Prevalence and Management of Immediate Adverse Reactions to Chemotherapy in Breast Cancer Patients: A Retrospective Study

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Abstract

Objective To analyze the prevalence, characteristics, and management of immediate adverse reactions (ARs) to chemotherapeutic agents in breast cancer patients treated at the National Cancer Institute (Instituto Nacional del Cáncer, INCAN, in Spanish) in Paraguay.

Materials and Methods A retrospective, observational, and cross-sectional study was conducted using clinical records of 200 breast cancer patients aged between 25 and 75 years submitted to outpatient chemotherapy at the INCAN between August 2022 and August 2023. The data collected included patient demographics, breast cancer subtype, chemotherapeutic agents used, and reported ARs.

Statistical Analysis Descriptive statistics were used to summarize the data. Chi-square tests were performed to evaluate the associations between ARs and specific chemotherapy agents, with statistical significance set at $p < 0.05$.

Results Among the 200 patients included, 61% (122/200) experienced ARs. The most common reactions were skin rash (17.1%), nausea (16.1%), and flushing (9.5%). Luminal A was the most prevalent breast cancer subtype (32.5%). Paclitaxel and docetaxel were the most frequently associated agents (29% each), but no statistically significant association was found involving specific drugs and ARs. The medications most commonly used in the management of ARs included chlorpheniramine (32%), dexamethasone (24%), and ondansetron (14%).

Conclusions Immediate ARs to chemotherapy are common among breast cancer patients, and they require effective monitoring and management protocols. These findings highlight the need for tailored strategies to mitigate ARs and improve treatment outcomes, particularly in resource-constrained settings.

Keywords

- antineoplastic agents
- drug-related side effects and adverse reactions
- breast neoplasms
- taxanes
- hypersensitivity

Introduction

Chemotherapy remains a cornerstone in cancer treatment, with expanding indications for various tumors, leading to a spectrum of toxicities that require management to improve patients' quality of life. This therapy employs specific drugs to target tumor cells by interfering with their DNA or RNA.[1,2] Adverse reactions (ARs), defined as undesired effects of medications or treatments, are classified as *immediate* or *delayed* based on the timing of symptom onset.[3] Immediate ARs are more common and are further divided into immunological and non-immunological types based on the underlying pathophysiological mechanisms.[4]

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Breast cancer originates in mammary glands influenced by estrogen, and it is a clonal disease capable of invasion and metastasis. The risk factors include age (older than 50 years), the female sex, sedentary lifestyle, alcohol consumption, and genetic predisposition, such as *BRCA1* and *BRCA2* mutations.[5] Breast cancer cells are classified into subtypes based on hormone receptor status:

- Luminal A: Estrogen and progesterone receptor-positive, associated with a good prognosis.
- Luminal B: Includes luminal B/human epidermal growth factor receptor 2 (HER2)-positive (worse prognosis) and luminal B/HER2-negative (high proliferation risk).
- HER2-positive: HER2 receptor-positive only, with an intermediate prognosis.
- Triple-negative: Lacks hormone receptors, responds to chemotherapy, but has a high recurrence rate.[6]

According to the Spanish Society of Medical Oncology (Sociedad Española de Oncología Médica, SEOM, in Spanish), the most common ARs associated with outpatient chemotherapy include hair loss, nausea and vomiting, fatigue, anemia, infections, dermatitis, acne, bruising, appetite loss, mouth sores, dry skin, and tiredness.[7] A study conducted at the Central Hospital of Instituto de Previsión Social, in Paraguay, in 2021 found that all patients receiving intravenous chemotherapy experienced ARs, with gastrointestinal (34.1%), dermatological (22.7%), and neurological (16.3%) events being the most prevalent.[8] The scientific literature[9] also documents hypersensitivity reactions (HSRs) to docetaxel and paclitaxel in approximately 30% of the patients, which can compromise the effectiveness of taxanes, especially during infusion.

Despite extensive global research on cancer and its symptoms, recent studies[10] focusing on the prevalence and intensity of ARs in patients undergoing chemotherapy are limited. Therefore, the primary objective of the current study is to analyze the prevalence of immediate adverse effects of chemotherapeutic agents in breast cancer patients at the Outpatient Medicine Service of Paraguay's National Cancer Institute (Instituto Nacional del Cáncer, INCAN, in Spanish).

Materials and Methods

A retrospective, observational, cross-sectional study was conducted in Capiatá, Paraguay, using clinical records of breast cancer patients treated at INCAN. The study population included women and men aged 25 to 75 years who received chemotherapy at the Outpatient service of Hospital Día between August 2022 and August 2023. The inclusion criteria were patients within the aforementioned age group with a confirmed diagnosis of breast cancer who received chemotherapy at INCAN during the specified period. The exclusion criteria were duplicate entries and incomplete records, particularly those lacking essential information on chemotherapy administration or AR documentation.

The main variables collected included sociodemographic data, the chemotherapeutic agents administered, the type of immediate ARs (occurring within 24 hours of infusion), and their severity. The specific ARs analyzed were: skin rash, nausea, facial flushing, headache, pain, dyspnea, gastrointestinal discomfort, and tachycardia. The severity of each event was graded using version 5.0 of the Common Terminology Criteria for Adverse Events (CTCAE). In accordance with institutional protocols, premedication was routinely administered prior to taxane-based chemotherapy, typically including dexamethasone, chlorpheniramine (a histamine H1 antagonist), and ranitidine or famotidine (a histamine H2 antagonist), 30 to 60 minutes before infusion, to reduce the risk of HSRs. Only immediate ARs were included in the analysis. Delayed effects, such as alopecia, were excluded due to their later onset and inconsistent documentation in immediate postinfusion records.

The sampling method was probabilistic and random. A minimum sample size of 151 participants was calculated based on a presumed AR rate of 88%, a total population of 2,084 patients receiving outpatient chemotherapy per year, a 95% confidence level, and a 5% margin of error. Final recruitment involved reviewing physical medical records obtained from the INCAN Archives Department, following a structured randomization protocol.

Clinical data were extracted exclusively from paper-based medical records. Each chart was reviewed manually using a standardized data collection form developed for the study. The ARs were identified based on documented nursing notes, infusion logs, and progress reports recorded during and immediately after chemotherapy sessions. Charts with incomplete or missing data were excluded to maintain data integrity.

Approval for access to patient records was obtained through a formal request submitted to the INCAN Medical Directorate and was contingent upon approval by the Ethics Committee of Universidad del Pacífico. After receiving ethical clearance, an Excel (Microsoft Corp.) database was created to input and organize the data collected.

To ensure data quality, a pilot test was conducted on 10 randomly-selected medical records to verify the presence and clarity of the required variables; these records were excluded from the final analysis. Statistical analyses were also performed using Excel. The quantitative variables were expressed through measures of central tendency (mean) and dispersion (standard deviation), while the qualitative variables were presented as absolute and relative frequencies. Associations between variables were evaluated using 2×2 contingency tables and Chi-squared (χ^2) tests, with statistical significance set at $p < 0.05$ and a 95% confidence level.

The present study was conducted in accordance with fundamental ethical principles. Patient confidentiality was always protected. The research posed no risk to the participants, as it was based on existing medical records.

Results

The current study included 200 patients with a mean age of 53 ± 11 years. The sample was composed of 94% (188/200) of female, and 6% (12/200) of male subjects ($p = 0.02$; $\chi^2 = 5.36$), with a statistical significance towards the female patients

Table 1 Chemotherapeutic agents and the occurrence of adverse reactions in the study sample

Chemotherapeutic qgent	n (%)
Docetaxel	58 (29)
Paclitaxel	58 (29)
Trastuzumab	35 (17)
Carboplatin	17 (9)
Doxorubicin	14 (7)
Cyclophosphamide	11 (5)
Pertuzumab	7 (4)
Total	**200 (100)**

who presented ARs. In total, 61% (122/200) of the patients experienced ARs, while 39% (78/200) reported no reactions. The most prevalent type of breast cancer was luminal A, accounting for 32.5% (65/200) of the cases, followed by HER2-positive breast cancer (31%; 62/200), luminal B (23.5%; 47/200), and triple-negative breast cancer (13%; 26/200).

The chemotherapeutics most frequently associated with ARs were paclitaxel and docetaxel, involved in 58% (116/200) of the cases. Trastuzumab accounted for 17% (35/200), carboplatin, for 9% (17/200), doxorubicin, for 7% (14/200), cyclophosphamide, for 5% (11/200), and pertuzumab, for 4% (7/200). The statistical analysis did not reveal any significant associations involving docetaxel ($p = 0.47$; $\chi^2 = 0.50$) and paclitaxel ($p = 0.80$; $\chi^2 = 0.06$) and the occurrence of ARs (►**Table 1**).

A total of 169 immediate ARs were documented among 200 patients, which represents a prevalence of 84.5%. Most ARs were mild (CTCAE grade 1; 139/169; 82.2%), with grade-2 reactions comprising 17.8% (30/169). No grade-3 or -4 events occurred.

Skin rash was nearly exclusively grade-1 (35/36; 97.2%), while nausea included grade-1 (21/34; 61.8%) and grade-2 (13/34; 38.2%) events. Transient reactions such as facial flushing (n = 20) were universally grade-1 (20/20, 100%). Cardiorespiratory symptoms (dyspnea: 14/15; 93.3%; tachycardia: 13/14; 92.9%) and gastrointestinal discomfort (13/14; 92.9%) were also predominantly grade-1. Full grading distributions are detailed in ►**Table 2**.

Regarding the management of ARs, chlorpheniramine was the most used medication (32%; 74/200), followed by dexamethasone (24%; 54/200) and ondansetron (14%; 31/200). Other interventions included metoclopramide (10%; 23/200), ketorolac (8%; 19/200), and hydrocortisone (4%; 10/200), as shown in ►**Table 3**.

Some patients experienced more than one AR or required multiple interventions, leading to variations in total counts.

Discussion

The current study highlights the high prevalence and clinical relevance of immediate ARs to chemotherapy among breast cancer patients. A total of 61% of patients experienced at least 1 AR, a figure that aligns with previous findings from Instituto de Previsión Social, in Paraguay,[8] where all patients undergoing intravenous chemotherapy reported ARs—most commonly gastrointestinal, dermatological, and neurological symptoms. These findings underscore the need for effective recognition and management of ARs to improve treatment adherence and patient outcomes.

As expected, most of our cohort were women (94%; 188/200), reflecting the gender-specific nature of breast cancer.[5,10,11] Although a statistically significant association was found between sex and the occurrence of ARs ($p = 0.02$; $\chi^2 = 5.36$), this result should be interpreted with caution, as the predominance of female patients may have introduced a bias. The mean age of 53 years corresponds with the postmenopausal onset typically observed in breast cancer, in line with global demographic data.[5] The distribution of molecular subtypes—luminal A (32.5%; 65/200), HER2-positive (31%; 62/200), luminal B (23.5%; 47/200), and triple-negative (13%; 26/200)—is consistent with the international literature,[6,12] in which luminal subtypes are most common and generally associated with more favorable prognoses.

Table 2 Types of adverse reactions

Adverse reaction	n (%)	CTCAE grade 1: n (%)	CTCAE grade 2: n (%)
Skin rash	36 (21.3)	35 (97.2)	1 (2.8)
Nausea	34 (20.1)	21 (61.8)	13 (38.2)
Facial flushing	20 (11.8)	20 (100)	0 (0)
Headache	18 (10.7)	13 (72.2)	5 (27.8)
Pain	18 (10.7)	10 (55.6)	8 (44.4)
Dyspnea	15 (8.9)	14 (93.3)	1 (6.7)
Gastrointestinal discomfort	14 (8.3)	13 (92.9)	1 (7.1)
Tachycardia	14 (8.3)	13 (92.9)	1 (7.1)
Total	**169 (100)**	**139 (82.2)**	**30 (17.8)**

Abbreviation: CTCAE, Common Terminology Criteria for Adverse Events.

Table 3 Medications used in the management of adverse reactions

Medications	n (%)
Chlorpheniramine	74 (32)
Dexamethasone	54 (24)
Ondansetron	31 (14)
Metoclopramide	23 (10)
Ketorolac	19 (8)
Hydrocortisone	10 (4)
Total	**229 (100)**

Among the chemotherapeutic agents studied, taxanes—specifically paclitaxel and docetaxel—were most frequently implicated in ARs, each accounting for 29% of the cases. This is consistent with previous reports[9,13,14] that associate taxanes with HSRs in up to 30% of the patients. However, we found no statistically significant link between a specific agent and the occurrence of ARs, suggesting that other factors—such as cumulative dose, infusion rate, or individual patient susceptibility—may also influence reaction risk. Future research should aim to identify predictive markers for ARs to enable the development of more personalized management strategies.

The types of ARs most frequently observed—skin rash, nausea, facial flushing, and dyspnea—mirror those commonly reported in the literature.[7,14,15] While most were mild (CTCAE grade 1), their impact on patient comfort and treatment adherence should not be underestimated. In our cohort, management strategies included the use of chlorpheniramine, dexamethasone, and ondansetron, which are well-established in the supportive care of chemotherapy-related toxicities.[7,15]

Notably, no grade-3 or -4 HSRs were reported. This may be attributed to our institution's standardized premedication protocols, which typically include corticosteroids, H1 antagonists, and H2 antagonists prior to taxane administration. This practice is supported by international guidelines, including those of Comité de l'évolution des pratiques en oncologie (CEPO),[16] which reports reductions in HSR incidence from approximately 30% to below 3% when premedication is used. Regimens that include dexamethasone, diphenhydramine, and H2 blockers have been shown to decrease severe HSRs to as low as 1 to 2%.[16]

Beyond premedication, the use of slow infusion rates and structured monitoring protocols at our center may have further reduced the risk of severe reactions. Evidence from recent studies[17] supports this approach, showing that infusion titration and vigilant observation significantly lower both the frequency and severity of HSRs. These practices are particularly important during the first and second cycles of chemotherapy, when most reactions tend to occur.

Our findings are consistent with recent literature[15,18] reporting that immediate HSRs to taxanes, particularly paclitaxel, often manifest early in the treatment course. A large retrospective study[15] of more than 6 thousand breast cancer patients receiving paclitaxel identified an 11.9% rate of immediate HSRs, with risk factors including younger age, Asian ethnicity, and a history of allergies. Moreover, excipients such as Cremophor EL, present in conventional paclitaxel formulations, have been implicated in complement-mediated (non-immunoglobulin E [IgE]) reactions, contributing to early-onset HSRs.[19] Nab-paclitaxel, which lacks Cremophor EL, has been shown to reduce this risk.[15] Although platinum agents such as carboplatin are typically associated with delayed HSRs, they can also cause acute reactions after multiple cycles or at higher cumulative doses.[20] These insights highlight the critical role of early-cycle monitoring and individualized premedication in minimizing risks. Desensitization protocols, when appropriately implemented, may enable patients with prior HSRs to safely continue chemotherapy.[21]

Despite its strengths, the present study has limitations. Its retrospective design, combined with reliance on paper-based records, may have led to underreporting mild or transient ARs. Although incomplete charts were excluded to ensure data integrity, variability in documentation remains a potential source of bias. Furthermore, the single-center setting may limit generalizability to other institutions with differing protocols or patient demographics.

In conclusion, the present study contributes to the growing body of evidence regarding immediate ARs to chemotherapy in breast cancer patients. The high prevalence of ARs observed reinforces the importance of proactive, protocol-driven management strategies—particularly the use of premedication and slow infusion practices. These measures are essential to safeguard patient safety and support continuity of care. Further prospective studies are needed to confirm these findings, explore predictive factors, and develop targeted interventions to minimize treatment-related toxicity in oncology.

Authors' Contributions

SB, SO, MP: conceptualization, data curation, investigation, methodology, resources, writing – original draft, writing – review & editing; GI: conceptualization, data curation, formal analysis, methodology, project administration, software, supervision, validation, visualization, writing – original draft, writing – review & editing.

Ethical Approval Statement

The present study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, and it was approved by the Institutional Review Board (IRB) of Universidad del Pacífico. Patient data were obtained from clinical files, and all identifying information was kept confidential. Names and other personal identifiers were not included in the main database to ensure privacy and confidentiality.

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Conflict of Interests

The authors have no conflict of interests to declare.

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