Int. J. Sci. R. Tech., 2026 3(9)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

Relationship Between Aminoglycoside-Induced Nephrotoxicity And Ototoxicity: Mechanisms, Risk Factors, Monitoring And Clinical Pharmacy Perspectives

Maddala Divya*

Vikas College Of Pharmacy

ABSTRACT

Objectives: To critically review the available evidence on aminoglycoside-induced nephrotoxicity and ototoxicity, and understanding whether the two adverse effects occur together, factors that increase risk, and practical approaches to monitoring and prevention. **Methods:** structured review article was developed from the uploaded clinical study by Smith et al. (1979) and supplemented with peer-reviewed literature identified through PubMed and related biomedical sources using terms covering aminoglycosides, nephrotoxicity, ototoxicity, therapeutic drug monitoring, risk factors and pharmacogenetics. Evidence was compared according to study design, population and clinical relevance. Because the literature is heterogeneous, findings were synthesized narratively rather than pooled statistically. **Key findings:** The classic study evaluated on 127 patients for both renal and auditory outcomes. Auditory toxicity occurred in 20 patients (15.7%), definite nephrotoxicity in 22 (17.3%), and both in four (3.1%); the association was not statistically significant (P=0.750). Later literature supports exposure control and renal monitoring, but also shows that ototoxicity can occur independently of measurable renal injury. Individual susceptibility, prolonged exposure, renal dysfunction and concomitant nephrotoxic treatment may increase risk. Recent pharmacogenetic evidence suggests that MT-RNR1 variants can increase susceptibility to aminoglycoside-related hearing loss, although evidence quality and clinical implementation remain variable. **Conclusions:** Aminoglycoside nephrotoxicity and ototoxicity should be treated as separate but clinically connected safety concerns. Dose individualization, therapeutic drug monitoring where appropriate, renal surveillance, careful review of concomitant medicines and attention to hearing and vestibular symptoms are important. Pharmacists can play a practical role in identifying avoidable exposure and coordinating monitoring of adverse reactions.

Keywords: Aminoglycosides; nephrotoxicity; ototoxicity; acute kidney injury; therapeutic drug monitoring; gentamicin; tobramycin; amikacin; clinical pharmacy.

INTRODUCTION

Aminoglycosides are older antibiotics, but they have not become clinically irrelevant. Gentamicin, tobramycin and amikacin are still used when their activity is needed, including in serious Gram-negative infections. while using them have to balance the adverse reactions such as nephrotoxicity and ototoxicity.

Since aminoglycosides are eliminated mainly through the kidneys, patient with renal impairment may cause drug accumulation in body and cause the drug toxicity. The important question is whether renal toxicity and auditory toxicity occur together in the same patient. The original study on which this review was based suggested the two side effects do not always occur together. A patient can experience hearing defects even if their kidneys are working normally. Even though the patients have normal renal findings the doctor have to monitor every parameter thoroughly to avoid toxicities

2. Review Questions

This review was guided by four questions:

(1) How do aminoglycosides produce kidney and inner-ear toxicity?

(2) Which factors increase the risk?

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

(3) What does the clinical evidence show about the relationship between nephrotoxicity and auditory toxicity? And

(4) What can pharmacists and other healthcare professionals do to reduce preventable toxicity?

3. Search and Review Approach

A structured narrative approach was used. The uploaded Smith et al. study was treated as the principal historical clinical study because it directly examined both renal and auditory outcomes. Additional peer-reviewed literature was identified through PubMed using combinations of the term's aminoglycoside, nephrotoxicity, ototoxicity, acute kidney injury, therapeutic drug monitoring, gentamicin, tobramycin, amikacin, risk factors and pharmacogenetics.

4. What Happens in the Kidney?

Aminoglycosides are filtered by the kidneys and can accumulate in proximal tubular cells. Intracellular accumulation can disturb phospholipid and cellular function and may contribute to oxidative stress and mitochondrial injury. The clinical result may be a rise in serum creatinine and acute kidney injury. The risk is not determined by the drug alone. Reduced renal clearance can increase exposure, while dehydration, critical illness and other nephrotoxic medicines can further increase the risk. This creates a practical reason for pharmacists to look at the patient's whole medication and clinical picture rather than interpreting an aminoglycoside concentration in isolation.

Importantly, serum creatinine is a relatively late marker of kidney injury. Therefore, waiting for a substantial creatinine increase before reassessing an aminoglycoside regimen may allow avoidable exposure to continue.

5. What Happens in the Inner Ear?

Aminoglycoside ototoxicity can affect cochlear and vestibular structures. Experimental literature describes uptake of aminoglycosides into sensory hair cells followed by oxidative stress, mitochondrial dysfunction and activation of cell-death pathways. These mechanisms help explain why hearing damage can persist even after the antibiotic has been stopped. The clinical problem is that ototoxicity is not always obvious during treatment. Hearing loss, tinnitus or balance problems may be subtle, and patients may not spontaneously report them. Unlike many episodes of aminoglycoside-associated renal injury,

6. Risk Factors

Risk factors for nephrotoxicity:

1. patient susceptibility and drug exposure,

2. Prolonged treatment,

3. high accumulating exposure,

4. renal impairment,

5. critical illness,

6. dehydration and

7. concomitant nephrotoxic medicines are commonly discussed risk factors for nephrotoxicity.

Ototoxicity is additionally influenced by:

1. cumulative exposure and individual susceptibility

2. Genetic susceptibility is an especially interesting recent development.

A 2024 systematic review reported the strongest evidence for MT-RNR1 variants m.1555A>G and m.1494C>T in aminoglycoside-related sensorineural hearing loss, although the available studies were generally of limited evidence level.

7. The Key Clinical Evidence: Do the Two Toxicities Occur Together?

The uploaded Smith et al. study provides the clearest direct answer to this question. Of 391 patients enrolled in three double-blind aminoglycoside studies, 127 could be evaluated for both renal and auditory toxicity. Auditory toxicity occurred in 20 patients (15.7%), definite nephrotoxicity in 22 (17.3%), and both events in four patients (3.1%). The association was not statistically significant (Fisher exact test, P=0.750). The authors therefore concluded that the two toxicities could occur independently under the treatment conditions studied.

This finding is useful, but it should be interpreted cautiously. The evaluable group represented only a subset of the original 391 patients, treatment lasted a mean of 7.7 days, and concentrations were maintained within predefined ranges. The study therefore does not show that nephrotoxicity and ototoxicity are always independent in prolonged or high-exposure treatment. It supports a narrower conclusion: under the studied conditions, renal toxicity did not reliably predict auditory toxicity.

8. Therapeutic Drug Monitoring:

Therapeutic drug monitoring can reduce avoidable exposure and is particularly useful when pharmacokinetics is unpredictable, treatment is prolonged or renal function changes. Older literature supports attention to peak and trough exposure, while modern practice increasingly uses regimen-specific approaches rather than one universal concentration target.

A critical point is that therapeutic drug monitoring should support clinical judgement, not replace it. A concentration result must be interpreted alongside renal function, dose, timing of the sample, treatment indication, duration and other medicines. Recent literature also shows that evidence for particular monitoring strategies is not equally strong for every patient group. Therefore, a pharmacist should avoid treating a single concentration as an automatic measure of toxicity.

9. Why Renal Monitoring Alone Is Not Enough

The most practical conclusion from the available evidence is that renal and auditory surveillance answer different questions. Serum creatinine and other renal measures help identify kidney injury, but they cannot rule out early or developing ototoxicity. Conversely, a patient with auditory symptoms may have no obvious renal deterioration.

Patients receiving aminoglycosides should therefore be asked about hearing changes, tinnitus, dizziness or imbalance when clinically relevant. Audiological assessment can be considered when symptoms develop or when the patient's treatment and risk profile make it appropriate. This is especially important because ototoxicity may be irreversible.

10. Role of the Clinical Pharmacist

The pharmacist plays a key role before, during and after aminoglycoside treatment. Before treatment, the indication, dose, renal function, body-size variables and concomitant medicines should be reviewed. During treatment, renal trends and drug concentrations should be interpreted, and the regimen should be reassessed when renal function changes.

Medication reconciliation is particularly important because other nephrotoxic medicines may increase overall risk. The pharmacist can also check treatment duration and question unnecessary continuation once the clinical indication has changed. Patient counselling should include simple warnings about reduced hearing, tinnitus, vertigo or imbalance.

11. Critical Appraisal of the Evidence

The evidence has several strengths. The Smith et al. study prospectively assessed renal and auditory outcomes and used defined toxicity criteria. More recent reviews have added mechanistic explanations and have explored therapeutic drug monitoring and genetic susceptibility.

However, there are also important limitations. Much of the direct renal–auditory relationship evidence is historical. Definitions of toxicity have changed, dosing strategies have evolved, and many contemporary patients receive different combinations of antimicrobials. Ototoxicity can also be under-recognised when formal audiometry is not performed. Pharmacogenetic findings are promising but are not yet sufficient to predict toxicity in every clinical situation.

The most defensible interpretation is therefore not that aminoglycoside nephrotoxicity and ototoxicity are unrelated. Rather, they should be regarded as distinct adverse effects that may share common exposure and susceptibility factors but do not reliably occur together.

12. Research Gaps

Future research should focus on prospective studies using standardised definitions of renal, cochlear and vestibular toxicity. Studies should also compare

contemporary dosing and therapeutic drug monitoring strategies rather than relying mainly on historical exposure data.

Another important area is early detection. Better biomarkers for kidney injury and inner-ear injury could potentially identify toxicity before permanent clinical damage occurs. Pharmacogenetic testing, particularly involving MT-RNR1, also deserves further evaluation in different populations and healthcare systems. Finally, studies evaluating pharmacist-led monitoring and medication-safety interventions could help quantify the practical benefit of clinical pharmacy involvement.

13. Limitations of This Review

This manuscript is a structured narrative review rather than a formal systematic review or meta-analysis.

The central historical study involved only 127 patients evaluable for both outcomes, and its findings were obtained under approximately one week of treatment with controlled drug concentrations.

Therefore, its toxicity percentages should not be treated as current universal incidence estimates. The additional literature is heterogeneous in design and population.

These limitations mean that conclusions should be applied clinically with appropriate judgement rather than as rigid rules.

CONCLUSION

Aminoglycosides continue to have an important place in antimicrobial therapy, but their safety depends on careful patient selection and monitoring. The available clinical evidence does not support assuming that kidney injury and auditory toxicity will necessarily occur together. A patient may develop one without the other.

For practice, this means that renal monitoring, therapeutic drug monitoring and assessment of auditory or vestibular symptoms should be considered complementary rather than interchangeable. Dose individualisation, avoidance of unnecessary nephrotoxic exposure, appropriate treatment duration and patient counselling remain practical ways to reduce harm. Pharmacists are well placed to coordinate these activities and to identify potentially preventable toxicity.

Outcome	Patients	Percentage
Auditory toxicity	20	15.7%
Definite nephrotoxicity	22	17.3%
Both toxicities	4	3.1%
Neither toxicity	89	70.1%
Either toxicity or both	38	30.0%

Table 1. Findings from the foundational clinical study

Area	What to assess	Possible pharmacist action
Before therapy	Indication, renal function, dose and concomitant medicines	Confirm appropriateness and identify modifiable risks
During therapy	Renal trend and drug exposure	Interpret TDM and recommend dose/interval changes when needed

Auditory/vestibular	Hearing change, tinnitus, dizziness or imbalance	Counsel patient and arrange assessment when indicated
Duration	Need for continued aminoglycoside exposure	Support de-escalation/stop decisions with clinical team
Medication safety	Other nephrotoxic medicines	Recommend alternatives or closer monitoring

Table 2. Practical safety approach

REFERENCES

1. Smith CR, Lipsky JJ, Lietman PS. Relationship between aminoglycoside-induced nephrotoxicity and auditory toxicity. Antimicrob Agents Chemother. 1979;15(6):780-782.
2. Le TA, Hiba T, Chaudhari D, et al. Aminoglycoside-Related Nephrotoxicity and Ototoxicity in Clinical Practice: A Review of Pathophysiological Mechanism and Treatment Options. Drugs R D. 2023;23(4):1357-1365. doi:10.1007/s40268-023-00433-5.
3. Mingeot-Leclercq MP, Tulkens PM. Aminoglycosides: nephrotoxicity. Antimicrob Agents Chemother. 1999;43(5):1003-1012.
4. Rybak LP, Ramkumar V. Ototoxicity. Kidney Int. 2007; 72:931-935.
5. Forge A, Schacht J. Aminoglycoside antibiotics. Audiol Neurootol. 2000;5(1):3-22.
6. Gaafar D, Baxter N, Cranswick N, et al. Pharmacogenetics of aminoglycoside-related ototoxicity: a systematic review. J Antimicrob Chemother. 2024;79(7):1508-1528. doi:10.1093/jac/dkae106.
7. Lebreton L, Hennart B, Baklouti S, et al. Pharmacogenetics of aminoglycoside ototoxicity: State of knowledge and practices. Therapie. 2024;79(6):709-717. DOI: 10.1016/j.therap.2024.05.006.
8. Wu P, Barros-Becker F, Ogelman R, et al. Multiple mechanisms of aminoglycoside ototoxicity are distinguished by subcellular localization of action. Front Neurol. 2024; 15:1480435.
9. Jackson GG, Arcieri G. Ototoxicity of gentamicin in man: a survey and controlled analysis of clinical experience in the United States. J Infect Dis. 1971;124: S130-S137.
10. Smith CR, Baughman KL, Edwards CQ, et al. Controlled comparison of amikacin and gentamicin. N Engl J Med. 1977; 296:349-363.
11. Wade JC, Smith CR, Petty BG, et al. Cephalothin plus an aminoglycoside is more nephrotoxic than methicillin plus an aminoglycoside. Lancet. 1978; 2:604-606.
12. Gailiunas P, Dominguez-Moreno M, Lazarus JM, et al. Vestibular toxicity of gentamicin: incidence in patients receiving long-term hemodialysis therapy. Arch Intern Med. 1978; 138:1621-1624.

HOW TO CITE: Maddala Divya*, Relationship Between Aminoglycoside-Induced Nephrotoxicity And Ototoxicity: Mechanisms, Risk Factors, Monitoring And Clinical Pharmacy Perspectives, Int. J. Sci. R. Tech., 2026, 3 (9), 506-510. https://doi.org/10.5281/zenodo.22939864