INVISIBLE SIDE EFFECTS: HEARING AT RISK IN CANCER THERAPY

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ABSTRACT

Chemotherapy, especially with platinum-derived agents, is recognized for its ototoxic effects, and can cause irreversible damage to auditory and vestibular function. This study aimed to evaluate the clinical and sociodemographic profile of cancer patients and to investigate the prevalence of hearing complaints associated with chemotherapy treatment. This is an observational, analytical, cross-sectional cohort study, carried out in a public oncology referral hospital. The sample consisted of patients over 18 years of age and with a confirmed medical diagnosis of cancer, excluding individuals with metabolic diseases, presence of metastases or previous oncological treatments. Data collection was conducted using a structured questionnaire, administered orally, containing 22 multiple-choice questions about personal identification, cancer history, and auditory manifestations. The study included 96 individuals, with a mean age of 54.14 years; Most of them were women with breast cancer (31.5%), living in the capital (42.2%) and without formal schooling (51.8%). The analysis revealed a high prevalence of auditory symptoms after the start of

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chemotherapy: tinnitus (78.1%), hearing difficulty (71.9%), otalgia (75%), dizziness (68.8%) and ear pruritus (56.3%). Carboplatin was used in 31.6% of the cases, and 44.6% of the participants were in the course of treatment. It is concluded that there is a high incidence of auditory complaints among patients undergoing chemotherapy, which highlights the need for systematic audiological monitoring, given the possibility of early manifestation of ototoxicity even before confirmation by conventional audiological tests. The role of the audiologist is essential in clinical surveillance and prevention of hearing problems in these patients.

Keywords: Cancer. Tinnitus. Dizziness. Hearing loss.

INTRODUCTION

Chemotherapy-induced ototoxicity is one of the most debilitating adverse effects, often underdiagnosed. This type of toxicity can trigger bilateral, progressive, and irreversible sensorineural hearing loss, starting at high frequencies and later extending to speech frequencies as the cumulative dose increases (CAMPOS et al., 2020). In addition to hypoacusis, manifestations such as tinnitus, otalgia, ear itching, vertigo, and imbalance are common and may precede detectable changes in conventional audiological tests (DA SILVA et al., 2021; PEPPÉ et al., 2023).

Data from the literature indicate that more than 50% of patients treated with cisplatin report auditory symptoms, and about a third have clinically significant hearing loss (GONÇALVES et al., 2022). In children, the prevalence is even higher, reaching up to 90% of cases (SANTOS; ALMEIDA; VASCONCELOS, 2021). Carboplatin, although considered less ototoxic, also imposes a relevant risk, especially in combined regimens or in high doses (FERREIRA et al., 2020).

The consequences of hearing loss and vestibular symptoms transcend the physical domain, negatively impacting communication, social life, educational and work performance, in addition to generating important emotional effects, such as anxiety, depression, and isolation (SANCHEZ et al., 2023; BARKER; LEIGHTON; FERGUSON, 2017). In this context, the early detection of ototoxicity is essential and can be made possible through the implementation of sensitive audiological monitoring protocols, with the use of tools such as high-frequency audiometry and distortion product otoacoustic emissions (LOURENÇO et al., 2019).

At the same time, although otoprotective strategies such as the use of antioxidants — e.g., N-acetylcysteine , dexamethasone — minimize the impact of cisplatin, there is still no consensus or standardized recommendations for its clinical application (ARAUJO et al., 2024; HENDERSON et al., 2020). Thus, the performance of the audiologist becomes essential, and must be inserted in the multiprofessional oncology teams to conduct the screening, periodic evaluation and auditory rehabilitation of patients at risk (JACOB et al., 2006).

In view of this scenario, the present study aims to evaluate the clinical and sociodemographic profile of cancer patients and to investigate the prevalence of hearing complaints associated with chemotherapy treatment, focusing on the impacts of ototoxicity on the quality of life of these individuals.

METHODOLOGY

This is a cross-sectional cohort study, of an analytical and observational nature, approved by the Research Ethics Committee of the institution (CAAE: 63341322.3.0000.5546; Opinion No. 5,792,977). The research was conducted in accordance with the ethical precepts established in Resolutions No. 466/2012 and No. 510/2016 of the National Health Council. All participants were previously informed about the objectives, risks and benefits of the study and, after voluntary agreement, signed the Informed Consent Form (ICF), ensuring the anonymity and confidentiality of the information collected.

The investigation was carried out in the oncology sector of a public reference hospital in the state of Sergipe. Data collection was carried out between January and October 2023, in the morning, in order to coincide with the greater flow of patients treated at the unit. Initially, an educational group activity was promoted in the waiting room, with the objective of informing users about the potential ototoxic effects of chemotherapy and the importance of hearing monitoring in the oncological context. During this action, an information leaflet was distributed containing guidance on hearing health, preventive strategies and the impacts of hearing loss on quality of life.

Then, patients who showed interest were referred to a reserved space, where they received additional clarification about the research. The sample was selected in a non-probabilistic manner, by convenience, including all patients who met the eligibility criteria and who were undergoing chemotherapy treatment at the unit during the study period.

INCLUSION CRITERIA

Individuals of both sexes, aged 18 years or older, born and residing in Brazil, with a confirmed medical and anatomopathological diagnosis of malignant neoplasm and undergoing active or recent chemotherapy treatment in the oncology sector of the hospital were included.

EXCLUSION CRITERIA

Individuals who had cognitive limitations or oral communication difficulties that prevented adequate comprehension and response to the data collection instrument were excluded. Those with a history of occupational or environmental exposure to high levels of noise or acoustic trauma, as well as patients who had already undergone otological surgeries or who had preexisting otological pathologies to the neoplasm, were also excluded. In addition, previous diagnoses of metabolic diseases, such as diabetes mellitus

or systemic arterial hypertension, as well as patients with a history of oncological treatments prior to the current study or with the presence of ongoing metastases, were considered exclusion criteria. Patients who underwent chemotherapy treatment at institutions other than the one where the study was conducted were also excluded. In addition, the participants could not present auditory complaints (such as tinnitus, hypoacusis, otalgia, ear pruritus or vertigo) before the start of cancer treatment.

COLLECTION PROCEDURES

The data were obtained through the application of a structured questionnaire, prepared by the advising researcher. The instrument contained 20 predominantly multiple-choice questions, distributed in four sections: (1) identification data (age and gender); (2) sociodemographic information (marital status, education and place of residence); (3) clinical history of the neoplasm (location of the primary tumor, time since diagnosis, time to the first specialized consultation, drugs used, clinical staging, number of chemotherapy sessions, surgeries performed, and family history of cancer); and (4) auditory complaints and otological history (presence of hypoacusis, tinnitus, vertigo, autophonia, pruritus or otalgia, as well as previous otological events).

To ensure the standardization of the collection and mitigate the interference of the researcher, the questionnaire was read aloud, and the participants provided their answers orally, according to the time needed for each one, respecting their physical and emotional conditions. When requested, the participant was allowed to resume or complete the questionnaire at another previously scheduled time.

At the end of the questionnaire application, all participants were invited to undergo complete audiological examinations, which were available at the audiology outpatient clinic of the same institution. The scheduling of the exams was carried out in a flexible manner, according to the availability and convenience of the patients, in order to ensure adherence to the diagnostic procedure.

STATISTICAL ANALYSIS

The data were analyzed with the aid of the Statistical Package for the Social Sciences (SPSS)® software, version 20.0. Initially, the normality of the distribution of the variables was verified using the Shapiro-Wilk test. The level of statistical significance was set at 5% ($p \leq 0.05$).

The main dependent variable was self-reported auditory complaints (presence or absence), while the independent variables included demographic characteristics (age,

gender), clinical characteristics (type of cancer, drug used, treatment time), and quality of life. Continuous variables with normal distribution were expressed as mean and standard deviation (±), while those without normal distribution were presented as median and interquartile range.

For the inferential analysis, the Student's t-test was used to compare two groups with normal distribution, and the Mann-Whitney test for groups without normal distribution. The chi-square test (χ^2) was applied for categorical variables. In analyses with more than two groups and multiple variation factors, analysis of variance (ANOVA) was used, complemented by Tukey's post hoc test when necessary.

RESULTS

Of the 89 individuals initially interviewed, 83 fully met the previously established inclusion criteria and were considered eligible to compose the final sample of this study. The mean age of the participants was 54.14 years (±13.49), with a predominance of females, representing 63.9% of the total sample. The mean interval between the onset of the first symptoms and the search for specialized medical care was 17 months (±17.9), indicating a substantial delay in access to diagnosis and initiation of cancer treatment.

Table 1 presents a detailed analysis of the sociodemographic, clinical, and treatment-related characteristics of the participants. The data indicate that most patients were married (45.8%) and lived in the state capital (42.2%). In terms of education, more than half of the sample (51.8%) had never attended school, which suggests a significantly low educational profile. Regarding the neoplastic typology, the most prevalent cancers in the sample were breast (31.5%), lung (9.6%) and bone marrow (9.6%).

Regarding the therapeutic modalities, 33.7% of the patients had already undergone surgical procedures and most of the participants (44.6%) were in the initial phase of chemotherapy treatment. The most frequently used antineoplastic drugs were carboplatin (31.6%), cyclophosphamide (25.3%) and oxaliplatin (16.9%). In addition, 59.0% of the interviewees reported having a family history of cancer, suggesting a possible hereditary component or relevant genetic predisposition.

Table 1 – Sociodemographic and clinical characteristics of the participants (n=83).

Variables	n (%)
Marital status	
Single	28(33,7)
Married	38(45,8)
Widower	9(10,8)
Divorced	8(9,16
Residence	
Capital	35(42,2)

Interior urban area	31(37,3)
Countryside	17(20,5)
Schooling	
Elementary school	25(30,1)
Middle school	7(8,4)
Higher education	8(9,6)
He never studied	43(51,8)
Type of cancer	
Anal	1(1,2)
Breast	26(31,5)
Head and neck	7(8,4)
Prostate	3(3,6)
Marrow	8 (9,6)
Lung	8(9,6)
Stomach	3(3,6)
Liver	1(1,2)
Leukaemia	7(8,4)
Lymphoma	3(3,6)
Skin	1(1,2)
Uterus	3(3,6)
Thyroid	1(1,2)
Pancreas	2 (2,4)
Underwent surgical procedure	
Yes	28 (33,7)
No need	37 (44,6)
He will still have surgery	18 (21,7)
Stage of chemotherapy	
Beginning	37 (44,6)
Middle	21(25,3)
Finalizing/Finalizing	24(30,1)
Chemotherapy drugs	
Carboplatin	26(31,6)
Cisplatin	12(14,5)
Oxaliplatin	14(16,9)
Vinscristina	8(9,6)
Doxorubicin	13(15,7)
Gemcitabine	7(8,4)
Cyclophosphamide	21(25,3)
Farmorrubicin	2(2,4)
Family history for cancer	
Present	49(59,0)
Absent	34(41,0)

Source: Authors' data

Regarding auditory aspects, 38.6% of the participants (n = 32) reported perception of hearing loss after the beginning of cancer treatment, representing the main self-reported auditory complaint. In addition, it was found that 83.1% of the participants had never undergone previous audiological evaluations, denoting a critical gap in the otological follow-up of these patients throughout the therapeutic process.

Table 2 presents the comparative analysis between the groups of participants with and without self-reported hearing difficulties, considering clinical and otological variables. A statistically significant association was observed between auditory complaints and the onset of symptoms after the administration of chemotherapy drugs ($p = 0.032$), suggesting the possible ototoxicity induced by the therapeutic regimen in question. In addition, symptoms

such as ear pruritus (p = 0.001), otalgia (p = 0.063), and sensation of ear fullness (p = 0.007) occurred significantly more frequently in the group that reported auditory complaints.

On the other hand, variables such as the presence of tinnitus (p = 0.628), dizziness (p = 0.833) and autophony (p = 0.266) did not show a statistically significant association with self-reported hearing loss, which may indicate different pathophysiological mechanisms or distinct clinical thresholds between these symptoms.

Table 2 – Comparison between participants with and without hearing complaints regarding clinical variables and otological symptoms (n = 83).

Variables	Self-reported listening well (%)	Self-reported not hearing well (%)	p (value)
Gender			**0,166**
Female	30 (58,8)	23 (71,9)	
Male	21 (41,2)	09 (28,1)	
Post-treatment hearing complaint			**0,032***
After chemotherapy	05(9,8)	09(28,1)	
After radiotherapy	46 (90,2)	23 (71,9)	
Presence of tinnitus			**0,628**
After chemotherapy	6(11,8)	6(18,8)	
After radiotherapy	44(86,3)	25(78,1)	
After radiotherapy and concomitant chemotherapy	1(2,0)	1(3,1)	
Presence of dizziness			**0,833**
After chemotherapy	12(23,5)	9(28,1)	
After radiotherapy	38(74,5)	22(68,8)	
After radiotherapy and concomitant chemotherapy	1(2,0)	1(3,1)	
Earache			**0,063***
Presence	5(9,8)	8(25,0)	
Absence	46(90,2)	24(75,0)	
Itch			**0,001***
Presence	11(21,6)	18(56,3)	
Absence	40(78,4)	14(43,8)	
Ear fullness			**0,007***
Presence	11(21,6)	16(50,0)	
Absence	40(78,4)	16(50,0)	
Autophony			**0,266**
Presence	13(25,5)	11(34,4)	
Absence	38(74,5)	21(65,6)	

Source: Authors' data

DISCUSSION

The survey indicated that breast cancer was the most prevalent type among the participants, representing 31.5% of the registered cases. These findings are in line with the estimates of the National Cancer Institute (INCA), which classifies breast cancer as the most common neoplasm in Brazil. INCA predicts a considerable increase in the incidence of this disease in the period from 2023 to 2025, with a projection of 73,610 new cases, corresponding to 30.1% of the total cancer cases in the country (INCA, 2023). This growth

is largely attributed to a multifactorial interaction involving biological, environmental, and social factors, such as the aging of the population, greater exposure to risk factors, and changes in social and dietary behavior patterns.

Regarding risk factors, the aging of the population has contributed substantially to the increase in the incidence of age-related cancers, such as breast cancer. In addition, behavioral factors, such as smoking, obesity, and exposure to carcinogenic agents, are strongly correlated with increased global cancer burden (Pan American Health Organization/World Health Organization – PAHO/WHO, 2024). In addition, changes in lifestyles, often associated with socioeconomic progress, have increased the population's exposure to inadequate eating habits, sedentary lifestyle, and environmental pollutants, further exacerbating this phenomenon.

The analysis of genetic influence, a preponderant factor in the development of breast cancer, was also central to this study. The data obtained show that 59% of the participants reported the presence of family history as a relevant factor in the manifestation of the disease. The scientific literature supports that genetic mutations, especially in genes such as BRCA1 and BRCA2, increase the predisposition to the development of breast cancer (Anderson, 1971; Fett-Conte; Salles, 2002). INCA (2022) estimates that between 5 to 10% of cancer cases are attributed to heredity, underscoring the importance of a personalized approach in assessing genetic risk and implementing preventive strategies.

The mean age of the participants, which was 54.4 years (ranging from 18 to 54 years), is also in line with the epidemiological pattern observed for breast cancer, since the incidence of cancer increases progressively after the age of 50 (INCA, 2023). The increase in longevity has been a determining factor in this scenario, because as the population ages, the probability of developing neoplasms increases. Factors such as long-term exposure to carcinogenic substances and the natural deterioration of cellular mechanisms over time may also contribute to this pattern (PAHO/WHO, 2024).

In terms of diagnosis and treatment, the literature indicates that early detection and initiation of treatment in the early stage are crucial determinants for reducing mortality and improving the patient's prognosis. The present research indicated that the participants started treatment on average 17 months after the appearance of the first symptoms. This data is alarming, as the Ministry of Health, through an ordinance issued in 2011, establishes a period of 60 days between diagnosis and the start of cancer treatment. The delay in starting treatment can be attributed to multiple factors, such as delay in recognizing symptoms, difficulty in accessing specialized services, and overloading the health system, factors that often result in diagnoses in more advanced stages of the disease (Coates,

1999). In fact, data from the Ministry of Health (2023) corroborate the hypothesis that delays in diagnosis and treatment are associated with an increased incidence of cancer in more advanced stages, compromising the chances of cure.

Another relevant aspect identified was the geographic distribution of the participants, with 42.2% living in the capital of Sergipe, where the study was conducted, which is explained by the greater concentration of health resources in the urban area. The IBGE survey (2019) and the implementation of the Surveillance of Risk and Protective Factors for Chronic Diseases by Telephone Survey (Vigitel) in 2006 reveal that the capitals have a more robust health infrastructure, favoring early diagnosis and access to appropriate treatments. The disparity in access to health between urban and rural areas is a factor that should be considered in public health policies, especially in peripheral regions where the coverage of medical services is insufficient (Ministry of Health, Vigitel Brasil, 2022).

Regarding socioeconomic aspects, it was observed that schooling has a significant correlation with the search for medical services. The sample studied revealed that 50.8% of the population had not attended school, while only 9.6% had higher education. This data is consistent with the INCA study (2022), which pointed to a significant disparity in cancer screening coverage between different educational levels. Women with a higher level of education demonstrated greater adherence to screening and regular medical follow-up, reflecting greater access to information and greater awareness of the importance of early detection of cancer. This disparity can be explained by the lack of access to adequate information, the scarcity of health education programs, and the level of social empowerment, which varies according to the educational level of the population (GUERRA et al, 2023).

Regarding marital status, it was observed that 45.8% of the participants were married. This finding corroborates evidence in the literature that indicates the positive influence of family support on clinical outcomes in oncology. According to Aizer et al. (2013), married patients are less likely to develop metastases and demonstrate better response rates to cancer treatment, a result often attributed to the emotional, psychological, and logistical support provided by the spouse and family nucleus. These results highlight the relevance of psychosocial factors in cancer management, suggesting that interventions focused on strengthening family support can contribute significantly to therapeutic adherence and clinical prognosis.

Regarding the therapeutic modalities adopted, it was identified that 33.7% of the patients underwent surgical intervention. This percentage is lower than the national average estimated by the National Cancer Institute (INCA, 2021), which points out that

approximately 80% of cancer patients require some type of surgical procedure throughout the treatment. This discrepancy can be attributed to the heterogeneity of the sample in terms of the anatomical location of the tumor, staging of the disease, and individual clinical conditions, which directly influence the surgical indication. The Brazilian Society of Oncological Surgery (SBCO, 2023) emphasizes that the decision for surgical intervention should consider multiple variables, such as the histological type of the neoplasm, extent of tumor dissemination, the patient's organic functionality, and the availability of adjuvant or neoadjuvant therapies, configuring a personalized and evidence-based approach.

All participants in the present study underwent chemotherapy protocols, with emphasis on the use of platinum-derived alkylating agents, notably carboplatin and cisplatin. Carboplatin has been widely administered and has been consistently associated with otoneurological adverse events, including ototoxicity and vestibular toxicity, clinically characterized by symptoms such as hearing loss, tinnitus, and vertigo. In this study, 46% of the patients reported at least one of these symptoms, a finding that corroborates previous evidence in the literature (FIGUEIREDO et al., 2004; SANCHEZ et al., 2023). Cisplatin, in turn, used by 14.5% of the sample, is recognized for its high ototoxic potential, with direct deleterious action on the hair cells of the cochlea, mediated mainly by processes of oxidative stress and cellular apoptosis (WINSTON; SRDJAN, 2023).

The high prevalence of auditory and vestibular manifestations observed reinforces the urgency of adopting prophylactic strategies and early monitoring of ototoxicity in cancer patients undergoing treatment with ototoxic chemotherapy drugs. Such strategies should include the judicious use of otoprotective agents — whose scientific evidence is progressively expanding — and the systematic implementation of audiological surveillance protocols based on objective tests, such as pure tone audiometry, high-frequency audiometry, and otoacoustic emissions (DILLARD et al., 2022).

It is necessary, however, to recognize the methodological limitations of this study, particularly with regard to hearing assessment based exclusively on self-reports. The absence of instrumental audiological tests restricts the diagnostic accuracy of the reported ototoxic manifestations, which may underestimate or overestimate the real prevalence of hearing impairments. Therefore, it is recommended that future investigations incorporate objective and standardized audiological evaluations, with longitudinal follow-up, in order to deepen the understanding of the auditory and vestibular impacts induced by chemotherapy.

CONCLUSION

The results indicated that 38.6% of the participants reported hearing difficulties after chemotherapy, such as tinnitus, dizziness and earache. The analysis revealed that the use of chemotherapy drugs, especially platinum derivatives, such as carboplatin and cisplatin, is directly related to the development of vestibular and auditory toxicity, affecting the quality of life of patients. These findings reinforce the need for systematic hearing monitoring protocols in cancer patients, in order to prevent and minimize ototoxic adverse effects, ensuring a more effective treatment and better support for patients' hearing health.

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