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Proteinuria as a Marker of Cochlear Microvascular Damage and Functional Hearing Deficit in Presbycusis: A Cross-Sectional Study

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Abstract

Background:
Presbycusis is the most prevalent sensory deficit in older adults, its metabolic subtype involves progressive strial microvascular degeneration. Proteinuria, a systemic marker of endothelial dysfunction, may reflect parallel cochlear microvascular damage.

Objective:
To investigate the association between proteinuria and cochlear dysfunction in elderly patients with presbycusis.

Methods:
In this cross-sectional study, 340 adults aged ≥60 years with clinically confirmed presbycusis were enrolled and classified by proteinuria status (urine albumin-creatinine ratio [ACR] ≥30 mg/g). The Hearing Handicap Inventory for the Elderly–Screening Version (HHIE-S) and the Absolute Bone Conduction (ABC) test were used to assess functional hearing deficit.

Results:
Of 340 participants, 112 (32.9%) had proteinuria. The proteinuria group showed significantly higher mean HHIE-S scores (20.4±8.6 vs. 8.2±6.4; $p<0.001$) and a greater prevalence of markedly reduced ABC results (42.9% vs. 14.0%; $p<0.001$). A moderately strong positive correlation was found between ACR and HHIE-S scores ($r=0.58$, $p<0.001$).

Conclusion:
Proteinuria is strongly associated with cochlear dysfunction and functional hearing handicap in presbycusis, supporting a shared renal–cochlear microvascular pathology.

Keywords: Presbycusis, Proteinuria, Albuminuria, Cochlear microvascular damage, HHIE-S

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Introduction:

Presbycusis, or age-related hearing loss (ARHL), is the most common sensory deficit among older adults and a leading cause of disability-adjusted life years worldwide.[1,2] Approximately one-third of adults aged 65 years and above are affected by disabling hearing loss, and the World Health Organization projects that by 2050 more than 700 million people globally will be affected—the majority being older adults.[3,4]

Presbycusis is classified into sensory, neural, metabolic (strial), and cochlear conductive

subtypes.[1,5] The metabolic subtype is characterised by progressive atrophy of the stria vascularis—the highly vascularised lateral cochlear wall that maintains the endocochlear potential (EP) through the blood-labyrinth barrier (BLB).[5,6] The EP provides the electromotive force essential for sound transduction; its decline produces a flat, sensorineural hearing loss across all frequencies.[2,7] The BLB and the renal glomerular filtration barrier share critical structural and molecular features, including dependence on the α3α4α5 network of type IV collagen for integrity and permselectivity.[8-10] This parallelism is compellingly demonstrated in Alport syndrome, a genetic collagen IV disorder that causes simultaneous progressive glomerulonephritis and sensorineural hearing loss.[9-11] In the broader aging population, systemic microvascular stressors chronic hypertension, diabetes mellitus, and oxidative stress cumulatively damage these shared basement membranes.[12]

Proteinuria, specifically albumin leakage through the glomerular basement membrane, is an established clinical surrogate for generalised endothelial dysfunction and microvascular damage.[12,13] The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines classify albuminuria by urine albumin-creatinine ratio (ACR) into A1 (<30 mg/g), A2 (30–300 mg/g), and A3 (>300 mg/g) categories.[14] Nitric oxide (NO) regulates vascular tone in both the spiral modiolar artery and renal afferent arterioles; reduced NO bioavailability causes chronic vasoconstriction and hypoperfusion in both organs.[6] Cross-sectional and prospective cohort data from Japan have demonstrated a statistically significant association between dipstick proteinuria and hearing impairment in working-age adults, suggesting that renal microvascular markers may predict auditory dysfunction.[13,15]

The Hearing Handicap Inventory for the Elderly–Screening Version (HHIE-S) is a validated 10-item questionnaire quantifying the social and emotional impact of hearing impairment on daily life.[16,17] Hearing loss in older adults contributes to social isolation, cognitive decline, and depression; albuminuria itself independently predicts hospitalisation, frailty, and functional decline in this population.[3,18-20] Despite this converging evidence, no study has comprehensively evaluated proteinuria in relation to functional hearing deficit in elderly patients with established presbycusis. This study investigates that association using the HHIE-S and ABC test in 340 adults aged ≥60 years.

Methods:

This cross-sectional clinical study was conducted at outpatient geriatric and audiology clinics. Ethical approval was obtained from the Institutional Review Board, and written informed consent was secured from all participants. A total of 340 participants aged ≥60 years with presbycusis defined as slowly progressive, bilateral, symmetrical sensorineural hearing loss without an identifiable alternative cause were enrolled.[1,5] Exclusion criteria included: sudden sensorineural hearing loss; ototoxic medications (aminoglycosides, high-dose loop diuretics); chronic middle ear disease or prior otologic surgery; noise exposure exceeding 85 dB for prolonged periods; cognitive impairment precluding questionnaire completion; and active urinary tract infection, fever, or recent intense exercise that could confound proteinuria results.[13,21]

The sensorineural nature of hearing loss was confirmed with a 512 Hz tuning fork.[22,23] The Rinne test was performed bilaterally; a positive result (air conduction > bone conduction) was required for inclusion, confirming absence of a significant conductive component.[22] The Weber test was conducted by placing the vibrating fork on the midline vertex; participants with lateralisation were excluded.[22] The Absolute Bone Conduction (ABC) test assessed cochlear sensitivity by comparing bone conduction duration between the participant (with occluded external auditory canal) and a normal-hearing examiner; results were categorised as normal, reduced, or markedly reduced.[23,24]

Functional hearing difficulty was quantified using the HHIE-S, a validated 10-item instrument assessing emotional (5 items) and social (5 items) dimensions of hearing handicap.[16,17] Responses were scored as: Yes (4 points), Sometimes (2 points), No (0 points), yielding a total of 0–40. Scores were categorised as: no handicap (0–8), mild-to-moderate (10–24), and significant handicap (26–40).[25,26]

All participants provided an early morning spot urine sample for dipstick testing.[13,21] Participants

with a positive dipstick result underwent confirmatory ACR testing.[14,27] Results were classified per KDIGO standards: A1 (normal, <30 mg/g), A2 (moderately increased, 30–300 mg/g), and A3 (severely increased, >300 mg/g).[14] Participants with ACR ≥30 mg/g were assigned to the proteinuria group.

Data were analysed using SPSS version 26.0. Continuous variables are expressed as mean ± SD and compared by independent samples t-test. Categorical variables are expressed as frequencies and percentages and compared by chi-square test. Pearson's correlation coefficient assessed the relationship between log-transformed ACR and HHIE-S scores. A p-value of <0.05 was considered statistically significant.

Results:

Of 340 enrolled participants with confirmed presbycusis, 112 (32.9%) had proteinuria (ACR ≥ 30 mg/g) and 228 (67.1%) did not. The proteinuria group was significantly older (73.5±7.1 vs. 70.1±6.2 years; p<0.001) and had higher prevalence of hypertension (73.2% vs. 50.9%; p<0.001) and diabetes mellitus (42.9% vs. 23.7%; p<0.001). Sex distribution did not differ significantly between groups (Table-I).

The proteinuria group demonstrated significantly higher mean HHIE-S scores compared to the non-proteinuria group (20.4±8.6 vs. 8.2±6.4; p<0.001), indicating a substantially greater perceived hearing handicap. Among participants with proteinuria, 87.5% reported some degree of hearing handicap (HHIE-S ≥10), compared to 36.0% in the non-proteinuria group. Significant handicap (HHIE-S 26–40) was found in 35.7% versus 8.8% of the non-proteinuria group (Table-II).

Both HHIE-S subscales were significantly higher in the proteinuria group (Table-III): the emotional subscale mean was 10.8±4.5 versus 4.2±3.1 (p<0.001), and the social subscale mean was 9.6±4.8 versus 4.0±3.6 (p<0.001).

Table-I: Demographic and clinical characteristics of the study population

Variable	Total (N=340) no. (%)	Proteinuria (+) (n=112) no. (%)	Proteinuria (-) (n=228) no. (%)	p-value
Age (years), Mean±SD	71.2±6.8	73.5±7.1	70.1±6.2	<0.001
Male sex	186(54.7)	64(57.1)	122(53.5)	0.523
Hypertension	198(58.2)	82(73.2)	116(50.9)	<0.001
Diabetes mellitus	102(30.0)	48(42.9)	54(23.7)	<0.001
Mean ACR (mg/g)	42.8±58.4	98.6±72.3	15.5±8.2	<0.001

Table-II: Distribution of Functional Hearing Deficit (HHIE-S Scores) by proteinuria status

HHIE-S Category	Proteinuria (+) (n=112) no. (%)	Proteinuria (-) (n=228) no. (%)	Total (N=340) no. (%)
No handicap (0–8)	14(12.5)	146(64.0)	160(47.1)
Mild-moderate (10–24)	58(51.8)	62(27.2)	120(35.3)
Significant (26–40)	40(35.7)	20(8.8)	60(17.6)
Mean HHIE-S Score±SD	20.4±8.6	8.2±6.4	12.2±9.4

Table-III: HHIE-S emotional and social subscale scores by proteinuria status

HHIE-S Subscale	Proteinuria (+) (n=112)	Proteinuria (-) (n=228)	p-value
Emotional (Max 20)	10.8±4.5	4.2±3.1	<0.001
Social (Max 20)	9.6±4.8	4.0±3.6	<0.001

Chi-square analysis revealed a significant association between proteinuria status and ABC test results (χ =38.6, p<0.001). Markedly reduced cochlear function was found in 42.9% of the proteinuria group versus 14.0% of the non-proteinuria group, while normal bone conduction was observed in only 16.1% versus 50.0% (Table-IV).

A dose-response relationship was observed between ACR severity and hearing handicap (Table-V). Mean HHIE-S scores increased progressively from 8.2±6.4 (A1) to 26.8±6.2 (A3), and the proportion with significant handicap rose from 8.8% to 53.8%. Pearson's correlation coefficient between log-transformed ACR and HHIE-S score was r=0.58 (p<0.001), indicating a moderately strong positive correlation.

Table-IV: Absolute Bone Conduction (ABC) test results by proteinuria status

ABC Test Result	Proteinuria (+) (n=112) no. (%)	Proteinuria (-) (n=228) no. (%)	p-value
Normal	18(16.1)	114(50.0)	<0.001
Reduced	46(41.1)	82(36.0)	
Markedly reduced	48(42.9)	32(14.0)	

Table-V: ACR severity categories and hearing handicap outcomes

ACR Category	no.	Mean HHIE-S±SD	Significant Handicap, no. (%)
A1 (Normal, <30 mg/g)	228	8.2±6.4	20(8.8)
A2 (Moderate, 30–300 mg/g)	86	18.6±7.8	26(30.2)
A3 (Severe, >300 mg/g)	26	26.8±6.2	14(53.8)

Discussion:

The principal finding of this study is that proteinuria is significantly associated with functional hearing deficits and reduced cochlear sensitivity in older adults with presbycusis. This association was consistent across all outcome measures total HHIE-S score, both subscales, and the ABC test and the dose-response gradient between ACR severity and hearing handicap strengthens the inference of a biological link between renal and cochlear microvascular pathology.

The biological plausibility of this association rests on the shared structural and molecular characteristics of the renal glomerulus and the stria vascularis.[6,8,9] Metabolic presbycusis results from progressive strial atrophy leading to decline in the endocochlear potential.[2,5,7] Both the BLB and the glomerular filtration barrier rely on the α3α4α5 type IV collagen network for their permselectivity.[6,10] In individuals with proteinuria, loss of permselectivity of the glomerular basement membrane likely reflects parallel deterioration of the BLB, disrupting the ionic gradients required for normal cochlear function.[12,14]

Our findings are consistent with prior reports. Umesawa et al demonstrated a significant cross-sectional association between dipstick proteinuria and hearing impairment among Japanese workers after adjustment for age, sex, and cardiovascular risk factors.[13] The same group subsequently reported a prospective association in which proteinuria at baseline predicted incident hearing impairment over five years.[15] The present study extends these observations to an older cohort with established presbycusis and adds validated functional outcome measures—HHIE-S and ABC test—not previously employed in this context.

Nitric oxide (NO) is a potent vasodilator regulating blood flow in the spiral modiolar artery and strial capillaries.[6] Systemic diseases such as hypertension and diabetes mellitus—both significantly more prevalent in our proteinuria group—impair NO bioavailability, resulting in chronic cochlear hypoperfusion and ischaemic

strial degeneration.[6,12] This is consistent with our finding that proteinuria was associated with significantly lower ABC test scores, indicating reduced cochlear sensitivity.

Elevation of both HHIE-S subscales in the proteinuria group has important clinical relevance. High emotional subscale scores signify embarrassment and frustration, while high social scores reflect difficulty following conversations in noise or at social events.[16,25] Such functional impairments are associated with social withdrawal, depression, and accelerated cognitive deterioration in the elderly.[18,28] Albuminuria additionally predicts frailty and increased hospitalisation rates, reinforcing that proteinuric elderly individuals constitute a high-risk population warranting targeted audiological surveillance.[19,20]

These findings carry several clinical implications. Urine dipstick screening is inexpensive and non-invasive, and can be readily integrated into primary care and audiology practice.[13,21] Detection of proteinuria in an elderly patient should prompt clinicians to consider a metabolic component to hearing loss and to anticipate greater difficulty with speech understanding in noise than audiometric thresholds alone might suggest.[2,28] Management of underlying microvascular disease through blood pressure and glycaemic control may potentially slow strial presbycusis progression, though longitudinal evidence is needed.[12,14]

This study has certain limitations. The cross-sectional design precludes causal inference. Pure-tone audiometry was not employed, limiting precision in hearing threshold quantification. The study population was derived from clinical outpatient settings, which may not fully represent the community-dwelling elderly population. Future prospective studies incorporating audiometric testing and longitudinal follow-up are warranted to confirm these findings.

Conclusion:

This cross-sectional study demonstrates that proteinuria is strongly associated with cochlear microvascular damage and functional hearing deficit in elderly adults with presbycusis. Proteinuric participants (ACR ≥30 mg/g) had significantly higher HHIE-S scores, worse ABC test outcomes, and a clear dose-response gradient across ACR severity categories—findings consistent with a shared renal–cochlear microvascular susceptibility. Proteinuria screening may serve as a useful diagnostic and prognostic adjunct in the evaluation of presbycusis, and a multidisciplinary approach integrating vascular risk management with auditory rehabilitation should be considered to optimise quality of life in this vulnerable population.

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