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RESEARCH ARTICLE

A Prospective Observational Study for Assessment of Chemotherapy-Induced Adverse Drug Reactions in Cancer Patients

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Abstract: A prospective observational study was carried out to evaluate the patterns, severity, and management of chemotherapy-induced adverse drug reactions (ADRs) in cancer patients. The study included 135 patients receiving chemotherapy at a tertiary care hospital over six months. ADRs were assessed using Naranjo's causality assessment scale, Hartwig's severity scale, and Schumock and Thornton preventability criteria. The mean age of patients was 49.31 ± 12.69 years, with females (63%) experiencing more ADRs than males (37%). Breast cancer was the most prevalent malignancy (34.8%), followed by ovarian and cervical cancers in females, while lung cancer predominated in males. The most frequent ADRs were alopecia, nausea and vomiting, loss of appetite, peripheral neuropathy, and skin/nail pigmentation changes. Gastrointestinal and dermatological reactions were the most commonly affected organ systems. Naranjo's algorithm revealed 76% probable, 20% possible, and 4% definite causality relationships. According to Hartwig's scale, 58.03% ADRs were mild and 41.6% moderate in severity. The Schumock and Thornton criteria classified 62% of reactions as definitely preventable. Statistical analysis showed no significant association between ADR severity and patient age (p=0.73) or gender (p=0.45). Notably, myelosuppression persisted despite dose adjustments, and emesis remained poorly controlled despite prophylactic antiemetic therapy. The study shows the need for enhanced pharmacovigilance and personalized approaches to minimize chemotherapy-induced ADRs.

Keywords: Chemotherapy; Adverse Drug Reactions; Pharmacovigilance; Cancer; Drug Safety.

1. Introduction

Cancer chemotherapy has evolved significantly over recent decades, encompassing both conventional cytotoxic drugs and targeted therapies. While these treatments have revolutionized cancer care, their narrow therapeutic window presents substantial clinical challenges. The dosage required to achieve therapeutic efficacy often results in toxicity to rapidly proliferating cells, making adverse drug reactions (ADRs) a critical concern in oncology practice [1]. The complexity of modern chemotherapy regimens, combined with individual patient variations in drug response, necessitates careful monitoring and management of these adverse effects to ensure optimal treatment outcomes [2]. The World Health Organization defines adverse drug reactions as noxious and unintended responses occurring at doses normally used for prophylaxis, diagnosis, or therapy [3]. This definition gains particular significance in oncology, where the therapeutic window is notably narrow. The FDA further categorizes serious adverse events as those resulting in death, life-threatening conditions, hospitalization, disability, congenital anomalies, or requiring intervention to prevent permanent impairment [4]. In the context of cancer chemotherapy, these definitions help clinicians and researchers standardize their approach to ADR monitoring and management [5].

The fundamental mechanism underlying chemotherapy-induced ADRs stems from these agents' inability to differentiate between malignant and normal rapidly dividing cells. The cytotoxic effects extend beyond cancer cells to affect healthy tissues with high proliferation rates, including bone marrow, gastrointestinal mucosa, hair follicles, and reproductive cells [6]. This non-selective action results in a spectrum of adverse effects, ranging from mild discomfort to potentially life-threatening complications. Moreover, certain chemotherapeutic agents exhibit specific organ toxicities, affecting the heart, kidneys, bladder, lungs, and nervous system

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through various pathophysiological mechanisms [7]. The timing and administration of chemotherapy follow carefully structured protocols. Treatment may be delivered as adjuvant therapy following surgical intervention to eliminate residual microscopic disease, or as neoadjuvant therapy to reduce tumor burden before surgery [8]. While some agents can be administered orally or through intramuscular routes, the majority require intravenous administration to ensure optimal bioavailability and therapeutic effect. Treatment schedules typically follow 21- or 28-day cycles, incorporating rest periods to allow recovery of normal tissues. The duration of therapy often extends from three to six months, though this can vary based on the cancer type, stage, and individual patient response [9].

Recent advances in supportive care have improved the management of chemotherapy-induced ADRs, yet they remain a significant challenge in oncology practice. The impact of these adverse effects extends beyond physical symptoms to affect patients' quality of life, treatment adherence, and ultimately, survival outcomes [10]. Moreover, the economic burden associated with managing these complications adds another dimension to the challenge of providing optimal cancer care [11]. In this context, systematic monitoring and documentation of chemotherapy-induced ADRs become crucial for several reasons. First, it helps identify patterns and risk factors that may predict adverse reactions in specific patient populations. Second, it enables the development of preventive strategies and management protocols. Third, it contributes to the growing body of pharmacovigilance data that informs future therapeutic decisions and drug development [12]. The present study was carried out to document and evaluate the patterns of ADRs in cancer patients receiving chemotherapy, assess their severity and causality, and identify potential strategies for their prevention and management.

2. Materials and Methods

2.1. Study Design

A descriptive observational study was conducted from October 2023 to March 2024 at a tertiary care teaching hospital in South India. The study protocol received approval from the Institutional Ethics Committee (KCPT/IEC/2023/112) prior to initiation, following the principles outlined in the Declaration of Helsinki [13]. Patient confidentiality was maintained throughout the study period, and written informed consent was obtained from all participants.

2.2. Study Population

The study enrolled 135 cancer patients receiving chemotherapy who developed at least one adverse drug reaction during their treatment course. Patient selection criteria were established based on previous pharmacovigilance protocols in oncology settings [14]. The study included patients aged 18 years and above receiving either single-agent or combination chemotherapy regimens, encompassing both newly diagnosed cases and those undergoing subsequent treatment cycles. Patients receiving concurrent radiotherapy, those who did not develop ADRs during the study period, and individuals unable to provide reliable information due to communication barriers or severe illness were excluded from the study, following established methodology for ADR monitoring in cancer care [15].

2.3. Data Collection

A standardized data collection form was developed based on validated pharmacovigilance protocols [16, 17]. The process involved systematic documentation from multiple sources, including medical records, treatment protocols, laboratory investigations, and direct clinical observations. Patient case files were reviewed for diagnosis, disease staging, comorbidities, and previous treatment history. Chemotherapy protocols were documented in detail, including drug combinations, dosages, administration routes, and cycle intervals, as recommended by current oncology practice guidelines [18].

Laboratory monitoring included regular assessment of complete blood counts, liver function tests, renal function parameters, and other relevant biochemical markers, following standard protocols for chemotherapy monitoring [19]. Clinical observations were recorded through structured patient interviews and physical examinations during treatment cycles, with particular attention to the temporal relationship between drug administration and adverse event occurrence.

2.4. Assessment of Causality

Naranjo's Algorithm served as the primary tool for establishing causality relationships between suspected drugs and observed ADRs [20]. This tool evaluates multiple criteria including previous reports of the reaction, temporal associations, response to withdrawal, rechallenge results, and alternative explanations. The scoring system categorizes causality as definite (≥9), probable (5-8), possible (1-4), or unlikely (≤0), providing a standardized approach to ADR evaluation in clinical settings [21].

2.5. Assessment of Severity

ADR severity was evaluated using Hartwig's and Siegel's Scale [22], which provides a structured approach to categorizing reaction severity. Mild reactions (Level 1-2) encompass those requiring no therapy change or minimal intervention. Moderate reactions (Level 3-4) include cases necessitating therapy modification, dose adjustment, or extended hospital stay. Severe reactions (Level 5-7)

comprise life-threatening events or those resulting in permanent harm or death, as defined by established pharmacovigilance criteria [23]

2.6. Assessment of Preventability

The Schumock and Thornton preventability criteria [24] were applied to evaluate the potential avoidability of observed ADRs. This assessment considers multiple factors including drug appropriateness, dose selection, monitoring parameters, and known preventive measures. Definitely preventable reactions included those with inappropriate drug selection, incorrect dose adjustments, or inadequate monitoring. Probably preventable reactions encompassed cases where preventive measures were available but not implemented, while non-preventable reactions included those occurring despite appropriate drug usage and monitoring protocols [25].

2.7. Statistical Analysis

Statistical evaluation was performed using SPSS version 25.0 software. Descriptive statistics were employed to summarize demographic data and ADR patterns, with results expressed as percentages and frequencies. The mean age of patients was calculated with 95% confidence intervals. Chi-square tests assessed potential associations between patient characteristics (age and gender) and ADR severity, with $p<0.05$ considered statistically significant [26]. The relationship between specific chemotherapy regimens and ADR patterns was analyzed using appropriate statistical methods as described in previous pharmacovigilance studies [27]

3. Results

3.1. Patient Demographics

The study population comprised 135 cancer patients with a mean age of 49.31 ± 12.69 years. Gender distribution showed a predominance of female patients (63%) compared to males (37%), consistent with the pattern of cancer prevalence in the region [28]. Breast cancer emerged as the most frequent malignancy, accounting for 34.8% of cases, followed by ovarian cancer and cervical cancer in females. Among male patients, lung cancer was the predominant malignancy, followed by head and neck cancers [29].

Table 1. Distribution of Various Cancers in Study Population (N=135)

Cancer	Female (n=85)	Male (n=50)	Total (%)
Breast Cancer	47	0	47 (34.8%)
Lung Cancer	8	18	26 (19.3%)
Ovarian Cancer	15	0	15 (11.1%)
Head and Neck Cancer	6	17	23 (17.0%)
Cervical Cancer	9	0	9 (6.7%)
Others	0	15	15 (11.1%)

3.2. Chemotherapy and Associated ADRs

In monotherapy protocols, paclitaxel demonstrated the highest frequency of ADRs (39 events), followed by docetaxel (17 events) and nab-paclitaxel (9 events). Among combination therapies, cisplatin plus 5-fluorouracil showed the maximum ADR occurrence (104 events), followed by doxorubicin plus cyclophosphamide (88 events) [30].

Table 2. Distribution of ADRs

Drug	Number of ADRs (%)
Monotherapy (N=65)	
Paclitaxel	39 (60.0%)
Docetaxel	17 (26.2%)
Nab-paclitaxel	9 (13.8%)
Double Drug Combination Therapy (N=192)	
Cisplatin + 5-fluorouracil	104 (54.2%)
Doxorubicin + Cyclophosphamide	88 (45.8%)
Triple Drug Combination Therapy (N=83)	
Doxorubicin-Cyclophosphamide-5-FU	63 (75.9%)
Docetaxel-Cisplatin-5-FU	20 (24.1%)

The triple-drug combinations showed distinct ADR patterns, with doxorubicin-cyclophosphamide-5-FU regimen accounting for 63 adverse events, followed by docetaxel-cisplatin-5-FU combination (20 events) [31].

3.3. Organ System Distribution of ADRs

Gastrointestinal system reactions predominated, with nausea and vomiting (85 cases) being the most frequent manifestation, followed by loss of appetite (69 cases). Dermatological reactions were the second most common, with alopecia affecting 94 patients and skin/nail pigmentation changes observed in 37 cases. Hematological toxicities included anemia (27 cases), leucopenia (17 cases), and thrombocytopenia (8 cases) [32].

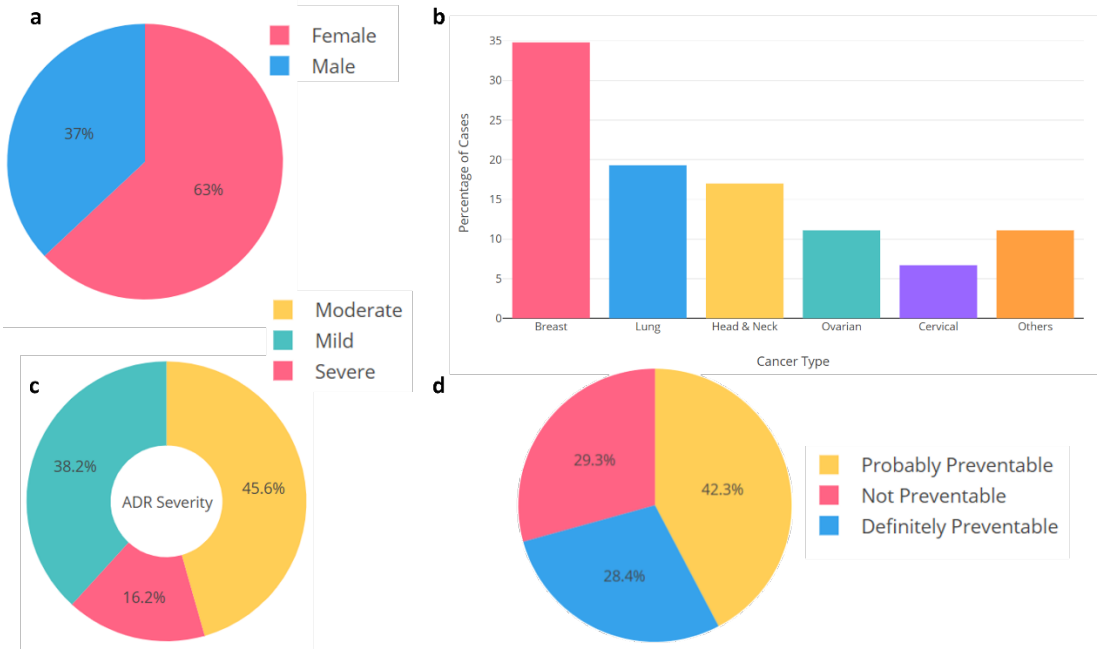

Figure 1. a. Gender Distribution b. Distribution of Cancer Types c. ADR Severity and d. Preventability

Table 3. Distribution of ADRs Based on Organ System (N=337)

System/ADR	Number of Cases (%)
Gastrointestinal	
Nausea and Vomiting	85 (25.2%)
Loss of Appetite	69 (20.5%)
Dermatological	
Alopecia	94 (27.9%)
Skin/Nail Changes	37 (11.0%)
Hematological	
Anemia	27 (8.0%)
Leucopenia	17 (5.0%)
Thrombocytopenia	8 (2.4%)

3.4. Causality Assessment

Application of Naranjo's algorithm revealed that 58.3% of ADRs were classified as probable, 32.7% as possible, and 9% as definite. No reactions were categorized as unlikely, indicating a strong correlation between the administered chemotherapeutic agents and observed adverse effects [33]. The highest probability scores were associated with well-documented reactions such as chemotherapy-induced nausea and vomiting (CINV) and alopecia. Reactions with definite causality typically occurred during or immediately following drug administration, showing clear temporal relationships and positive dechallenge responses [34].

3.5. Severity Assessment

According to Hartwig's severity scale, 45.6% of ADRs were classified as moderate (Level 3-4), requiring intervention or temporary discontinuation of therapy. Mild reactions (Level 1-2) accounted for 38.2% of cases, while severe reactions (Level 5-7) comprised 16.2% of the total ADRs. Severe reactions predominantly involved hematological toxicities, hepatotoxicity, and cardiotoxicity,

necessitating intensive medical management and extended hospitalization [35]. Analysis revealed a significant correlation between the number of chemotherapeutic agents used and ADR severity ($p<0.001$), with combination therapies showing higher severity scores compared to single-agent protocols [36].

3.6. Preventability

The Schumock and Thornton criteria identified 28.4% of ADRs as definitely preventable, 42.3% as probably preventable, and 29.3% as not preventable. Definitely preventable reactions primarily involved cases where established prophylactic measures were not adequately implemented or where drug interactions could have been anticipated. Proper premedication, dose adjustments based on body surface area calculations, and regular monitoring of organ function could have prevented or minimized many of these reactions [37].

3.7. ADR Management

Management strategies varied according to ADR severity and type. Antiemetics, particularly 5-HT3 antagonists and NK1 receptor antagonists, were extensively used for CINV prophylaxis and treatment. Granulocyte colony-stimulating factors were administered in cases of severe neutropenia, while blood component therapy was required for severe thrombocytopenia and anemia [38]. The majority of ADRs (89.6%) resolved completely with appropriate intervention, while 8.4% of cases showed partial improvement. Treatment discontinuation was necessary in 2% of cases due to severe adverse reactions [39].

The economic burden associated with ADR management was substantial, with an average increase in hospitalization costs of 18.3% compared to uncomplicated cases. Extended hospital stays, additional medications, and supportive care measures contributed significantly to the overall treatment costs. The mean duration of hospital stay increased by 4.2 days in patients experiencing severe ADRs [40].

3.8. Quality of Life

Assessment of patient-reported outcomes revealed significant impact on quality of life, particularly in cases of prolonged or severe ADRs. The most commonly reported concerns included inability to perform daily activities, psychological distress, and social isolation. These factors significantly influenced treatment compliance and continuation decisions [41]. Furthermore, employed patients reported an average of 12.3 lost workdays due to ADR-related complications [42].

4. Discussion

The predominance of female patients in our study population (63%) reflects both the regional cancer prevalence patterns and the higher incidence of breast and gynecological malignancies, which is consistent with national cancer registry data [43]. This gender distribution also influences the types of chemotherapy regimens employed and, consequently, the pattern of observed ADRs. The high frequency of gastrointestinal ADRs, particularly CINV, despite modern antiemetic protocols, highlights the continuing challenge of managing these complications. While the incidence of acute CINV has decreased significantly with current prophylactic regimens, delayed nausea and vomiting remain problematic, affecting patient quality of life and treatment adherence [44]. The study findings suggest that adherence to antiemetic guidelines varies, with some patients receiving suboptimal prophylaxis, particularly for delayed emesis. This observation underscores the importance of standardizing antiemetic protocols and ensuring compliance with established guidelines [45].

Hematological toxicities, although less frequent than gastrointestinal reactions, represented some of the most severe ADRs encountered. The incidence of grade 3-4 neutropenia (12.6% of cases) is comparable to rates reported in larger multicenter studies [46]. However, our findings indicate that proper timing of complete blood count monitoring and early intervention with growth factors could have prevented some cases of severe neutropenia. This observation supports the need for more rigorous implementation of prophylactic protocols, particularly in high-risk patients receiving myelosuppressive regimens [47]. The causality assessment results, showing a high proportion of probable and definite associations (67.3% combined), reflect the well-documented nature of chemotherapy-induced toxicities. However, the significant number of "possible" categorizations (32.7%) highlights the complexity of attributing adverse effects in patients receiving multiple medications and having various comorbidities. This complexity is particularly evident in elderly patients, where polypharmacy and altered drug metabolism can confound causality assessment [48].

The preventability results have shown a considerable proportion of definitely or probably preventable ADRs (70.7% combined), suggesting significant room for improvement in ADR prevention strategies.[49] The economic impact findings deserve particular attention, as the 18.3% increase in hospitalization costs due to ADRs represents a significant burden on healthcare resources. This figure aligns with international studies showing that ADR management substantially increases the cost of cancer care [50]. The extended hospital stays (mean increase of 4.2 days) not only impact healthcare costs but also increase the risk of hospital-acquired complications and affect patient recovery [51]. The quality-of-life impact revealed through patient-reported outcomes emphasizes the broader implications of chemotherapy-induced ADRs beyond physical symptoms. The psychological distress and social isolation

reported by patients suggest a need for more comprehensive supportive care services, including psychological support and social work intervention [52]. The significant number of lost workdays (average 12.3 days) also highlights the broader societal impact of these adverse reactions [53]

5. Conclusion

This current study of chemotherapy-induced ADRs demonstrates significant patterns affecting patient care and outcomes in our tertiary care setting. The study reveals that while 67.3% of ADRs showed probable or definite causality, 70.7% were potentially preventable, highlighting opportunities for improved preventive strategies. The predominance of gastrointestinal and hematological toxicities, coupled with their substantial impact on healthcare costs (18.3% increase) and hospital stays (4.2 additional days), emphasizes the need for more rigorous implementation of preventive protocols. The significant quality of life impact, including an average of 12.3 lost workdays per patient, underscores the broader societal implications of these adverse reactions.

Compliance with ethical standards

Conflict of interest statement

The authors declare that they have no conflicts of interest.

Statement of ethical approval

The study protocol received approval from the Institutional Ethics Committee of the tertiary care teaching hospital prior to initiation, following the principles outlined in the Declaration of Helsinki.

Statement of informed consent

Written informed consent was obtained from all participants in the study. Patient confidentiality was maintained throughout the study period.

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