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Determinants of hearing outcomes in pediatric oncology: Insights from South Africa's public health context

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Abstract

Hearing loss is a major morbidity among pediatric cancer survivors, particularly in low- and middle-income countries (LMICs) such as South Africa, where platinum-based chemotherapy agents are widely used. Although prior research has described the prevalence of ototoxicity in this population, limited evidence exists on the determinants of hearing outcomes in resource-constrained health systems. This study investigated demographic, diagnostic, and treatment-related factors influencing hearing loss in children receiving platinum-based chemotherapy within South Africa's public healthcare context. A retrospective review of 47 records (ages 5–18) from two public hospitals (2018–2022) was conducted. Data included demographic (age, sex, race), diagnostic (cancer type, treatment duration), and treatment (cisplatin, carboplatin) variables. Audiological outcomes were determined using pure tone audiometry and otoacoustic emissions. Descriptive statistics, chi-square tests, ANOVA, and logistic regression were applied. \Hearing loss occurred in 36.2% of patients. Younger age significantly predicted hearing loss ($p = .03$), and age effects on high-frequency thresholds were confirmed ($p < .05$). CNS cancers ($\chi^2 = 8.12$, $p = .004$), treatment duration beyond six months ($p < .01$), and cisplatin therapy ($p < .001$) were all associated with greater ototoxicity risk. Younger age, CNS malignancies, prolonged treatment, and cisplatin exposure are key determinants of ototoxicity in South African pediatric oncology. Strengthening ototoxicity monitoring through context-specific protocols, expanded audiological capacity, and interdisciplinary collaboration is essential to improve equitable care and long-term outcomes.

Keywords: Pediatric cancer, Ototoxicity; cisplatin, Carboplatin, Hearing loss, South Africa, Audiology; chemotherapy

Introduction

Childhood cancer in South Africa, though less common than adult cancers, remains a major public health concern with 800–1,000 new cases annually.[1] Treatment often requires aggressive chemotherapy with platinum-based drugs, notably cisplatin and carboplatin, which, while lifesaving, are highly ototoxic.[2–5] Up to 70% of children treated with cisplatin may develop permanent hearing loss, influenced by cumulative dose, treatment duration, and age at treatment onset.[6] In South Africa, these risks are amplified by resource limitations, uneven access to audiological monitoring, and broader social determinants of health, highlighting ototoxicity as both a clinical and public health challenge.

Chemotherapy-induced hearing loss typically presents as high-frequency sensorineural impairment, leading to speech and language delays, academic challenges, and social isolation.[7–9] These impacts are often more severe in low- and middle-income countries (LMICs), where affected children may lack access to hearing technology, specialized services, and educational support.[10,11]

Platinum-related ototoxicity is mediated by oxidative stress and reactive oxygen species damaging cochlear outer hair cells.[12] Cisplatin is more ototoxic than carboplatin but remains indispensable for some aggressive childhood cancers such as medulloblastoma.[6,13] International evidence identifies younger age, cumulative dose, and co-exposure to other ototoxic agents (e.g., aminoglycosides, loop diuretics) as principal risk factors.[6,8,13] However, evidence from LMICs—where health system constraints and socioeconomic inequities may modify risk patterns—remains limited.

Previous research from this cohort has reported the prevalence and audiological profile of ototoxic hearing loss in South African pediatric oncology.[14] To avoid duplication, this manuscript performs a secondary, inferential analysis of the same cohort and focuses on determinants of hearing outcomes (demographic, diagnostic and treatment variables) and on practical implications for ototoxicity

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monitoring in South Africa's public hospitals. This approach contributes novel insight into the contextual drivers of hearing loss in a resource-constrained setting.

Age is a consistent predictor of ototoxic vulnerability, with younger children particularly vulnerable.[8] In this study, children under 5 years were excluded because routine behavioral audiometry in that age group was not consistently recorded, reflecting a broader challenge in reliably monitoring very young pediatric patients with cancer in public settings. Findings on sex and race are inconsistent in the literature,[15,16] but in South Africa racial categories often intersect with socioeconomic disadvantage and healthcare access, so demographic effects must be interpreted in context.[17] Treatment characteristics - including drug type, dosing schedule, and multimodal therapies - further influence ototoxic risk.[18,19] Cisplatin confers the greatest risk, especially at cumulative doses above 400 mg/m^2.[6,8] When combined with cranial irradiation, the risk of auditory damage increases.[9] In this cohort, documentation of radiotherapy and concurrent ototoxic co-medications was inconsistent, a common limitation of retrospective LMIC record reviews that highlights the need for improved clinical documentation.

What distinguishes the South African context are not only the biological risk factors but also systemic barriers to effective monitoring and mitigation.[20,21] Public hospitals serving the majority of children face shortages of audiologists, limited access to high-frequency audiometry and inconsistent implementation of standardized monitoring protocols.[22–25,36] International bodies such as the International Society of Pediatric Oncology recommend structured ototoxicity monitoring with validated grading systems,[6] yet these are infrequently operationalized in LMICs practice. Consequently, hearing loss is often identified late and rehabilitation delayed.

By framing ototoxicity through both biological determinants and health-system constraints, this study adds analytic and contextual insight to the previously reported descriptive data. The aim is to identify predictors of hearing outcomes among pediatric patients with cancer and to inform feasible, context-sensitive monitoring and policy responses for South Africa.

Methodology

Aim and Objectives:

This study aimed to explore factors influencing hearing outcomes in pediatric patients with cancer in South Africa. Specific objectives were to:

- Determine factors influencing overall hearing function in this population.
- Examine relationships between demographic factors (age, sex, race) and hearing outcomes.
- Assess diagnostic factors (cancer type, treatment duration) in relation to hearing outcomes.
- Evaluate treatment factors (cisplatin vs carboplatin) and their association with hearing outcomes.

Research design

Study design and setting

A descriptive, retrospective record review[26] was conducted at two tertiary public hospitals in Johannesburg: Chris Hani Baragwanath Academic Hospital (CHBAH) and Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). Both institutions serve predominantly low-income populations and provide oncology and audiology services for pediatric patients with cancer. Descriptive findings from this cohort have been reported previously.[14] The current analysis uses the same dataset but extends the work through inferential analysis to identify demographic, diagnostic, and treatment-related predictors of hearing outcomes. The earlier paper presented prevalence and audiological characteristics, whereas this study focuses on determinants and contextual factors affecting ototoxicity risk in South Africa's public healthcare context.

Sampling and study population

A non-probability purposive sampling strategy[27] was used to identify patient records that met the inclusion criteria. Eligible participants were pediatric patients

aged 5–18 years, diagnosed with cancer and treated with platinum-based chemotherapy (cisplatin and/or carboplatin) at CHBAH or CMJAH between 2018 and 2022.

Inclusion criteria:

- Age 5–18 years.
- Treatment with cisplatin and/or carboplatin.
- At least two audiological assessments recorded.

Exclusion criteria:

- Children <5 years, due to reduced reliability of behavioral audiometry.
- Cognitive impairment affecting audiological test validity.
- Incomplete or missing audiological data (<2 assessments).

Data collection procedures

Ethical approval was obtained from the University of the Witwatersrand Human Research Ethics Committee (M221128). Data were extracted from hospital records a using a structured form that captured:

1. *Demographics:* age, sex, race (as documented).
2. *Diagnostic factors:* cancer type and duration of treatment.
3. *Treatment factors:* chemotherapy agent (cisplatin/carboplatin). Where available, the number of cycles, cumulative dose, radiotherapy, and co-exposure to ototoxic drugs (aminoglycosides, loop diuretics) were recorded, though documentation was inconsistent.
4. *Audiological data:* hearing thresholds, tympanometry, distortion product otoacoustic emissions (DPOAEs), and pure-tone audiometry (PTA). Both conventional and high-frequency audiometry were included where available. Rehabilitation details (hearing aid referral, fitting, and educational support) were recorded if noted.

Ototoxicity grading

Where high-frequency audiometric thresholds (≥4 kHz) were available, the SIOP Boston/Chang (Brock) ototoxicity grading system[6] was retrospectively applied. Records lacking adequate data were summarized descriptively.

Data analysis

Descriptive statistics were used to summarize demographic, diagnostic, treatment, and audiological variables. Inferential tests included[28]:

- *Chi-square tests* for associations between categorical variables (e.g., sex and hearing loss).
- *ANOVA and t-tests* for differences across diagnostic or treatment groups.
- *Logistic regression* to assess predictors of hearing loss (independent variables: age, sex, race, cancer type, treatment type; dependent variable: hearing function).

Hearing loss classification followed established pediatric norms.[29] Pure-tone thresholds >20 dB HL at any frequency (0.5–8 kHz; up to 12 kHz when high-frequency data were available) were considered abnormal. Both ear-specific thresholds and the better-ear four-frequency pure-tone average (0.5, 1, 2, 4 kHz) were calculated. Hearing loss was recorded if either ear exceeded 20 dB HL at one or more frequencies, to capture early high-frequency losses. Where possible, severity was classified using the SIOP Boston/Chang system.[6] Significance was set at $p < 0.05$. Statistical analyses were performed with IBM SPSS v26.0.[28]

Reliability and validity measures

Validity was supported by strict inclusion/exclusion criteria and by requiring at least two audiological assessments per patient. Audiological procedures conformed to HPCSA standards,[29] ensuring data accuracy. Reliability was maintained through standardized testing across both hospitals,

structured data collection, and data quality checks.

Ethical considerations and data management

Ethical approval was granted (M221128). As a retrospective record review, informed consent was waived under national guidelines permitting use of anonymized data.

Each patient was assigned a unique study code. Data were stored on password-protected, access-controlled systems, with regular verification for accuracy. Upon study completion, anonymized data were archived according to University of the Witwatersrand retention policies for potential secondary analysis.

Results

Demographic Profile of the Sample

Records from 47 pediatric patients were reviewed. The sample showed an approximately equal sex distribution and diverse racial composition reflective of Johannesburg's population (Table 1).

The mean age at diagnosis was 12.3 years (SD = 3.1; range 5–18 years).

Table 1: Demographic profile of participants

Variable	N = 47	%
Sex		
Male	26	55.3%
Female	21	44.7%
Race		
Black	31	66.0%
White	8	17.0%
Mixed Race	6	12.8%
Other	2	4.3%

Most diagnoses occurred between ages 10 and 15 (59.6%), followed by 5–9 years (23.4%) and 16–18 years (17.0%) (Table 2).

Table 2: Age distribution of pediatric patients with Cancer

Age Group (years)	Number of Patients	Percentage (%)
5–9	11	23.4
10–15	28	59.6
16–18	8	17.0
Total	**47**	**100**

The predominance of patients aged 10–15 likely reflects increased incidence of certain cancers in early adolescence and greater exposure to intensive treatment protocols in this developmental phase — a relevant consideration for ototoxicity vulnerability.

Audio logical findings

Hearing loss was identified where pure-tone thresholds exceeded 20 dB HL at any test frequency (0.5–8 kHz; extended to 12 kHz where available), in accordance with HPCSA guidelines. Severity was graded using the SIOP Boston/Chang scale when data permitted. Overall, 36.2% (n = 17) of patients exhibited hearing loss, predominantly bilateral high-frequency sensorineural loss (42.6%).

Table 3: proportion of hearing loss by frequency range

Frequency Range	Number of Patients with Hearing Loss	Percentage (%)
High Frequency	14	82.4
Low-to-Mid Frequency	3	17.6
Total	**17**	**100**

High-frequency hearing loss predominated (82.4% of affected patients), consistent with the typical ototoxic profile of platinum-based agents.

Objective 1: Factors influencing hearing function

Logistic regression analysis examined the effects of age, sex, and race on hearing loss. Age was a significant predictor, $\chi^2(3, N = 47) = 10.68$, $p < .05$, with younger patients showing higher risk ($p = .03$). Neither sex nor race showed significant associations ($p > .05$) (Table 4).

Table 4. Logistic regression results for factors influencing hearing loss

Predictor	B	SE	OR	p-value
Age	0.91	0.42	2.5	0.03*
Sex	-0.22	0.51	0.81	0.64
Race	0.13	0.32	1.14	0.72

*Significant at p < .05

Although age-related susceptibility was evident, interpretation should be cautious given the modest sample size.

Objective 2: Demographic factors and hearing outcomes

ANOVA confirmed a significant effect of age on high-frequency thresholds ($F = 4.67$, $p < .05$), indicating younger children were more affected. No statistically significant differences were observed by sex or race ($p > .05$). These findings align with international reports suggesting that younger age increases ototoxic vulnerability, while demographic variables such as sex and race play minimal direct roles but may intersect with structural inequities.

Objective 3: Relationship between diagnostic factors and hearing function

Children with central nervous system (CNS) cancers exhibited a greater prevalence of hearing loss than those with other cancer types. A significant association was observed between CNS cancer and hearing loss ($\chi^2(1, N = 47) = 8.12$, $p = .004$). Treatment duration also influenced outcomes: patients treated for more than six months had higher hearing loss prevalence (52.9%) compared to those treated for shorter durations (21.7%) ($t = 3.45$, $p < .01$) (Table 5).

Table 5. Hearing loss prevalence by cancer type and treatment duration

Cancer Type	Hearing Loss (%)	Duration (>6 months)	Hearing Loss (%)
CNS	67%	Yes	52.9%
Non-CNS	21%	No	21.7%

Extended treatment duration likely reflects cumulative ototoxic exposure, though this may also be confounded by multimodal therapies and incomplete dosing data.

Objective 4: Relationship between treatment factors and hearing function

Cisplatin-treated patients demonstrated substantially higher hearing loss rates than those receiving carboplatin (53.8% vs. 15.8%; Table 6). The difference was statistically significant ($t = 5.22$, $p < .001$), confirming cisplatin's stronger ototoxic profile.

Table 6. Hearing loss prevalence by treatment type

Treatment Type	Hearing Loss (n)	% of Group with Hearing Loss
Cisplatin	14	53.8%
Carboplatin	3	15.8%

This pattern reinforces international evidence of cisplatin's dose-related cochleotoxicity. Limited high-frequency testing in public sector settings may, however, underestimate early ototoxic effects.

Discussion

Unlike the earlier report on prevalence within this cohort,[14] the present study provides a secondary inferential analysis examining determinants of ototoxicity. This analytic extension enables contextual interpretation of hearing outcomes in relation to demographic, diagnostic, and treatment variables, offering insights relevant to risk stratification and health system strengthening in South Africa.

The findings highlight that young age, cancer type, treatment duration, and chemotherapy agent were key determinants of hearing outcomes. Rather than reiterating well-established risk factors, this study situates them within South Africa's public healthcare system, where ototoxicity monitoring remains inconsistent and constrained by limited resources.[22,23] The results thus advance understanding of how structural and contextual

factors amplify biological vulnerabilities.

Age emerged as a significant determinant of hearing loss, with children under ten showing greater susceptibility.[8,17] Their developing auditory systems are more vulnerable to high-frequency damage from platinum compounds.[6] The exclusion of children under five, due to limited audiometric reliability, is acknowledged as a weakness that future work should address through objective measures such as auditory brainstem response. No associations were found between hearing outcomes and sex or race, consistent with Brooks and Knight.[13] However, in the South African context, "race" reflects socioeconomic disparities that shape access to care. Hendricks et al.[30] have shown that socioeconomic status—rather than race per se—drives childhood cancer outcomes, underscoring the need to disentangle biological from structural contributors to ototoxicity risk.

Diagnostic variables also played a role. Children with CNS cancers were more likely to experience hearing loss, aligning with Tillmanns et al.[9] and Brock et al.[6] This may relate to the frequent use of cisplatin in CNS protocols and potential exposure to cranial radiotherapy, which was not consistently captured here. Treatment duration exceeding six months was also associated with poorer hearing outcomes. Duration served as a proxy for cumulative exposure due to incomplete dosing data, though this is confounded by multimodal regimens. Future studies in South Africa should systematically record cumulative doses (mg/m^2) to improve dose–toxicity modelling. These findings are consistent with global evidence that extended exposure to platinum agents heightens auditory risk. In South Africa, longer treatment courses may also increase delays in audiological follow-up, reflecting systemic barriers to continuity of care.[20,22,23]

Cisplatin was again confirmed as the most ototoxic agent, with significantly higher rates of hearing loss compared with carboplatin.[6] A key contextual insight is that high-frequency audiometry—critical for early detection—is seldom available in South African public hospitals.[22,23] As a result, ototoxicity is typically identified only when it affects speech frequencies, delaying rehabilitation. Implementation of HPCSA guidelines[29] remains inconsistent due to shortages of audiologists, limited equipment, and competing clinical priorities. Practical solutions could include adoption of portable audiometry, mobile health tools for community-based screening, and integration of ototoxicity monitoring within oncology care pathways through stronger oncologist–audiologist collaboration.

The observed hearing loss prevalence of 36.2% aligns with findings from LMICs such as Richard and Andrea's Tanzanian study[17] but exceeds many high-income country (HIC) estimates.[6] This reflects inequities in monitoring infrastructure. In HICs, baseline and follow-up testing are routine; in LMICs, detection often occurs only after communication difficulties arise, leading to underestimation of true prevalence. Clinically, reducing cumulative ototoxic exposure remains a priority. Adhering to antibiotic stewardship can limit aminoglycoside use in febrile neutropenia, and substituting furosemide with less ototoxic diuretics could mitigate risk. Randomized trials and international guidelines have shown that sodium thiosulfate effectively reduces cisplatin-induced hearing loss, with promising real-world uptake.[9,17,31–35] Even where thiosulfate is unavailable, these context-sensitive strategies are feasible and impactful.

The implications of this study are twofold: first, it provides inferential evidence on ototoxicity determinants among South African pediatric oncology patients; second, it highlights systemic gaps in monitoring and intervention capacity. Addressing these requires national policy commitment, integration of ototoxicity screening into standard oncology care, workforce development for audiologists, and cross-sector partnerships to enhance access to equipment and services.

Study limitations include its retrospective design, reliance on incomplete clinical records, and small sample size (n = 47) from two hospitals, which limits generalizability. Variations in audiological procedures may have influenced consistency of results. Missing data on radiotherapy, concurrent ototoxic medications, and genetic susceptibility represent additional constraints.

Prospective studies with larger cohorts, precise dose documentation, and genomic analyses within African populations are needed to strengthen predictive modelling and inform contextually appropriate interventions.[8,14]

Conclusion

This study identified younger age, CNS cancers, prolonged treatment duration, and cisplatin exposure as key determinants of hearing loss among South African children with cancer. Its contribution lies in framing these risks within the realities of South Africa's under-resourced public health system, where structured ototoxicity monitoring is rarely standardized. These findings reinforce the need for locally adapted guidelines, expanded audiology capacity, and integrated multidisciplinary care. Future research should include cumulative dose and radiotherapy data and explore genetic susceptibility to inform equitable, evidence-based ototoxicity prevention and monitoring strategies for African pediatric oncology settings.

Brief points

What is already known on this topic

- Platinum-based chemotherapy agents, particularly cisplatin, are effective in pediatric oncology but highly ototoxic.
- Younger children are more vulnerable to chemotherapy-induced hearing loss, often presenting with high-frequency sensorineural loss.
- Standardized ototoxicity monitoring protocols exist in high-income countries but are inconsistently applied in low- and middle-income countries (LMICs).

What this paper adds

- Provides the first analysis of demographic, diagnostic, and treatment-related factors influencing hearing outcomes in pediatric patients with cancer in South Africa.
- Highlights the absence of standardized ototoxicity monitoring protocols in South Africa's public healthcare system and the systemic barriers to their implementation.
- Offers context-specific recommendations for improving ototoxicity monitoring in LMICs, including integration of audiology into oncology care and feasible strategies to reduce additional ototoxic exposures.

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