | | |
| | No. | % | No. | % | |
| Normal | 0 | 0.0% | 2 | 2.9% | 0.980* ^c |
| Mild SNHL | 13 | 43.3% | 29 | 41.4% | |
| Moderate SNHL | 6 | 20.0% | 12 | 17.1% | |
| Severe SNHL | 11 | 36.7% | 27 | 38.6% | |

*. Statistically insignificant p-value (p>0.05). ^c. Chi-square test.

A significant association was found between CHD and HCV, and SNHL. The majority of patients with mild and severe SNHL had DM & HTN, while 33.3% of patients with moderate SNHL had HTN (Table 3).

Table (3): Distribution of patients according to SNHL and comorbidities

| Comorbidities | SNHL | | | | | | | | p-value |
|---------------|----------------|-------|---------------|--------------|------------------|--------------|-----------------|--------------|---------------|
| | Normal N= 2 | | Mild N= 42 | | Moderate N=18 | | Severe N= 38 | | |
| | No. | % | No. | % | No. | % | No. | % | |
| CHD | 1 | 50.0% | 7 | 16.7% | 10 | 55.6% | 6 | 15.8% | 0.004* |
| DM | 0 | 0 | 9 | 21.4% | 1 | 5.6% | 14 | 36.8% | 0.054 |
| HTN | 2 | 100% | 17 | 40.5% | 6 | 33.3% | 11 | 28.9% | 0.221 |
| HCV | 0 | 0 | 5 | 11.9% | 3 | 16.7% | 0 | 0 | 0.044* |

*. Statistically significant p-value (p<0.05), Fisher’s exact test

In the present study, the prevalence of PEX among SNHL patients was estimated in the current study as 36% with a 95% confidence interval of (23.8%– 49.8%). Unilateral PEX was represented by 10 patients (55.6%), while bilateral PEX was represented by 8 patients (44.4%) (Table 4).

Table (4): Prevalence of PEX among study participants (N=50)

| PEX Presence | | No. | % | 95% Confidence Limits | |
|------------------------------|-------------------|-----------|-------|-----------------------|-------|
| | | No | 32 | 64.0% | 50.2% |
| Yes | | 18 | 36.0% | 23.8% | 49.8% |
| PEX Laterality (n=18) | Unilateral | 10 | 55.6% | 33.2% | 76.3% |
| | Bilateral | 8 | 44.4% | 23.7% | 66.8% |

Assessment of patients’ lens revealed that clear lens was found in 48 eyes (48%), while 12 eyes (12%) were pseudophakic. Nuclear cataract was the most common type of cataract (18%), followed by cortical (8%) and posterior subcapsular (7%). Mature cataract was identified in only two eyes (2%) while the mixed type was identified in 5 eyes (5%) (Table 5).

Table (5): Distribution of study participants according to lens status (N=100 eyes)

| Lens status | No. | % |
|--------------------------------|-----|-------|
| No Cataract | 48 | 48.0% |
| Pseudophakic | 12 | 12.0% |
| Nuclear cataract | 18 | 18.0% |
| Cortical cataract | 8 | 8.0% |
| Posterior subcapsular cataract | 7 | 7.0% |
| Mature cataract | 2 | 2.0% |
| Mixed | 5 | 5.0% |

Fundus examination revealed that 50% of the examined eyes had normal fundus. The most prevalent fundus abnormalities were tigroid fundus (20%), NPDR (14%), and high C/D ratio (> 0.5 in 11%), while Macular drusen represented the least common abnormality (1%) (Table 6).

Table (6): Distribution of the examined eyes according to findings of fundus examination (N=100)

| | No. | % |
|------------------------|-----|-------|
| Normal | 50 | 50.0% |
| Tigroid fundus | 20 | 20.0% |
| NPDR | 14 | 14.0% |
| high C/D Ratio | 11 | 11.0% |
| PVD | 4 | 4.0% |
| Pale optic disc | 4 | 4.0% |
| Macular drusen | 1 | 1.0% |

Associations between the presence of PEX and the degree of SNHL were tested for statistical significance. There were no statistically significant associations between PEX and patients’ SNHL status. However, patients without PEX showed higher percentages of moderate and severe SNHL compared to those with PEX (Table 7).

Table (7): Distribution of patients according to SNHL and PEX status

| SNHL | No PEX | | PEX | | p-value |
|----------|--------|-------|-----|-------|---------------------|
| | No. | % | No. | % | |
| None | 1 | 1.6% | 1 | 2.8% | 0.563 ^{*c} |
| Mild | 24 | 37.5% | 18 | 50.0% | |
| Moderate | 13 | 20.3% | 5 | 13.9% | |
| Severe | 26 | 40.6% | 12 | 33.3% | |

*. Statistically insignificant p-value (p>0.05).

^c. Chi-square test.

There were no statistically significant associations between PEX and patients' age, sex, or comorbidities (Table 8). However, compared to patients without PEX; BCVA was significantly lower and IOP was significantly higher with gonioscopy revealed more frequency of narrow-angle among patients with PEX (Table 9).

Table (8): Distribution of patients with PEX according to patients' demographics and comorbidities (N=50)

| | | SNHL (n=50 patients) | | | | p-value |
|--------------------|------------------|----------------------|-------|------------|-------|---------------------|
| | | No PEX (n=32) | | PEX (n=18) | | |
| Age (years) | Mean ± SD | 60.0 ± 8.0 | | 63.0 ± 6.0 | | 0.278 ^{*t} |
| Sex | Male | 10 | 31.3% | 5 | 27.8% | 0.797 ^{*F} |
| | Female | 22 | 68.8% | 13 | 72.2% | |
| Comorbidity | None | 9 | 28.1% | 8 | 44.4% | - |
| | CHD | 8 | 25.0% | 4 | 22.2% | 0.825 ^{*F} |
| | DM | 9 | 28.1% | 3 | 16.7% | 0.497 ^{*F} |
| | HTN | 12 | 37.5% | 6 | 33.3% | 0.768 ^{*F} |
| | HCV | 4 | 12.5% | 0 | 0 | 0.283 ^{*F} |

*. Statistically insignificant p-value (p>0.05).

^t. Independent-samples t-test, ^F Fisher's exact test.

Table (9): Distribution of patients with PEX according to study variables (N=100)

| | | SNHL (n=100) | | | | p-value |
|-----------------------------|---------------------------------------|---------------|-------|--------------|-------|---------------------------|
| | | No PEX (n=64) | | PEX (n=36) | | |
| Visual Acuity | Mean ± SD | 0.60 ± 0.20 | | 0.33 ± 0.20 | | <0.001 [*] |
| IOP | Mean ± SD | 12.59 ± 1.66 | | 16.14 ± 5.64 | | 0.018[*] |
| Cataract | None | 41 | 64.1% | 7 | 19.4% | <0.001 ^{*F} |
| | Pseudophakic | 7 | 11% | 5 | 13.9% | |
| | Nuclear cataract | 7 | 11% | 11 | 30.6% | |
| | Cortical cataract | 2 | 3.1% | 6 | 16.7% | |
| | Posterior subcapsular cataract | 5 | 7.8% | 2 | 5.5% | |
| | Mature cataract | 0 | 0 | 2 | 5.5% | |
| | Mixed | 2 | 3.1% | 3 | 8.3% | |
| Fundus abnormalities | Normal | 38 | 59.4% | 12 | 33.3% | <0.001 ^{*F} |
| | Tigroid fundus | 14 | 21.9% | 6 | 16.7% | |
| | NPDR | 8 | 12.5% | 4 | 11.1% | |
| | high C/D Ratio | 0 | 0 | 11 | 30.6% | |
| | PVD | 0 | 0 | 1 | 2.8% | |
| | Pale optic disc | 0 | 0 | 2 | 5.5% | |
| | Macular drusen | 4 | 6.2% | 0 | 0 | |
| Gonioscopy | Narrow angle | 15 | 23.4% | 25 | 69.4% | <0.001 ^{*c} |
| | Open angle | 49 | 76.6% | 11 | 30.6% | |
| C/D ratio | Mean ± SD | 0.37 ± 0.07 | | 0.50 ± 0.16 | | 0.004^{*t} |

*. Statistically significant p-value (p<0.05).

^c. Chi-square test; ^F Fisher's exact test; ^t Student T-test.

DISCUSSION

Pseudoexfoliation syndrome (PEX) is a complex, age-related systemic disorder of the extracellular matrix primarily affecting the eye and visceral organs⁽⁷⁾. Sensorineural hearing loss (SNHL) can be attributed to various etiologies as demonstrated with its association with PEX syndrome⁽⁸⁾. This study aimed to describe the prevalence of pseudoexfoliation syndrome among patients with sensorineural hearing loss to confirm the reciprocal correlation between both conditions.

In the present study, most participants (35 patients, 70%) were females. Similar to **Shuster et al.**⁽⁹⁾ study in which females with SNHL were more than males. Their study showed that hearing loss affects both men and women but physiological differences between both sexes are often hormone-driven where the hormone estrogen and its related signaling pathways may in part, modulate the differences in hearing.

In the current study, there was no significant difference regarding mean age between PEX and non-PEX patients. This was in contrast with other studies that indicate the increasing frequency of PEX among higher age group individuals^(1,3,10,11).

In the PEX group, although not significant, the female occurrence was 72.2% (13 patients) compared to male affection (27.8%, 5 patients), a finding that was not in agreement with various results on the gender distribution of PEX. In **Yildirim et al.**⁽³⁾ study, of 100 patients diagnosed with PEX, 53 (53.0%) were women and 47 (47.0%) were men. Other studies reported no difference⁽¹²⁾ or slightly higher male prevalence⁽¹³⁾.

There was statistically significant association existed between comorbidities as CHD and HCV; and SNHL. These results agreed with a review-based study examining cohort studies that were published in the years 2010–2018 and examined associations of hearing loss with other health conditions, namely visual impairment, mobility restrictions, cognitive impairment, psychosocial health problems, diabetes, cardiovascular diseases, stroke, arthritis, and cancer. For all of these health conditions, it was found that prevalence was larger in people with hearing loss⁽¹⁴⁾.

An interesting study by **Friedland and Colleagues**⁽¹⁵⁾ showed that the audiometric patterns strongly correlated with cardiovascular disease. The researchers reported that patients with low-frequency hearing loss should be regarded as “at-risk” for cardiovascular events, and appropriate medical referrals should be considered.

Moreover, the majority of patients with mild and severe SNHL had DM and HTN, while 33.3% of patients with moderate SNHL had HTN. Investigating the association between hearing loss and diabetes, **Bainbridge and Colleagues**⁽¹⁶⁾ looked

at 5,140 adult participants from 1999-2004. The researchers report that hearing impairment was found to be more prevalent among those participants with diabetes. Following multivariate analyses, they found that people with diabetes had significantly increased likelihoods of hearing impairment in worse and better ears at all severity levels and frequencies. Other systematic reviews involving 20,194 participants and 7,377 individual cases revealed that the prevalence of hearing loss among those with diabetes was more than twice that than those without diabetes with a stronger association among those people younger than age 60⁽¹⁷⁾. The study of **Kim and Colleagues**⁽¹⁸⁾ in 2016 also supported the previous findings.

In the current study, no significant association was found between PEX patients with systemic morbidities such as CHD, DM, or HTN. This contrasted with other studies that found an increased association of PEX and systemic diseases, such as HTN, coronary artery disease, myocardial infarction, peripheral artery disease, ischemic neurological disease, stroke, and Alzheimer's disease^(3,19,20).

Association between SNHL and pseudoexfoliation was described by many reports and its prevalence among PEX patients was reported to fluctuate between 34% and 88.6% according to different methods of hearing assessment^(1,3,8, 21-23). On the other hand, there was a paucity of reports to confirm the reciprocal relation between the two associated conditions. To the best of author's knowledge except for the study of **Singham et al.**⁽⁴⁾ who indirectly reported the occurrence of PEX in 51 patients (60%) among their studied SNHL group.

The frequency of unilateral PEX was found to be more than bilateral occurrence (55.6% and 44.4% respectively) finding that was also reported by many researchers^(3,24,25). On the other hand, bilateral involvement was reported to be higher by other studies^(22,26). Proving the nonexistence of the so-called unilateral pseudoexfoliation, Thomas et al 2005 reported ultrastructural alterations in anterior segment tissues of all noninvolved eyes in clinically unilateral PEX⁽²⁷⁾.

In the current study, mild SNHL constituted the largest proportion among study subjects followed by severe SNHL and moderate hearing loss. Comparable results were obtained from different studies confirming the prevailed occurrence of mild SNHL among patients with pseudoexfoliation^(3,22).

This study also found no statistically significant associations between PEX and patients' SNHL status. However, patients without PEX showed higher percentages of moderate and severe SNHL compared to those with PEX. **Elshafei and Elbadry**⁽²²⁾ study found no statistically significant difference in SNHL between cases of unilateral and

bilateral PEX or between the ear towards the affected side in unilateral cases.

The prevalence of cataract was significantly higher in PEX patients in the current study. Similarly, many studies reported that the development of cataracts was greater in PEX patients compared to non-PEX ones. The presence of PEX was reported to increase the risk of developing cataracts by 2.3 (odds ratio) ^(3,28). As previously reported the recent study found that nuclear cataract was the most common type encountered followed by cortical type in PEX patients while others reported nuclear cataract to be the second most common type following mixed type ^(29,30). Increased incidence of cataract among PEX patients may be explained by increase oxidative stress and ocular ischemia and evidenced by a significant reduction of ascorbic acid in the aqueous of cataract patients PEX ^(21,32).

The current study results found that PEX was associated with significantly lower BCVA, higher IOP, and more C/D ratio compared to those without PEX. This was in agreement with the other studies that found glaucoma to be significantly more common in subjects with PEX but it was not associated with below-average hearing in any of the study groups. ^(3,23). **Samarai et al.** ⁽⁸⁾ compared the severity and prevalence of SNHL between PEX patients and patients with concomitant PEX and glaucoma. But in contrast to our results, the results demonstrated that the difference was not statistically significant.

Higher frequencies of narrow-angle on gonioscopy were found among PEX patients. This agreed with other studies reporting significantly lower AC angle and depth ^(33,34). On the other hand, **Moreno-Montanes et al.** ⁽³⁵⁾ reported no difference between PEX patients compared to controls.

CONCLUSION

This study establishes the reciprocal association between pseudoexfoliation and sensorineural hearing loss. The main reason for this association remains unclear although the infiltrative nature of PEX can still explain this concurrence.

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