

Laboratory Biomarkers of Auditory Dysfunction in Chronic Kidney Disease: From Uremic Burden and Anemia to Iron Status, Mineral Metabolism, Inflammation, and Dialysis Adequacy

D. M. Nabiyeva^{1*},
N. E. Makhkamova¹

ABSTRACT

Background: Hearing impairment is increasingly recognized as an extra-renal complication of chronic kidney disease (CKD). Although pure-tone audiometry remains the conventional method for documenting hearing loss, a laboratory-centered approach may provide earlier and more mechanistically relevant information. Uremic burden, anemia, iron deficiency, disordered mineral metabolism, inflammation, malnutrition, electrolyte abnormalities, and dialysis-related factors can alter cochlear perfusion, outer-hair-cell function, endocochlear ion homeostasis, and neural conduction.

Objective: To synthesize current evidence on the relationship between laboratory biomarkers and auditory dysfunction in CKD, with particular emphasis on serum urea, creatinine, estimated glomerular filtration rate (eGFR), hemoglobin, ferritin and iron status, albumin, C-reactive protein (CRP), electrolytes, calcium-phosphate metabolism, fibroblast growth factor 23 (FGF23), parathyroid hormone (PTH), and hemodialysis adequacy.

Methods: A targeted narrative review of contemporary and foundational clinical studies was performed, prioritizing studies that combined laboratory measurements with pure-tone audiometry, high-frequency audiometry, otoacoustic emissions (OAE), speech audiometry, or auditory evoked potentials. Particular attention was paid to studies published from 2020 through 2026, supplemented by earlier mechanistic and clinical reports when needed to interpret conflicting findings.

Results: The most reproducible laboratory pattern is an association between greater renal dysfunction and poorer high-frequency hearing. Higher urea and creatinine frequently accompany hearing loss, although their independent predictive value is inconsistent across studies. Lower eGFR is associated with progressively worse high-frequency thresholds in several cohorts. Anemia represents a biologically plausible and clinically modifiable risk factor: lower hemoglobin is associated with worse hearing or speech performance, while iron deficiency anemia is linked to increased odds of sensorineural hearing loss in population data. Ferritin requires cautious interpretation in CKD because it reflects both iron stores and inflammation; recent population data suggest higher ferritin may be associated with a lower risk of high-frequency hearing loss, but these results cannot be directly extrapolated to inflamed or dialysis populations without concurrent transferrin saturation. Emerging data identify FGF23 and D-serine as potential biomarkers of hearing impairment in maintenance hemodialysis. CRP, albumin, calcium-phosphate balance, electrolyte shifts, Kt/V, ultrafiltration volume, and intradialytic hypotension may further define high-risk auditory phenotypes.

Conclusions: Auditory dysfunction in CKD is better conceptualized as the clinical expression of a laboratory-defined metabolic, hematological, inflammatory, and dialysis-related milieu than as an isolated otological complication. A practical laboratory-audiological panel should combine renal function (creatinine, urea, eGFR), anemia and iron indices (hemoglobin, ferritin, transferrin saturation), inflammatory/nutritional markers (CRP, albumin), mineral metabolism (calcium, phosphate, PTH, FGF23 when available), and dialysis metrics (Kt/V, ultrafiltration, blood-pressure stability) with high-frequency audiometry and OAE.

Keywords: Chronic kidney disease; hearing loss; laboratory biomarkers; urea; creatinine; eGFR; haemoglobin; ferritin; iron deficiency; FGF23; C-reactive protein; otoacoustic emissions; haemodialysis.

¹Department of Otorhinolaryngology, Tashkent State Medical University, Tashkent, Uzbekistan.

***Send correspondence to:**

D. M. Nabiyeva

Department of Otorhinolaryngology, Tashkent State Medical University, Tashkent, Uzbekistan.

E-mail: 998973334501g@gmail.com

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INTRODUCTION

Chronic kidney disease is a systemic disorder in which declining renal function produces a progressively complex biochemical environment. Accumulation of nitrogenous metabolites, altered acid-base and electrolyte balance, anemia, oxidative stress, chronic inflammation, endothelial dysfunction, and mineral-bone abnormalities are not merely laboratory consequences of CKD; together they shape the functional status of multiple organs. The inner ear is particularly vulnerable because cochlear transduction depends on stable ion gradients, adequate microvascular perfusion, intact mitochondrial metabolism, and highly energy-dependent transport within the stria vascularis.

The relationship between renal disease and hearing is biologically credible. The kidney and cochlea share specialized epithelial transport mechanisms, basement-membrane components, ciliary biology, and dependence on tightly regulated ionic composition. A recent comprehensive review in *Nature Reviews Nephrology* emphasized that hearing loss and CKD are linked by developmental, genetic, physiological, pharmacological, and treatment-related mechanisms, and that the risk of hearing loss rises with worsening kidney function, reaching its highest level in patients receiving hemodialysis¹.

Historically, most clinical studies approached this problem from the otological side: they measured pure-tone thresholds and then compared the prevalence of hearing loss between patients and controls. That design established that sensorineural hearing loss is common in CKD, but it does not fully answer a more clinically actionable question: which biochemical abnormalities identify patients whose auditory system is at greatest risk, and how does correction or deterioration of those abnormalities relate to cochlear function?

A laboratory-centered framework is important for three reasons. First, many biochemical abnormalities in CKD are modifiable. Anemia can be treated, iron status can be corrected, dialysis adequacy can be improved, ultrafiltration can be individualized, and inflammatory or nutritional problems can be addressed. Second, laboratory abnormalities often precede symptoms. A patient can have no major communication complaint while OAE amplitude is already reduced or high-frequency thresholds are elevated. Third, the laboratory profile can help distinguish potentially reversible metabolic dysfunction from established structural damage.

High-frequency hearing deserves particular attention. Contemporary data show that CKD patients who are not yet receiving hemodialysis already demonstrate significantly worse thresholds in the 4–8 kHz region than individuals with preserved renal function, while patients on hemodialysis generally have the poorest thresholds². Earlier work using DPOAE likewise showed that objective outer-hair-cell abnormalities can appear in later CKD stages before a major deficit is evident on conventional

audiometry³. This suggests that biochemical stress initially affects the basal cochlea and outer hair cells.

The concept of a single ‘renal hearing marker’ is unlikely to be correct. Serum urea and creatinine reflect retention of nitrogenous products but are influenced by volume status, muscle mass, dietary intake, and dialysis timing. eGFR is a better overall index of renal function but is not a direct measure of uremic neurotoxicity. Hemoglobin reflects oxygen-carrying capacity, yet it is influenced by iron status, erythropoietin, inflammation, and blood loss. Ferritin is especially complex in CKD because it is both an iron-storage protein and an acute-phase reactant. Calcium, phosphate, PTH, and FGF23 reflect CKD-mineral and bone disorder but may also have independent effects on neural and sensory tissues. A clinically meaningful model must therefore integrate several markers rather than relying on a single laboratory value.

Recent literature has expanded the biomarker field. In 2023, Yuan and colleagues reported markedly higher FGF23 and D-serine levels in maintenance-hemodialysis patients with hearing impairment than in hemodialysis patients with normal hearing and controls, identifying both as potential risk biomarkers⁴. A 2024 Cytokine study further demonstrated a positive relationship between serum FGF23 and mean binaural hearing threshold in chronic renal failure, with experimental data suggesting that FGF23 changes can precede some traditional renal markers⁵. In 2026, a population-based analysis of 2,971 adults reported that higher ferritin was associated with a lower risk of high-frequency hearing loss and that Mendelian-randomization findings were compatible with a potentially protective relationship⁶. These results are provocative but require cautious CKD-specific interpretation.

The purpose of this review is therefore not merely to summarize the prevalence of hearing loss in CKD. Its central question is laboratory and mechanistic: when renal, hematological, iron-related, inflammatory, mineral, or dialysis indicators change, what direction of auditory change is supported by current evidence? The review also proposes a practical laboratory-audiological monitoring model for predialysis CKD, maintenance hemodialysis, and kidney transplantation.

REVIEW APPROACH

This article was designed as a targeted narrative review rather than a systematic review or meta-analysis. Contemporary peer-reviewed reports were prioritized when they evaluated both laboratory parameters and objective auditory outcomes, including conventional pure-tone audiometry, high-frequency or extended high-frequency audiometry, transient-evoked or distortion-product otoacoustic emissions, speech audiometry, or auditory evoked potentials.

The evidence base included studies of predialysis CKD, maintenance hemodialysis, and kidney transplant recipients. Reports published from 2020 through 2026

were given greatest weight for current interpretation, while earlier studies were retained when they directly evaluated the relationship between biochemical variables and hearing. Because the objective was mechanistic and clinically interpretive, inconsistent findings were not averaged or forced into a single direction; instead, possible reasons for heterogeneity were examined.

The principal laboratory domains were:

(1) renal function and uremic burden: serum urea/BUN, creatinine, eGFR; (2) hematological and iron markers: hemoglobin, ferritin, transferrin saturation and iron-deficiency state; (3) electrolytes and mineral metabolism: sodium, potassium, calcium, phosphate, PTH and FGF23; (4) inflammation and nutrition: CRP and albumin; and (5) renal-replacement variables: Kt/V, ultrafiltration volume, blood-pressure instability, dialysis duration and transplant-associated improvement of metabolic parameters.

Why Laboratory Abnormalities Can Affect Hearing

The cochlea is a metabolically active organ with limited collateral blood supply. The stria vascularis maintains the endocochlear potential by active transport of potassium and other ions. Outer hair cells convert electrical energy into mechanical amplification and are highly sensitive to mitochondrial dysfunction, ischemia, oxidative stress, and changes in extracellular composition. Spiral ganglion neurons and central auditory pathways are additionally vulnerable to uremic neurotoxicity and chronic metabolic stress.

Uremia can influence hearing through several pathways. Retained metabolites may interfere with membrane enzymes and neuronal conduction; oxidative stress can damage lipid membranes and mitochondria; and endothelial dysfunction can reduce cochlear microvascular stability. Because the basal turn of the cochlea is especially susceptible to metabolic and toxic injury, high-frequency hearing is often affected before speech frequencies.

Anemia provides a second major pathway. Lower hemoglobin decreases systemic oxygen-carrying capacity. In the cochlea, where perfusion is end-arterial and metabolic demand is high, chronic hypoxia may impair the stria vascularis, reduce ATP-dependent ion transport, and increase susceptibility of outer hair cells to additional metabolic insults. Iron deficiency may add mechanisms beyond anemia because iron is essential for mitochondrial enzymes and myelin-related processes.

Inflammation and malnutrition may modify both cochlear perfusion and interpretation of laboratory markers. CRP identifies systemic inflammatory activity, while albumin reflects a combination of nutritional status, inflammation, protein loss, and systemic illness. In CKD, these markers are interdependent with anemia and ferritin, which complicates causal interpretation.

Mineral metabolism adds a newer dimension. FGF23 rises early in CKD and is closely linked to phosphate handling, vitamin D metabolism and secondary hyperparathyroidism. Experimental and clinical data now suggest that FGF23 may be associated with hearing impairment, potentially through direct or indirect effects on cochlear tissue. PTH, phosphate and calcium abnormalities may influence neuronal excitability, microvascular calcification, and inner-ear fluid regulation, although human evidence is still less consistent than for renal function and anemia.

Dialysis introduces acute physiological oscillations on top of chronic metabolic disease. Rapid changes in plasma osmolality, electrolytes, intravascular volume and blood pressure can transiently change cochlear homeostasis. A 2026 study using DPOAE demonstrated significant post-hemodialysis decreases in amplitude and signal-to-noise ratio at 1,000, 2,000, 4,000 and 6,000 Hz after a single session, supporting the concept that acute dialysis-associated shifts can influence outer-hair-cell function even when conventional hearing appears normal⁷.

Renal Function and Uremic Burden

Serum urea and BUN

Serum urea/BUN is the most intuitive marker of uremic burden, but its relationship with hearing is not uniform. Several studies report that patients with hearing loss have higher urea concentrations than those without hearing loss. In a 2023 CKD study, mean serum urea was approximately 202 mg/dL in patients with hearing loss compared with approximately 111 mg/dL in those without hearing loss, with a highly significant between-group difference⁸. This finding supports a dose-related association between retained nitrogenous products and auditory dysfunction.

Older hemodialysis data likewise suggested that patients with plasma urea above 200 mg/dL had a higher frequency of hypoacusis than those with lower urea, although the difference narrowly missed conventional statistical significance⁹. These observations are biologically plausible because uremic toxins can disrupt neuronal membrane function, energy metabolism, and possibly Na⁺/K⁺-ATPase-dependent cochlear processes.

However, urea should not be treated as a stand-alone predictor. Some modern dialysis cohorts have found no independent relationship between BUN and hearing after adjustment, and a recent prospective dialysis study reported that elevated urea and creatinine did not reliably predict the presence of sensorineural hearing loss¹⁰. Pediatric CKD data have also shown impaired cochlear function without a clear association with blood urea¹¹.

The most reasonable interpretation is therefore conditional rather than absolute: persistently high urea identifies greater uremic exposure and may accompany poorer hearing, especially high-frequency dysfunction, but a fall in urea does not guarantee immediate auditory recovery. Structural cochlear damage accumulated over

years may remain despite biochemical correction. Urea is best interpreted together with eGFR, dialysis adequacy, hemoglobin, inflammatory status, and objective cochlear tests.

Serum creatinine

Creatinine is strongly associated with the severity of renal impairment and frequently differs between CKD patients with and without hearing loss. In the 2023 study noted above, mean creatinine was substantially higher in patients with hearing loss than in those without it (approximately 9.7 versus 5.6 mg/dL)⁸. Population-based work has also identified creatinine as a marker associated with hearing impairment in specific subgroups¹².

At the mechanistic level, creatinine itself is unlikely to be directly ototoxic at clinically observed concentrations. It should be considered a surrogate for the broader metabolic environment of reduced renal clearance. Thus, the clinically important direction is: rising creatinine generally indicates worsening renal function and, across populations, is often accompanied by higher high-frequency thresholds or poorer cochlear function. Falling creatinine after successful kidney transplantation can occur in parallel with improvement in hearing, but this does not prove that creatinine reduction itself is the causal mechanism.

Studies of kidney transplant recipients are particularly informative because they provide a quasi-longitudinal model of metabolic recovery. Transplant cohorts often show marked differences in renal-function markers between hemodialysis, transplant and control groups and persistent high-frequency hearing abnormalities despite improved creatinine and eGFR¹³. This demonstrates both reversibility and residual injury: renal biochemical normalization reduces metabolic stress, but established cochlear damage may remain.

Estimated glomerular filtration rate

eGFR is conceptually more useful than creatinine alone because it integrates serum creatinine with demographic variables and provides a staging index of renal function. Contemporary frequency-specific research demonstrates a graded worsening of high-frequency hearing as renal function declines. In a 2025 Renal Failure study, high-frequency hearing loss was observed in 25.0% of participants with preserved renal function, 68.8% of nondialysis CKD patients and 78.8% of hemodialysis patients².

These data support a practical interpretation: falling eGFR should increase suspicion for subclinical high-frequency hearing loss even when speech-frequency audiometry remains near normal. The relationship is not perfectly linear in every population, partly because age, hypertension, diabetes, noise exposure and ototoxic medication strongly influence hearing. Nevertheless, eGFR is one of the most clinically useful laboratory markers for deciding when audiological screening should become more intensive.

A 2021 population-based study also found relationships between kidney function and hearing impairment, although the direction and magnitude varied by age and sex, illustrating the importance of confounding and model specification¹². This heterogeneity argues against a single threshold of eGFR at which hearing loss 'begins'. Instead, progressive eGFR decline should be interpreted as a continuous risk signal.

Hemoglobin, Iron Deficiency, Ferritin and Transferrin Saturation

Hemoglobin and anemia

Among routinely measured CKD laboratory variables, hemoglobin has one of the strongest mechanistic links to auditory function because it determines oxygen delivery. In the 2023 CKD cohort, mean hemoglobin was lower in participants with hearing loss than in those without hearing loss (7.69 versus 8.85 g/dL; $p=0.047$)¹³. Although the absolute values reflect a severely anemic CKD population, the direction of association is clinically consistent with cochlear hypoxia.

Evidence outside CKD supports the same biological concept. In a large adult cohort, iron deficiency anemia was associated with increased odds of sensorineural hearing loss (adjusted OR 1.82) and combined hearing loss (adjusted OR 2.41)¹⁴. The study defined iron deficiency anemia using both hemoglobin and ferritin, making it particularly relevant to the interpretation of CKD-related iron markers.

Lower hemoglobin can influence hearing through chronic tissue hypoxia, reduced oxygen availability to the stria vascularis, endothelial dysfunction, and increased susceptibility to ischemic or dialysis-related stress. Speech understanding and high-frequency thresholds may both deteriorate as oxygen delivery worsens. Conversely, correction of anemia may improve the reversible component of auditory dysfunction, although there is insufficient evidence to recommend a hemoglobin target specifically for hearing preservation.

Importantly, anemia in CKD is multifactorial. Erythropoietin deficiency, functional iron deficiency, absolute iron deficiency, inflammation, shortened red-cell survival, blood loss during dialysis, and nutritional deficiency can coexist. Thus, hemoglobin should trigger a search for mechanism rather than be interpreted in isolation.

Ferritin: a useful but potentially misleading auditory biomarker

Ferritin is especially attractive for a laboratory-focused hearing study because iron metabolism is biologically relevant to cochlear oxygenation and mitochondrial function. However, ferritin is also one of the easiest markers to misinterpret in CKD. Low ferritin generally supports depleted iron stores, but normal or high ferritin does not reliably exclude iron-restricted erythropoiesis because ferritin rises during inflammation.

Population evidence suggests that iron deficiency is associated with hearing loss. The large JAMA Otolaryngology study of more than 300,000 adults found higher odds of sensorineural and combined hearing loss in patients with iron deficiency anemia¹⁴. This supports a clinically plausible model in which depleted iron stores and reduced hemoglobin impair cochlear oxygen delivery or neural metabolism.

Newer data add complexity. In 2026, Lu and colleagues analyzed 2,971 NHANES participants and found that high serum ferritin was associated with a lower risk of high-frequency hearing loss after multivariable adjustment (OR 0.600, 95% CI 0.390-0.922). Mendelian-randomization analysis was also compatible with a potentially protective relationship between ferritin and sensorineural hearing loss⁶. This is an important new finding, but it was not a CKD-specific study and therefore cannot be translated directly into a recommendation that higher ferritin is always protective in dialysis patients.

In CKD, high ferritin can reflect adequate iron stores, intravenous iron exposure, inflammation, liver disease or a combination of these factors. For that reason, contemporary anemia guidance recommends interpreting ferritin together with transferrin saturation (TSAT), not alone. The 2026 KDIGO anemia guideline specifically uses combined ferritin and TSAT thresholds when considering iron therapy in hemodialysis¹⁵.

The most clinically defensible auditory interpretation is therefore nonlinear. Very low ferritin, especially with low TSAT and anemia, may identify iron deficiency and a potentially modifiable risk environment for hearing. Moderately adequate ferritin with adequate TSAT may support normal erythropoiesis and tissue oxygenation. Very high ferritin in the presence of elevated CRP may primarily reflect inflammation rather than beneficial iron stores and should not be assumed to protect hearing.

For future CKD hearing studies, ferritin should be analyzed jointly with TSAT, hemoglobin and CRP. A four-variable model is more informative than ferritin alone: hemoglobin reflects the final oxygen-carrying phenotype; ferritin reflects storage plus inflammation; TSAT reflects immediately available circulating iron; and CRP helps identify inflammatory distortion of ferritin **Table 1**.

Electrolytes and Acid-Base Homeostasis

The inner ear depends on precise ionic gradients, particularly potassium-rich endolymph. Sodium, potassium, calcium, chloride and acid-base balance can therefore plausibly influence cochlear receptor potentials and synaptic transmission. CKD and hemodialysis alter these variables chronically and acutely.

Despite strong biological plausibility, cross-sectional human evidence is inconsistent. In the 2023 study comparing CKD patients with and without hearing loss, sodium, potassium and chloride were not significantly different between groups⁸. Other studies have similarly failed to demonstrate a stable one-to-one relationship between serum electrolyte concentrations and hearing thresholds.

This does not mean electrolytes are irrelevant. Serum values represent only a snapshot, while cochlear fluid regulation depends on tissue and membrane transport processes that may be affected by rapid shifts. Acute hemodialysis can alter osmolality and electrolyte composition over several hours. The 2026 DPOAE study showing post-dialysis reduction in cochlear emission amplitude supports the concept that dynamic change may matter more than a single predialysis serum concentration⁷.

Therefore, a laboratory hearing study should distinguish static electrolyte level from dialysis-associated delta. The change in potassium, calcium, sodium, bicarbonate and osmolality across a session may be more informative than the absolute value alone. Future protocols should ideally pair pre- and post-dialysis laboratory sampling with OAE before and after the same session.

Calcium-Phosphate Metabolism, PTH and FGF23

CKD-mineral and bone disorder represents an emerging auditory research domain. Calcium is essential for synaptic vesicle release, hair-cell transduction and neuronal excitability, while phosphate and PTH reflect systemic mineral dysregulation. Secondary hyperparathyroidism, vascular calcification and altered vitamin D metabolism may indirectly affect cochlear perfusion and neural function.

Historical studies did not consistently show a direct correlation between PTH and hearing loss, and early vestibular work concluded that the role of calcium-

Table 1: Proposed iron-hearing interpretation.

Laboratory pattern	Likely interpretation in CKD	Expected auditory implication	Clinical caution
Low Hb + low ferritin + low TSAT	Absolute iron deficiency with anemia	Higher risk of cochlear hypoxia and SNHL; possible worse high-frequency thresholds	Treat according to CKD anemia guidance; hearing benefit not yet proven as an endpoint
Low Hb + normal/high ferritin + low TSAT	Functional iron deficiency/ inflammation	Risk may remain high despite 'normal' ferritin	Check CRP/inflammation; ferritin alone is misleading
Normal Hb + adequate ferritin/TSAT	Better oxygen-delivery and iron status	Potentially lower metabolic auditory risk	Does not exclude age/noise/ototoxic causes
Very high ferritin + high CRP	Inflammatory ferritin elevation or iron overload context	Direction uncertain; inflammation may worsen cochlear risk	Do not infer protection from ferritin alone

phosphate disturbances remained uncertain. This inconsistency should be acknowledged because it shows that not every plausible laboratory mechanism becomes a strong clinical biomarker.

FGF23 has changed the discussion. Yuan and colleagues reported that maintenance-hemodialysis patients with hearing impairment had substantially higher FGF23 and D-serine levels than hemodialysis patients with normal hearing and healthy controls. In their model, elevated FGF23 and D-serine were identified as risk factors for hearing impairment, with odds ratios of 16.54 and 15.22, respectively⁴.

A subsequent 2024 Cytokine study combined human and animal data. Serum FGF23 was higher in chronic renal failure patients with hearing loss and positively correlated with mean binaural hearing threshold. In renal-failure rats, FGF23 increased along with ABR threshold, creatinine, BUN and PTH; importantly, FGF23 elevation appeared earlier than several traditional indicators⁵.

These findings position FGF23 as one of the most interesting candidate laboratory biomarkers for CKD-related hearing dysfunction. It may act as a marker of CKD-mineral and bone disorder severity, a mediator of systemic toxicity, or both. However, routine use is premature. External validation, standardized assays, adjustment for phosphate, PTH, vitamin D and eGFR, and longitudinal evidence are needed before FGF23 can be used to guide hearing surveillance.

D-serine is similarly promising but less established. It is involved in N-methyl-D-aspartate receptor signaling and could theoretically influence excitotoxic or neural auditory mechanisms. Its measurement is not part of routine nephrology practice, which currently limits clinical applicability.

Inflammation, CRP and Albumin

CKD is characterized by chronic low-grade inflammation, especially in advanced disease and dialysis. Inflammation promotes endothelial dysfunction, oxidative stress, erythropoietin resistance, functional iron deficiency and malnutrition. These pathways converge on cochlear microcirculation and metabolism.

CRP is not a hearing-specific biomarker, but it can materially change how other laboratory values are interpreted. This is particularly important for ferritin. A patient with high ferritin and high CRP may have significant functional iron restriction despite apparently adequate iron stores. Thus, CRP can act as an interpretive modifier in laboratory-audiological analysis.

Albumin provides complementary information. Lower albumin may reflect malnutrition, inflammation, protein loss and chronic illness severity. In kidney transplant research, patients with auditory abnormalities have sometimes shown differences in albumin and renal-function parameters, although causal relationships are not established¹³.

A useful conceptual model is that inflammation and malnutrition lower auditory resilience. They may not independently produce a predictable number of decibels of hearing loss, but they can amplify the effects of anemia, vascular disease and uremia. For this reason, future multivariable models should include CRP and albumin as covariates whenever ferritin, hemoglobin or dialysis parameters are analyzed.

Dialysis Adequacy, Ultrafiltration and Hemodynamic Instability

Hemodialysis is both corrective and potentially stressful for the auditory system. It lowers uremic toxin burden but creates repetitive changes in fluid volume, osmolality, electrolytes and blood pressure. This dual effect explains why studies of hearing immediately before and after dialysis have reported improvement, no change, or worsening.

Kt/V is a practical marker of small-solute dialysis adequacy and an indirect measure of urea removal. A low Kt/V indicates insufficient clearance and potentially greater cumulative uremic exposure. Although direct Kt/V-hearing evidence remains limited, it is biologically reasonable to expect poorer long-term auditory outcomes when dialysis adequacy is consistently suboptimal.

Ultrafiltration volume and intradialytic hypotension may be equally important. The labyrinthine artery behaves as an end-arterial system; recurrent hypotension can reduce cochlear perfusion. Large ultrafiltration volumes may increase hemodynamic instability and rapid osmotic change. In a laboratory-oriented protocol, these variables should be treated as 'functional biomarkers' alongside serum tests.

The 2026 single-session DPOAE study provides modern evidence that dialysis can acutely reduce OAE amplitude and signal-to-noise ratio⁷. This finding is particularly relevant because OAE detects outer-hair-cell function and may change before conventional thresholds. It also argues that timing of audiological testing relative to dialysis must be standardized.

Systematic reviews confirm substantial heterogeneity in the literature but consistently identify CKD and especially hemodialysis populations as high-risk groups for hearing impairment^{16,17}. The most informative future studies will integrate biochemical change, ultrafiltration, blood-pressure trajectories and objective cochlear measurements within the same dialysis session.

Kidney Transplantation as a Model of Metabolic Reversal

Kidney transplantation offers a unique opportunity to examine whether auditory dysfunction improves when uremia, anemia and electrolyte abnormalities are corrected. If hearing improves in parallel with creatinine reduction, eGFR recovery and hemoglobin normalization, this supports the presence of a reversible metabolic component.

However, transplant data show that recovery is incomplete. In a 2022 study, kidney transplant recipients continued to demonstrate elevated high-frequency thresholds compared with healthy controls despite substantially better renal function than hemodialysis patients¹³. Hearing abnormalities were particularly evident at extended high frequencies. No clear correlation was found between hearing thresholds and blood tacrolimus or mTOR inhibitor levels, although drug-related neurotoxicity remains a theoretical concern.

The important laboratory message is that normalization of creatinine and eGFR does not erase cumulative cochlear injury. Long-standing uremia, anemia, microvascular damage, previous ototoxic exposure and years of dialysis may create irreversible lesions. Therefore, post-transplant hearing should be interpreted as the balance between metabolic recovery and residual structural damage.

Longitudinal transplant protocols should ideally measure creatinine, eGFR, hemoglobin, ferritin, TSAT, CRP, albumin, calcium, phosphate and immunosuppressant levels at the same visits as high-frequency audiometry and OAE. Such designs could identify which biochemical

improvements are most strongly associated with auditory recovery **Table 2**.

A Laboratory-Audiological Risk Model for Clinical Practice

A practical screening model should be simple enough for routine nephrology but sensitive enough to identify early auditory risk. The proposed approach uses a two-layer strategy: a core panel available in most hospitals and an extended biomarker panel for research or high-risk cases.

The core laboratory panel should include serum creatinine, urea/BUN, eGFR, hemoglobin, ferritin, TSAT, CRP, albumin, sodium, potassium, calcium and phosphate. In hemodialysis, Kt/V, ultrafiltration volume and intradialytic blood-pressure instability should be recorded. In transplant recipients, tacrolimus or other immunosuppressant trough levels may be added when clinically relevant.

The core audiological panel should include conventional pure-tone audiometry plus high-frequency assessment at least through 8 kHz, and OAE. Speech audiometry is particularly valuable when the patient reports difficulty

Table 2: Evidence Matrix: What Happens to Hearing When a Laboratory Marker Changes?

Marker	When marker worsens	Expected auditory direction	Strength/consistency of evidence	Best paired hearing test
Urea/BUN	Rises / remains persistently high	Often poorer thresholds; high-frequency dysfunction may be more common	Moderate but inconsistent	High-frequency PTA + OAE
Creatinine	Rises	Generally greater probability/severity of hearing impairment as renal function worsens	Moderate	High-frequency PTA
eGFR	Falls	Progressive increase in high-frequency hearing-loss risk	Moderate-to-strong observational	4–8 kHz or extended high-frequency PTA
Hemoglobin	Falls	Greater hypoxic risk; poorer thresholds and speech function in some cohorts	Moderate; mechanistically strong	PTA + speech audiometry
Ferritin	Falls with low TSAT	Iron-deficiency phenotype may increase SNHL risk	Indirect/moderate	High-frequency PTA
Ferritin	Rises	Not inherently harmful or protective in CKD; depends on TSAT and CRP	Uncertain; 2026 population data suggest possible protection	Interpret with TSAT/Hb/CRP
TSAT	Falls	Suggests reduced available iron and potential anemia-related cochlear risk	Mechanistic; limited direct hearing data	PTA + speech testing
CRP	Rises	May amplify inflammatory/vascular auditory risk and distort ferritin interpretation	Emerging/indirect	OAE + PTA
Albumin	Falls	May mark malnutrition-inflammation and lower auditory resilience	Limited direct evidence	PTA/OAE
Potassium/sodium/calcium	Large or rapid shifts	Potential transient cochlear dysfunction	Mechanistic; static values inconsistent	Pre/post dialysis OAE
Phosphate/PTH	Rise	Possible neural/cochlear risk; evidence inconsistent	Limited	PTA + ABR
FGF23	Rises	Higher hearing thresholds / higher probability of hearing impairment	Promising emerging evidence	PTA, possibly ABR
Kt/V	Falls	Potentially poorer long-term hearing due to inadequate clearance	Emerging	High-frequency PTA + OAE
Ultrafiltration	Large volume	Potential transient or cumulative cochlear perfusion stress	Plausible/emerging	OAE before/after HD
Intradialytic BP	Hypotension episodes	Potential ischemic cochlear injury	Plausible/emerging	OAE + high-frequency PTA

understanding speech that is disproportionate to pure-tone thresholds. ABR can be reserved for asymmetry, suspected neural involvement, unexplained speech-audiometry abnormalities, or research protocols.

Patients should be considered laboratory-audiologically high risk when several adverse domains cluster: advanced CKD or rapidly falling eGFR; persistent azotemia; hemoglobin reduction; iron-deficiency pattern; elevated inflammatory markers with low albumin; substantial mineral-bone disorder; long dialysis duration; inadequate Kt/V; high ultrafiltration; recurrent intradialytic hypotension; or exposure to ototoxic medications.

The value of clustering is that no individual laboratory variable is sufficiently specific. For example, a patient with creatinine elevation but normal hemoglobin, stable electrolytes, low CRP, adequate dialysis and no hearing complaints may be at lower immediate risk than a patient with similar creatinine plus severe anemia, iron restriction, inflammation and recurrent intradialytic hypotension

Table 3. Interpretation of Individual Markers: Clinical Scenarios

Scenario 1: Urea and creatinine rise while eGFR falls, but hemoglobin remains stable. The principal auditory concern is increasing uremic exposure. High-frequency audiometry and OAE are preferable to waiting for a speech-frequency deficit. If hearing worsens, the relationship should be interpreted as association with overall renal deterioration rather than direct creatinine toxicity.

Scenario 2: Hemoglobin falls and ferritin is low with low TSAT. This pattern strongly supports iron-deficiency anemia. From an auditory perspective, reduced oxygen delivery and iron-dependent metabolic function provide a credible mechanism for worsening cochlear performance. Correction should follow nephrology guidelines, and hearing can be reassessed after hematological stabilization to determine whether a reversible component exists.

Scenario 3: Hemoglobin falls, ferritin is high, TSAT is low and CRP is high. This is a typical inflammatory/functional iron-deficiency phenotype. Ferritin should not be interpreted as evidence of abundant usable iron. Auditory risk may remain elevated because anemia and inflammation are both active.

Scenario 4: Ferritin is high, hemoglobin and TSAT are adequate, CRP is low. The 2026 general-population study raises the possibility that higher ferritin within a non-inflammatory context may not be harmful and could correlate with lower high-frequency hearing-loss risk⁶. In CKD, however, no hearing-specific ferritin target can currently be recommended.

Scenario 5: Kt/V falls below target and predialysis urea rises while high-frequency thresholds deteriorate. The temporal association supports inadequate uremic clearance as a potentially modifiable contributor, although confounding by dialysis vintage and comorbidity must be considered.

Scenario 6: OAE amplitude falls immediately after dialysis despite stable pure-tone thresholds. This pattern may represent transient outer-hair-cell dysfunction related to acute hemodynamic or osmotic changes, consistent with 2026 DPOAE data. Ultrafiltration, blood pressure and electrolyte deltas should be reviewed.

Scenario 7: Creatinine falls markedly and eGFR rises after transplantation, but high-frequency hearing remains impaired. This suggests that the metabolic component has improved while irreversible cochlear damage persists. Rehabilitation rather than further metabolic correction may become the dominant audiological need.

Areas of Uncertainty and Research Priorities

The current literature is limited by heterogeneous definitions of hearing loss, different frequency ranges, variable timing of testing relative to dialysis, small sample sizes, inconsistent adjustment for age and diabetes, and incomplete documentation of ototoxic medications. These limitations explain why a marker such as urea can be strongly associated with hearing loss in one study and non-predictive in another.

Ferritin is a priority research marker because of the apparent tension between iron-deficiency data and the new 2026 observation that higher ferritin may be associated with reduced high-frequency hearing-loss risk in the general population. CKD studies should test whether the relationship is U-shaped, modified by CRP, or dependent on TSAT. Ferritin must never be analyzed without inflammation and iron-availability markers.

FGF23 is another major research opportunity. Existing human and experimental results are sufficiently strong

Table 3: Suggested Monitoring Algorithm.

Clinical stage	Laboratory focus	Audiological testing	Suggested interval
CKD G2–G3 with stable function	Creatinine/eGFR, Hb, ferritin/TSAT, electrolytes	Baseline PTA + 4–8 kHz; OAE if available	Every 12 months or sooner if eGFR declines
CKD G4–G5 predialysis	Add CRP, albumin, Ca/P/PTH; review ototoxic drugs	PTA + high-frequency PTA + OAE + speech testing	Every 6 months
Maintenance hemodialysis	Hb, ferritin/TSAT, urea, Kt/V, UF, BP instability, CRP/albumin, Ca/P	High-frequency PTA + OAE; standardize timing in interdialytic period	Every 3–6 months; 1–3 months if high risk
Kidney transplant, first year	Creatinine/eGFR, Hb, ferritin/TSAT, CRP, albumin, electrolytes, drug levels as indicated	Pre-transplant baseline; repeat PTA/OAE	3, 6 and 12 months
Stable transplant > 1 year	Routine graft and anemia/iron markers	PTA/high-frequency PTA; OAE if prior abnormality	Annually

to justify prospective validation, but not yet sufficient for routine screening. Studies should examine whether FGF23 predicts OAE decline or high-frequency threshold change independently of eGFR, phosphate, PTH, age and dialysis duration.

Dynamic rather than static laboratory analysis may be particularly informative in hemodialysis. The change in urea, osmolality, calcium, potassium, blood pressure and body weight across a single session should be paired with pre/post OAE and possibly extended high-frequency audiometry. This could distinguish acute reversible changes from chronic structural damage.

Longitudinal transplantation studies should investigate whether the magnitude of creatinine reduction, eGFR recovery, anemia correction and CRP normalization predicts the magnitude of hearing improvement. Such studies should also account for calcineurin-inhibitor levels and previous dialysis exposure.

Finally, future work should define a multivariable laboratory-audiological risk score. A useful score would not attempt to predict hearing from a single marker but would combine renal-function severity, anemia/iron status, inflammation, mineral metabolism and dialysis stress. The endpoint should include both threshold change and objective cochlear measures such as OAE.

DISCUSSION

The principal conclusion of this review is that CKD-associated hearing impairment should be understood as a phenotype generated by several interacting laboratory domains. Renal-function decline determines the background uremic burden; anemia and iron restriction determine oxygen-delivery capacity; inflammation and malnutrition modify vascular and metabolic resilience; mineral-bone abnormalities provide additional endocrine and neural stress; and hemodialysis adds repeated hemodynamic and osmotic fluctuations.

The strongest current clinical signal is the graded association between renal dysfunction and high-frequency hearing loss. This is consistent across recent frequency-specific data, systematic reviews and earlier OAE studies. High-frequency audiometry therefore appears to be the hearing test most naturally aligned with laboratory monitoring of CKD progression.

Urea and creatinine are useful but imperfect. They should be interpreted as markers of the uremic environment rather than direct ototoxins. Their association with hearing is strongest at a group level and less reliable for individual prediction. eGFR provides a more standardized measure of renal severity but remains influenced by age and underlying patient characteristics.

Hemoglobin and iron status represent the most clinically modifiable laboratory domain. The cochlea's dependence on oxygen supply makes anemia biologically important, and population evidence links iron deficiency anemia to sensorineural hearing loss¹⁴. In CKD, however, iron

biology cannot be represented by ferritin alone. Ferritin's dual identity as storage protein and acute-phase reactant is central to interpretation.

The new ferritin literature is particularly important because it warns against simplistic assumptions. Low ferritin in an anemic patient can support iron deficiency and plausible auditory risk, yet higher ferritin was associated with lower high-frequency hearing-loss risk in a recent general-population analysis⁶. These findings are not contradictory if ferritin is understood in context: adequate iron stores may be beneficial, while inflammation-driven ferritin elevation may represent a different biological state. CKD research must therefore separate iron sufficiency from inflammatory hyperferritinemia using TSAT and CRP.

FGF23 provides a model for the next generation of CKD auditory biomarkers. Unlike creatinine or urea, which mainly reflect renal function and nitrogenous retention, FGF23 may connect kidney disease, mineral metabolism and tissue-level effects more directly. The strong associations reported in hemodialysis and chronic renal failure studies justify further work on whether FGF23 can predict early OAE or high-frequency changes.

Dialysis adequacy should also be incorporated into auditory studies. The auditory system is exposed not only to the chronic pre-dialysis biochemical state but also to the speed and magnitude of change during treatment. The 2026 demonstration of acute post-dialysis DPOAE deterioration makes timing a major methodological issue. Audiometry performed immediately after dialysis cannot be assumed to represent the same physiological state as testing on a stable interdialytic day.

The practical implication is that nephrologists and otologists should share data rather than work in parallel. An audiogram without laboratory context may miss the mechanism, while a laboratory profile without high-frequency audiometry or OAE may miss early organ damage. The proposed combined panel is feasible in most tertiary centers and can be adapted to resource availability¹⁸.

The review also highlights an important distinction between association and causation. A reduction in urea, creatinine or CRP that occurs at the same time as hearing improvement does not prove that one marker directly caused the change. These markers may move together because a broader metabolic environment improved. For publication-quality research, multivariable analysis and longitudinal within-patient data are essential.

Despite these limitations, a laboratory-centered framework has substantial clinical value. It transforms hearing loss from a late symptomatic complication into a potentially monitorable systemic manifestation of CKD. It also identifies modifiable domains—anemia, iron status, dialysis adequacy, inflammatory burden and hemodynamic stability—that can be optimized for established nephrological reasons while their auditory consequences are prospectively evaluated¹⁹. **Table 4**

Table 4: Key Laboratory Takeaways.

Question	Evidence-based answer
If urea rises, what happens to hearing?	Higher urea often accompanies worse hearing and greater uremic burden, but it is not a reliable stand-alone predictor.
If creatinine rises / eGFR falls?	Risk of high-frequency hearing impairment generally increases as renal function worsens.
If hemoglobin falls?	Cochlear hypoxic risk rises; several studies associate anemia with poorer hearing.
If ferritin falls?	When accompanied by low TSAT and anemia, it supports iron deficiency and may increase auditory risk.
If ferritin rises?	Interpret with CRP and TSAT. Higher ferritin may reflect adequate iron or inflammation; a 2026 non-CKD study found lower HFHL risk with high ferritin.
If CRP rises?	Inflammatory burden increases and ferritin becomes harder to interpret; cochlear vascular/metabolic risk may rise.
If FGF23 rises?	Emerging evidence associates higher FGF23 with higher hearing thresholds and hearing impairment in renal failure.
If Kt/V falls?	Inadequate dialysis may increase cumulative uremic exposure and potentially worsen auditory risk.
If ultrafiltration is high or hypotension occurs?	Cochlear perfusion may be compromised; objective OAE monitoring is especially relevant.

CONCLUSION

Laboratory abnormalities in CKD are meaningfully linked to auditory function, but no single marker is sufficient. The most consistent pattern is that worsening renal function—higher creatinine and uremic burden with lower eGFR—is associated with a greater probability of high-frequency hearing impairment. Urea is a useful marker of uremic exposure but has inconsistent independent predictive value.

Anemia and iron metabolism are clinically important because they are modifiable. Lower hemoglobin and iron-deficiency anemia are associated with hearing impairment, whereas ferritin requires contextual interpretation with TSAT and CRP. Recent evidence suggesting a potentially protective association of higher ferritin with high-frequency hearing in the general population should stimulate CKD-specific research rather than immediate clinical extrapolation.

FGF23 and D-serine are promising emerging biomarkers, while CRP, albumin, calcium-phosphate metabolism, dialysis adequacy, ultrafiltration and intradialytic hypotension can refine risk assessment. The most rational monitoring strategy combines laboratory data with high-frequency audiometry and OAE.

For a laboratory-oriented journal, the key message is that hearing dysfunction in CKD is not merely an ENT endpoint. It is a functional readout of renal, hematological, inflammatory, mineral and dialysis-related physiology. Future prospective studies should test multivariable biomarker panels and determine whether correction of specific laboratory abnormalities produces measurable improvement in cochlear function.

DECLARATIONS

Ethics Approval

Not applicable; this manuscript is a narrative review and does not report a new interventional or observational patient cohort.

Consent for Publication

Not applicable.

Competing Interests

The authors should confirm the final statement before submission.

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Author Contributions

To be finalized according to actual contributions, preferably using the CRediT taxonomy.

Data availability

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REFERENCES

- Greenberg D, Rosenblum ND, Tonelli M. The multifaceted links between hearing loss and chronic kidney disease. *Nat Rev Nephrol.* 2024;20:295-312.
- Şahin MF, Karataş M. High-frequency hearing loss in chronic kidney disease: a frequency-specific analysis across renal function stages. *Ren Fail.* 2025;47(1):2590865.
- Govender SM, Govender CD, Matthews G. Cochlear function in patients with chronic kidney disease. *S Afr J Commun Disord.* 2013;60:44-49.
- Yuan D, Li J, Guo M, et al. Correlation study of FGF23/D-serine in maintenance hemodialysis patients with combined hearing impairment. *PLoS One.* 2023;18(1):e0280378.
- Li J, Nie J, Zhou Z, Guo M, et al. Changes of FGF23 and hearing in chronic renal failure and their correlation analysis. *Cytokine.* 2024;174:156478.
- Lu C, Wei Z, Li Y, et al. Higher serum ferritin associated with reduced risk of hearing loss: a cross-sectional analysis of NHANES and causal inference. *Acta Otolaryngol.* 2026;146(4):485-493.
- Cakmak Karaer I, Pembegul I. The effect of a single hemodialysis session on cochlear function of patients with end-stage renal disease. *Audiol Res.* 2026;16(3):71.
- Harshvardhan R, Phageria K, Meena R, et al. Prevalence of hearing loss and factors association in chronic kidney disease patients. *Indian J Otolaryngol Head Neck Surg.* 2023;75(3):2196-2200.
- Bazzi C, Venturini CT, Pagani C, et al. Hearing loss in short- and long-term haemodialysed patients. *Nephrol Dial Transplant.* 1995;10(10):1865-1868.
- Pandit A, Makwana P, Patel V. A prospective study of auditory functions in patients undergoing dialysis. *Bengal J Otolaryngol Head Neck Surg.* 2025;32(3):119-127.

11. Li X, Wang J. Association between kidney function and hearing impairment among middle-aged and elderly individuals: a cross-sectional population-based study. *Postgrad Med.* 2021;133(6):701-706.
12. Simsir M, Yildiz MG, Karatas M, et al. Hearing impairments as an overlooked condition in kidney transplant recipients. *Transpl Int.* 2022;35:10198.
13. Schieffer KM, Chuang CH, Connor J, et al. Association of iron deficiency anemia with hearing loss in US adults. *JAMA Otolaryngol Head Neck Surg.* 2017;143(4):350-354.
14. Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO 2026 Clinical Practice Guideline for the Management of Anemia in Chronic Kidney Disease. *Kidney Int.* 2026.
15. Kohansal B, Fathollahzadeh S, Bahadori Ghezeljeh A, et al. A systematic review on hearing and balance in patients with chronic kidney disease with and without hemodialysis. *Indian J Otolaryngol Head Neck Surg.* 2024;76(4):2939-2947.
16. Kumar KA, Hishamudin ADB, Krishnan DA, et al. The effect of hemodialysis on hearing in chronic kidney disease patients - a systematic review. *Indian J Med Sci.* 2022;74(1):32-39.
17. Ozturan O, Lam S. The effect of hemodialysis on hearing using pure-tone audiometry and distortion-product otoacoustic emissions. *ORL J Otorhinolaryngol Relat Spec.* 1998;60:306-313.
18. Usamatu A, Iseh KR, Amutta SB et al. Cochlear function in patients with chronic kidney disease: a cross-sectional evaluation in Sokoto, Northwestern Nigeria. *Saudi J Otorhinolaryngol Head Neck Surg.* 2026;28(2):79-84.
19. World Health Organization. World Report on Hearing. Geneva: World Health Organization; 2021.