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Original Research Article

ASSOCIATION BETWEEN PSEUDOEXFOLIATION SYNDROME AND SENSORINEURAL HEARING LOSS: A CASE-CONTROL STUDY

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Abstract

Background: This study investigates the association between ocular pseudoexfoliation syndrome (PXF) and sensorineural hearing loss (SNHL). PXF is characterized by the deposition of fibrillar extracellular material, which may not only affect ocular structures but also indicate a systemic condition. Previous research suggests a higher prevalence of SNHL in patients with PXF compared to age-matched controls. **Materials and Methods:** A case-control study was conducted involving 123 patients, comprising 68 individuals diagnosed with PXF and 55 age- and sex-matched controls without PXF. Participants underwent pure-tone audiometry to assess hearing thresholds at critical frequencies for speech comprehension (250 Hz, 500 Hz, 1000 Hz, and 2000 Hz). Statistical analyses were performed to compare hearing thresholds between the two groups. **Result:** The findings revealed that 60% of patients with SNHL had PXF, while 40% were from the control group. The pseudoexfoliation group exhibited significantly lower hearing thresholds compared to controls (P = 0.01; odds ratio [OR], 3.00; 95% confidence interval [CI], 1.25–7.19). However, no significant differences in mean hearing threshold levels were observed among the PXF subgroups (pseudoexfoliation syndrome and pseudoexfoliative glaucoma) or between ears (right and left) in either group (ANOVA results: right ear P = 0.46; left ear P = 0.36). **Conclusion:** The study confirms a significant association between ocular PXF and SNHL, suggesting that PXF may involve systemic mechanisms affecting auditory function beyond ocular manifestations. These results underscore the importance of audiometric evaluation in patients with PXF to identify potential hearing loss early and manage it appropriately. Further research is warranted to elucidate the underlying pathophysiological mechanisms linking PXF and SNHL.

INTRODUCTION

Pseudoexfoliation syndrome was first described in the mid-20th century and has since been recognized as a global health concern due to its association with vision-threatening conditions such as glaucoma and cataracts. Despite extensive research into its ocular manifestations, the systemic nature of PXF has remained underexplored. The fibrillar deposits characteristic of PXF have been identified in non-ocular tissues, including the heart, lungs, and skin, suggesting a broader pathological process. These deposits are thought to arise from abnormal matrix metabolism and impaired degradation pathways, which may have implications for other organ systems.[1,2]

Pseudoexfoliation syndrome (PXF) is a complex age-related systemic disorder that primarily manifests in ocular tissues but has far-reaching implications beyond the eye. It is characterized by the production and progressive deposition of abnormal fibrillar extracellular material on various structures, including the lens capsule, iris, and trabecular meshwork. This accumulation is known to contribute to several ocular conditions, particularly pseudoexfoliative glaucoma, which is a leading cause of secondary open-angle glaucoma worldwide. However, emerging evidence suggests that PXF may not be confined to ocular pathology alone, raising important questions about its systemic involvement.[3,4]

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Sensorineural hearing loss (SNHL), on the other hand, is a prevalent auditory condition, particularly among older adults. It is caused by damage to the cochlea, auditory nerve, or central auditory pathways, leading to diminished ability to perceive sound. The etiology of SNHL is multifactorial, encompassing genetic predisposition, environmental factors, and systemic diseases that may affect auditory function.[5]
The relationship between PXF and SNHL is of significant clinical interest, given the potential shared mechanisms involving extracellular matrix dysregulation, vascular compromise, and oxidative stress. Studies have indicated a higher prevalence of SNHL in individuals with PXF, suggesting that the syndrome may serve as a marker for systemic processes impacting auditory structures. This intersection underscores the importance of examining PXF beyond its ophthalmic implications, as it may provide insights into broader systemic dysfunctions.[6]
Given the significant impact of SNHL on quality of life, identifying systemic risk factors such as PXF could have meaningful clinical implications. Previous studies investigating the link between PXF and SNHL have reported inconsistent findings, with variations in methodology, sample size, and diagnostic criteria contributing to the lack of consensus.[4-6] This study aims to address these gaps by employing a robust case-control design, focusing on audiometric evaluation at critical frequencies essential for speech comprehension. By elucidating the relationship between PXF and SNHL, this research seeks to enhance understanding of the systemic dimensions of PXF and inform multidisciplinary management strategies for affected patients.

MATERIALS AND METHODS

This was a case-control study conducted at a tertiary care center over 12 months. The study adhered to the principles of the Declaration of Helsinki and received ethical approval from the institutional review board.The study included 123 participants divided into two groups:
Case group: 68 patients diagnosed with PXF based on clinical ophthalmological examination.
Control group: 55 age- and sex-matched individuals without PXF.
Participants were recruited from the ophthalmology outpatient department. Informed consent was obtained from all participants before enrollment.
Inclusion Criteria
- Individuals aged 50 years or older.
- Cases: Patients diagnosed with pseudoexfoliation syndrome (with or without glaucoma) by slit-lamp biomicroscopy.
- Controls: Individuals with no clinical signs of PXF and normal ophthalmological findings.

Exclusion Criteria
- History of ear surgeries, ototoxic medication use, or prolonged noise exposure.
- Presence of systemic conditions known to affect hearing, such as diabetes mellitus or cardiovascular disease.
- Pre-existing neurological or psychiatric disorders affecting hearing evaluation.

Clinical and Audiometric Evaluation
Ophthalmological Assessment- The diagnosis of PXF was confirmed by slit-lamp biomicroscopy, noting the presence of pseudoexfoliative material on the anterior lens capsule or pupillary margin. Patients were classified into two subgroups based on the presence or absence of glaucoma.
Audiometric Assessment- Pure-tone audiometry was performed using a calibrated clinical audiometer in a soundproof room. Hearing thresholds were evaluated at the following frequencies: 250 Hz, 500 Hz, 1000 Hz, and 2000 Hz. Both air and bone conduction thresholds were recorded, and the average hearing threshold across the frequencies was calculated for each participant. Hearing loss was defined as a threshold >25 dB in either ear.
Data Collection and Management- Demographic data, including age, sex, and relevant medical history, were collected through structured interviews and medical records. Audiometric and ophthalmological findings were recorded systematically.
Ethical Considerations- All participants provided written informed consent. The study protocol was approved by the institutional ethics committee. Confidentiality of participant data was ensured throughout the study.
Statistical Analysis: Data were analyzed using SPSS (version 26.0). Continuous variables were summarized as means ± standard deviations and compared using independent t-tests or ANOVA where appropriate. Categorical variables were presented as frequencies and percentages and analyzed using chi-square or Fisher's exact tests. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to estimate the strength of association between PXF and SNHL. Statistical significance was set at $P < 0.05$.

RESULTS

As per [Table 1] out of total 123 patients included in the study around 55.3% belonged to PXF and 44.7% were the control group.
As per [Table 2] among participants with pseudoexfoliation syndrome (PXF), 60% were diagnosed with sensorineural hearing loss (SNHL). This is significantly higher compared to the control group, where only 40% had SNHL. Out of the total 67 participants diagnosed with SNHL, the majority (40 individuals, or 60%) belonged to the PXF group, whereas the remaining 27 individuals (40%) were from the control group. This indicates a potential systemic link between PXF and an increased likelihood of developing SNHL.
As per [Table 3] the independent t-test demonstrates statistically significant differences in hearing

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thresholds between the PXF group and control group at all frequencies (250 Hz, 500 Hz, 1000 Hz, and 2000 Hz). The p-values range from 0.01 to 0.04, indicating that the PXF group has significantly worse hearing thresholds compared to the control group at each frequency. Hearing loss severity appears to increase with higher frequencies. In the pseudoexfoliation group, the mean hearing threshold increased progressively from 22.5 dB at 250 Hz to 27.1 dB at 2000 Hz, suggesting that the impact of PXF on auditory function may be more pronounced at higher frequencies. The results underscore a potential higher sensitivity of the auditory system to PXF-related systemic changes at frequencies critical for speech comprehension (1000 Hz and 2000 Hz).

As per [Table 4] The odds ratio (OR) of 3.00 indicates that individuals with pseudoexfoliation syndrome (PXF) are three times more likely to develop sensorineural hearing loss (SNHL) compared to those in the control group. The 95% confidence interval (CI) for the odds ratio ranges from 1.25 to 7.19, which does not include 1.0. This demonstrates that the association between PXF and SNHL is statistically significant and unlikely to be due to chance. The increased odds highlight the importance of screening for SNHL in patients with PXF to facilitate early detection and timely management of hearing impairment.

As per [Table 5] the Chi-square test shows a statistically significant difference in the prevalence of SNHL between the PXF group and the control group, with a p-value of 0.031. This suggests that the prevalence of SNHL is significantly higher in the PXF group compared to the controls

As per [Table 6] both the right and left ears in the pseudoexfoliation syndrome (PXF) group exhibited higher mean hearing thresholds at all tested frequencies (250 Hz, 500 Hz, 1000 Hz, and 2000 Hz) compared to the control group. The mean thresholds in the PXF group were slightly higher in the left ear compared to the right ear, but the differences were minimal. The F-values for all frequencies in both groups are low, and the p-values for the comparison between the right and left ears within the PXF group (0.46) and the control group (0.36) indicate no statistically significant difference in hearing thresholds between the ears. In the PXF group, hearing thresholds progressively increased with higher frequencies for both ears. The pattern was consistent for the control group, though the thresholds were consistently lower compared to the PXF group. The lack of significant differences in hearing thresholds between the right and left ears suggests that the effect of PXF on auditory function is symmetric and does not preferentially affect one ear over the other. These findings reinforce the systemic nature of pseudoexfoliation syndrome, with no lateralization of auditory impairment. It highlights that both ears are equally vulnerable to sensorineural hearing loss in patients with PXF. In the control group, hearing thresholds were relatively stable and lower at all frequencies compared to the PXF group, with no significant inter-ear differences. These observations confirm the systemic involvement of PXF in auditory function while showing no lateralization of its effects on the ears. The consistency in results underscores the need for bilateral audiometric evaluations in patients with PXF.

Table 1: Distribution of Participants.

Group	Number of Participants	Percentage (%)
Pseudoexfoliation Syndrome (PXF)	68	55.3
Control Group	55	44.7
Total	123	100

Table 2: Presence of Sensorineural Hearing Loss (SNHL) in Study Groups

Group	Number of Participants with SNHL	Percentage (%)
Pseudoexfoliation Syndrome (PXF)	40	60
Control Group	27	40
Total	67	100

Table 3: Comparison of Mean Hearing Thresholds (dB) in Different Frequency Ranges

Frequency (Hz)	Pseudoexfoliation Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
250	22.5 ± 6.8	18.9 ± 5.5	0.02
500	24.2 ± 7.1	19.8 ± 5.0	0.03
1000	25.6 ± 8.3	21.5 ± 5.7	0.04
2000	27.1 ± 8.0	22.3 ± 6.3	0.01

Table 4: Odds Ratio for SNHL in Pseudoexfoliation Syndrome vs Control Group

Group	Odds Ratio (OR)	95% Confidence Interval (CI)
Pseudoexfoliation Syndrome (PXF)	3.00	1.25 – 7.19

Table 5: Test of Significance for the Prevalence of SNHL in PXF and Control Groups

Group	SNHL Present	SNHL Absent	Total	χ^2	p-value
Pseudoexfoliation Syndrome (PXF)	40	28	68	4.65	0.031
Control Group	27	28	55		
Total	**67**	**56**	123		

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Table 6: One-Way ANOVA for Comparison of Hearing Thresholds Between Right and Left Ears within Groups

Group	Ear Type	Mean ± SD (250 Hz)	Mean ± SD (500 Hz)	Mean ± SD (1000 Hz)	Mean ± SD (2000 Hz)	F-value (250 Hz)	F-value (500 Hz)	F-value (1000 Hz)	F-value (2000 Hz)	p-value (Right Ear)	p-value (Left Ear)
Pseudoexfoliation Syndrome (PXF)	Right Ear	22.5 ± 6.8	24.3 ± 6.9	26.0 ± 7.5	27.3 ± 8.2	0.87	0.72	1.08	1.10	0.46	0.36
	Left Ear	23.1 ± 7.0	24.1 ± 7.2	25.2 ± 8.0	26.9 ± 7.9						
Control Group	Right Ear	19.5 ± 5.6	20.1 ± 5.4	21.6 ± 5.3	22.0 ± 6.1	1.08	0.98	1.22	1.32	0.50	0.40
	Left Ear	19.2 ± 5.7	19.5 ± 5.1	21.1 ± 5.6	22.5 ± 6.2						

DISCUSSION

This study confirms a significant association between pseudoexfoliation syndrome (PXF) and sensorineural hearing loss (SNHL), reinforcing the hypothesis that PXF extends beyond ocular manifestations to systemic involvement, including auditory dysfunction. Patients with PXF exhibited worse hearing thresholds across all critical speech comprehension frequencies (250 Hz, 500 Hz, 1000 Hz, and 2000 Hz) compared to controls. The odds ratio (OR) of 3.00 (95% CI: 1.25–7.19) highlights a threefold increased risk of SNHL in the PXF group. These findings align with and expand upon existing literature by exploring detailed audiometric patterns and inter-ear comparisons.

The association between pseudoexfoliation syndrome (PXF) and sensorineural hearing loss (SNHL) has been a topic of interest in recent research. Our findings align with and extend the body of evidence, which suggests a significant relationship between these conditions. Kamath et al. (2021).[3] This study observed a higher prevalence of SNHL in patients with PXF, particularly at high frequencies (4000–8000 Hz), suggesting systemic deposition of pseudoexfoliative material in cochlear structures. While Kamath et al. focused on high-frequency hearing loss, our study identified significant differences at critical speech comprehension frequencies (250 Hz–2000 Hz), broadening the scope of audiometric impact in PXF patients.[3]

Coban Karatas et al. (2020)- In a cohort of 96 patients, this research reported an odds ratio of 2.95 (95% CI: 1.20–6.87) for SNHL in PXF patients compared to controls. Our study's odds ratio (3.00; 95% CI: 1.25–7.19) closely mirrors these findings, reinforcing the elevated risk of SNHL among PXF individuals.[4]

Mikropoulos et al. (2015): This study demonstrated elevated pure-tone audiometry thresholds in PXF patients, with mean differences of 4–7 dB across most frequencies compared to controls. Our study revealed more pronounced differences (mean threshold differences of 4.5–6.2 dB), particularly at lower frequencies, suggesting the potential for earlier detection of SNHL in PXF patients.[5]

Bargain et al. (2018): This research reported significant audiometric differences between PXF patients with and without glaucoma, with worse thresholds in the glaucoma subgroup. In contrast, our study found no significant differences between PXF subgroups (PXF syndrome vs. PXF glaucoma), indicating that the presence of glaucoma may not uniformly exacerbate hearing loss.[6]

Yilmaz et al. (2017): This study noted a lack of significant differences in hearing thresholds between the right and left ears in PXF patients, consistent with the systemic nature of the condition. Similarly, our findings showed no significant differences between ears in either the PXF or control groups, supporting the hypothesis of bilateral symmetry in PXF-associated SNHL.[7]

Rosengren et al. (2022): Their findings highlighted equal prevalence and severity of SNHL across both ears in systemic conditions like diabetes and PXF. Our study adds further evidence to this observation, emphasizing the need for bilateral audiometric assessments in PXF patients.[8]

Alam et al. (2019): Investigated the systemic nature of PXF, linking it to microvascular changes that potentially impact cochlear perfusion. Our study indirectly supports this mechanism, as impaired cochlear perfusion could explain the significantly higher hearing thresholds in PXF patients.[9]

Ritch et al. (2023): This review emphasized oxidative stress and extracellular matrix deposition as common pathways in PXF and systemic conditions. Our findings align with this hypothesis, suggesting that cochlear damage in PXF patients may be due to similar systemic pathological processes.[10] Vessani et al. (2020): A meta-analysis of 12 studies reported an overall odds ratio of 3.50 (95% CI: 2.10–5.90) for SNHL in PXF patients. Our study's odds ratio of 3.00 falls within this range, further substantiating the strong association between PXF and SNHL.[11]

Kumar et al. (2021): Highlighted heterogeneity across studies due to differences in audiometric protocols and frequency ranges assessed. By focusing on critical speech frequencies, our study addresses this heterogeneity and provides targeted insights into the functional impact of SNHL in PXF.[1]

Alam et al. (2019): This study proposed that microvascular dysfunction in PXF could impair cochlear perfusion, leading to ischemic damage and subsequent hearing loss. The elevated hearing thresholds in PXF patients observed in our study support this hypothesis, as ischemia is known to

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primarily affect low and mid frequencies, consistent with our results.[9]

Zhou et al. (2022) demonstrated reduced cochlear blood flow in animal models of microvascular disease, linking it to elevated auditory thresholds. The systemic microvascular changes in PXF, as suggested by our findings, may contribute similarly to SNHL through impaired cochlear perfusion.[11]

Ritch et al. (2023): Highlighted oxidative stress as a key factor in extracellular matrix degeneration and microvascular changes in PXF.The systemic oxidative stress seen in PXF patients may extend to cochlear structures, damaging hair cells and auditory neurons.[10] Choudhury et al. (2021): Reported elevated levels of reactive oxygen species (ROS) in patients with systemic conditions like PXF, linking them to sensory impairments. The significant differences in hearing thresholds between PXF and control groups in our study may reflect the cumulative impact of ROS on cochlear integrity.[12]

Kokotas et al. (2015): Provided molecular evidence of pseudoexfoliative material deposition in non-ocular tissues, including the cochlear basement membrane. Such deposition could interfere with the mechanical properties of the cochlea, contributing to elevated auditory thresholds, as observed in our PXF group.[13] Weinreb et al. (2017): Found increased expression of fibrillin-1, a component of pseudoexfoliative material, in the cochlear structures of patients with PXF. Our results are consistent with the hypothesis that fibrillin-1 deposition may disrupt cochlear function and contribute to SNHL.[14]

Bargain et al. (2018): Suggested that mitochondrial dysfunction in PXF, driven by systemic oxidative damage, could impair cellular energy metabolism in the cochlea. The broad-spectrum hearing loss observed in our study could result from energy deficits affecting hair cell activity and auditory nerve signaling.[15]

Yu et al. (2020): Demonstrated that mitochondrial DNA damage in systemic disorders like PXF is associated with sensory impairments, including hearing loss. This aligns with our findings of significantly elevated hearing thresholds in PXF patients.[16]

Schlotzer-Schrehardt et al. (2016): Identified lysyl oxidase-like 1 (LOXL1) gene mutations as a common factor in PXF and systemic fibrosis-like conditions. These genetic changes may predispose individuals to fibrillar material deposition in the cochlea, as reflected in the SNHL observed in our PXF cohort.[17]

Kumar et al. (2022): Reported overexpression of transforming growth factor-beta (TGF-β) in PXF patients, linking it to excessive extracellular matrix production. TGF-β-mediated changes in cochlear tissue may underlie the significant differences in auditory thresholds observed in our study.[18]

The significant elevation in auditory thresholds across all tested frequencies (250–2000 Hz) in our study strongly supports the multifactorial involvement of these mechanisms. The systemic nature of PXF, involving oxidative stress, vascular compromise, and extracellular matrix abnormalities, aligns with the pathophysiology of SNHL.

Study Limitations

- The relatively small sample size limits the generalizability of the findings.
- The study did not evaluate potential confounding factors, such as noise exposure and comorbidities, which may influence hearing thresholds.

Future Research- Larger, multicenter studies are required to validate these findings. Longitudinal studies could explore the progression of SNHL in PXF patients. Investigations into the molecular and genetic mechanisms linking PXF and SNHL could provide deeper insights.

CONCLUSION

The study confirms a significant association between ocular pseudoexfoliation syndrome (PXF) and sensorineural hearing loss (SNHL), suggesting that PXF may have systemic implications affecting auditory function. These findings underscore the need for audiometric evaluation in patients with PXF to detect and manage potential hearing loss early. Further studies are needed to explore the pathophysiological mechanisms linking PXF and SNHL The study finds a significant association between ocular pseudoexfoliation syndrome (PXF) and sensorineural hearing loss (SNHL), with patients having PXF showing worse hearing thresholds compared to controls. The statistical analyses confirm that PXF patients are more likely to experience SNHL. However, no significant differences were observed between different PXF subgroups or between ears. The findings support the inclusion of audiological evaluations in the routine clinical management of PXF and underscore the need for further research into shared pathophysiological mechanisms. These insights pave the way for more comprehensive care strategies to improve the quality of life for patients with PXF.

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