Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

# Pattern, Severity and Preventability of Chemotherapy-induced Adverse Drug Reactions in Head and Neck Cancer Patients: A Prospective Observational Study from a tertiary care hospital in Gujarat

**Kruti Sharma**[1]
Ganpat University
**Nilesh Patel**[1]
nilesh.patel@ganpatuniversity.ac.in

Ganpat University
**Nirav Asarawala**[2]
M.S Patel Cancer Centre, Shree Krishna Hospital and Medical Research Centre

**Research Article**

**Keywords:** Adverse drug reactions, Chemotherapy toxicity, Head and neck cancer, Pharmacovigilance, Preventability

**Posted Date:** November 20th, 2026

**DOI:** https://doi.org/10.21203/rs.3.rs-11244487/v1

**License:** This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

**Additional Declarations:** No competing interests reported.

**Pattern, Severity and Preventability of Chemotherapy-induced Adverse Drug Reactions in Head and Neck Cancer Patients: A Prospective Observational Study from a tertiary care hospital in Gujarat**

[1] Research Scholar, Department of Pharmacology, Shree S. K. Patel College of Pharmaceutical Education and Research, Ganpat University, Mehsana, Gujarat – 384012.

[1] Professor, Department of Pharmacology, Shree S. K. Patel College of Pharmaceutical Education and Research, Ganpat University, Mehsana, Gujarat – 384012.

[2] Medical Oncologist, Department of Oncology, M.S. Patel Cancer Centre, Shree Krishna Hospital, Karamsad, Anand, Gujarat-388325.

**Corresponding Author:**

**Dr. Nilesh Patel**

Professor,

Department of Pharmacology,

Shree S. K. Patel College of Pharmaceutical Education and Research,

Ganpat University, Mehsana, Gujarat – 384012.

E-mail ID: nilesh.patel@ganpatuniversity.ac.in

Contact: +91 94276 84312

| Name of Authors | ORCID ID |
|---|---|
| Kruti B. Sharma | 0000-0002-1461-2978 |
| Nilesh Patel | 0000-0001-5142-8128 |
| Nirav Asarawala | 0009-0003-3755-0225 |

**ABSTRACT**

**Background:** Chemotherapy plays an important role in management of head and neck cancer; however, its use is frequently associated with adverse drug reactions (ADRs) that may negatively affect. Therefore, monitoring of chemotherapy-related ADRs is essential to improve patient safety and to optimize therapeutic outcomes.

**Methods:** A prospective observational study was conducted among head and neck cancer patients receiving chemotherapy at a tertiary care hospital in Central Gujarat. A total of 386 patients were included in study. ADRs were documented through active surveillance and evaluated for causality, severity, and preventability using the WHO–UMC causality assessment scale, Naranjo's algorithm, Modified Hartwig and Siegel severity scale, and Modified Schumock and Thornton preventability scale. Descriptive analysis was performed using Microsoft Excel.

**Results:** Among the 386 patients receiving chemotherapy, 355 patients (91.97%) experienced at least one ADR, resulting in a total of 1508 ADR events. Musculo-skeletal pain-related reactions and gastrointestinal disturbances were most frequently reported ADR categories. The most common individual ADRs included constipation, change in body weight, alopecia, dizziness/fatigue and body pain. Cisplatin-based chemotherapy showed highest proportion of ADR events, followed by paclitaxel with carboplatin. Most ADRs were categorized as probable in causality assessment and were moderate in severity, while a considerable proportion were found to be preventable.

**Conclusion:** Chemotherapy-induced ADRs are common among head and neck cancer patients. Continuous monitoring through pharmacovigilance programs is essential to identify ADRs early, improve patient safety, and optimize chemotherapy management.

**Keywords:** Adverse drug reactions, Chemotherapy toxicity, Head and neck cancer, Pharmacovigilance, Preventability

**INTRODUCTION:**

Head and neck cancer (HNC) is a heterogeneous group of malignancies involving oral cavity, pharynx, larynx, nasal cavity and salivary glands.[1] Head and neck cancer remains a major public health burden in developing regions. In India, prevalence of HNC is high largely due to widespread exposure to risk factors such as tobacco use and alcohol consumption as well as human papillomavirus (HPV) infection.[1,2]

Chemotherapy is an essential component in management of HNC as it is used either alone or in combination with surgery and/or radiotherapy.[3] Despite its therapeutic benefits, chemotherapy is commonly associated with adverse drug reactions (ADRs). Furthermore, cancer patients frequently have reduced physiological reserves and poor nutritional status. These factors, along with comorbid conditions increases risk of drug-related toxicities.[4]

World Health Organization defined adverse drug reaction (ADR) as unintended, noxious response to a drug occurring at doses normally used for prevention, diagnosis or treatment of disease. [5] Chemotherapy related adverse drug reactions can adversely affect on treatment adherence and resulting in prolong hospital stay, increase healthcare costs as well as reduced patients' quality of life. However, severe ADRs may also contribute to increased morbidity and mortality.[3,6]

Pharmacovigilance is a core public health activity focused on detection and prevention of adverse drug reactions. Although Pharmacovigilance Programme of India (PvPI) supports national ADR reporting, region-specific evidence on chemotherapy-related adverse drug reactions in head and neck cancer patients from tertiary care hospitals remains limited.[6]

Several studies have evaluated chemotherapy-related adverse drug reactions in Oral and HNC patients, as well as in mixed oncology populations.[3,7-11] However, data describing the pattern, severity, and preventability of chemotherapy-induced ADRs specifically among head and neck cancer patients in Central Gujarat are still limited. Therefore, present study was undertaken with the aim to comprehensively assess and analyze adverse drug reactions associated with chemotherapy used in patients with head and neck cancer treated at a tertiary care hospital in Anand region of Central Gujarat.

## METHODOLOGY:

**Ethical approval:** The study protocol (IEC/BU/148/Faculty/31/342/2023) was reviewed and approved by Institutional Ethics Committee-2 (IEC-2) of Bhaikaka University, Karamsad. Written informed consent was obtained from all participants. Patient confidentiality and anonymity were strictly maintained throughout the study in accordance with institutional ethical guidelines and the principles of the Declaration of Helsinki.

**Study design and site:** This hospital-based, prospective observational study was conducted at Oncology department, Shree Krishna Hospital, Karamsad, a tertiary care hospital in Anand region of Central Gujarat, India.

**Study population:** Based on Cochran's formula with an assumed prevalence of 50%, a 95% confidence level, and a 5% margin of error, the minimum required sample size was 384 patients. Accordingly, a total of 386 newly diagnosed patients with head and neck cancer, who fulfilled the eligibility criteria were included in the study. The study was conducted over a period from November 2023 to September 2025.

**Study inclusion and exclusion criteria:** Newly diagnosed head and neck cancer patients of either gender, aged ≥18 years, receiving chemotherapy, completed their treatment and who provided informed consent for participation in study are included. However, patients receiving only surgical or radiotherapy treatment without chemotherapy, who have not completed their treatment and those who unwilling to participate in study were excluded.

**Data collection:** Data were collected using predesigned structured case record form. Patient information including socio-demographic details, cancer characteristics, prescribed treatment regimen including chemotherapy agents was recorded. All suspected adverse drug reactions (ADRs) occurring during chemotherapy were documented through patient interview, active surveillance as well as through review of patient case files, laboratory reports and treatment charts.

**Assessment of adverse drug reactions**:

Patients were monitored for adverse drug reactions (ADRs) through questioning for symptoms as well as laboratory investigations performed during their hospital admission period. All suspected ADRs were documented using Central Drugs Standard Control Organization (CDSCO) adverse drug reaction reporting forms.[12] Any invasive investigations were not undertaken or recommended to treating physician as part of study. Adverse drug reactions reported by patients as well as those diagnosed and documented by treating physicians were included in analysis.

The incidence of adverse drug reactions (ADRs) according to chemotherapy regimen was calculated using the number of patients experiencing at least one ADR as the numerator and the total number of patients receiving that specific regimen as the denominator. ADR incidence was expressed as a percentage using the following formul[13]:

$$\%\ \text{ADR incidence} = \frac{\text{Number of patients experiencing} \geq 1\ \text{ADR}}{\text{Total number of patients receiving the regimen}} \times 100$$

This analysis was performed on a patient basis rather than ADR events, where each patient was counted once if at least one ADR occurred during the treatment period.

For the system-wise analysis, each patient was counted once in a particular organ system if at least one adverse drug reaction related to that system was observed. Since patients could experience multiple ADRs, the organ system categories were not mutually exclusive. In addition, ADRs were classified based on affected organ system and type of reactions. In addition, reported adverse drug reaction(s) evaluated for causality assessment, drug-reaction assessment, severity level and its preventability.

**Causality assessment** of reported ADRs was performed using ***WHO-UMC causality assessment scale*** [World Health Organization - Uppsala Monitoring Centre], which is WHO Collaborating Centre for International Drug Monitoring to evaluate causal relationship between suspected drug and reported adverse event(s), which categorized ADRs as certain, probable, possible or unlikely.[14]

**Drug-reaction assessment** of ADRs was performed using ***Naranjo's algorithm***, a structured questionnaire consists of objective questions with responses categorized as yes, no or do not know. Based on cumulative score, ADRs were classified as definite, probable, or possible.[15]

**Preventability** of ADRs was assessed using ***Modified Schumock and Thornton preventability scale***, which categorizes reactions as definitely preventable, probably preventable or not preventable based on predefined criteria.[16]

**Severity** of ADRs was evaluated using ***Modified Hartwig and Siegel severity scale***, which classifies ADRs as mild, moderate or severe, by taking consideration of factors such as need for treatment modification, prolongation of hospital stay and extent of disability caused by reaction(s).[17]

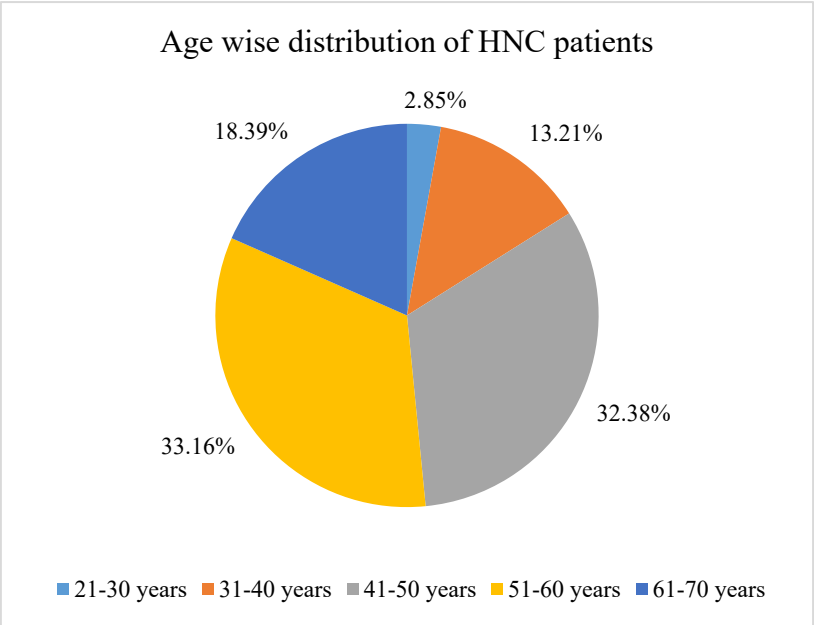
**Statistical analysis:** All collected data were entered into Microsoft Excel and analyzed using STATA (USA). Descriptive statistics were used to summarize demographic characteristics, clinical variables, chemotherapy

regimens and adverse drug reaction (ADR) profiles. Continuous variables were expressed as mean ± standard deviation (SD) where applicable, while categorical variables were presented as frequencies and percentages. System-wise distribution of ADRs and regimen-wise ADR patterns were analyzed using frequency distributions and proportions. Causality, severity, and preventability of ADRs were assessed using standardized scales including the WHO–UMC causality assessment scale, Naranjo's algorithm, Modified Hartwig and Siegel severity scale and Modified Schumock and Thornton preventability scale and results were summarized using frequencies and percentages. Associations between selected patient characteristics (such as age group, gender, and chemotherapy regimen) and occurrence of ADRs were evaluated using Chi-square test, $p<0.05$ was considered statistically significant in all analyses.

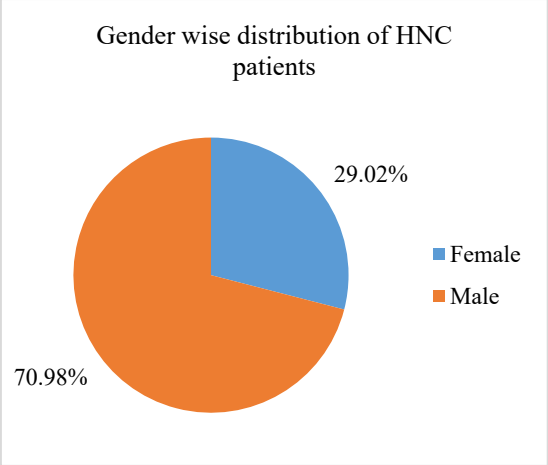
**RESULTS:**

A total of 454 patients with head and neck cancer were initially screened during study period from November 2023 to September 2025. Based on predefined inclusion and exclusion criteria, 386 patients were included in final analysis. Out of 386 patients receiving chemotherapy, 91.97% patients (n=355) experienced at least one adverse drug reaction, while 8.03% patients (n=31) did not report any ADRs. A total of 1,508 ADR events were documented among the study population. These reactions were categorized into approximately 54 distinct ADR types, corresponding to an average of 4.25 ADRs per patient.

**Demographic characteristics:** The majority of HNC patients belonged to age group of 51-60 years (33.16%, n=128) followed by 41-50 years (32.38%, n=125) and 61-70 years (18.39%, n=71). [Figure 1] About 70.98% were male patients (n=274), while 29.02% were female (n=112) patients. [Figure 2]




[Figure 1. Age wise distribution of HNC patients]

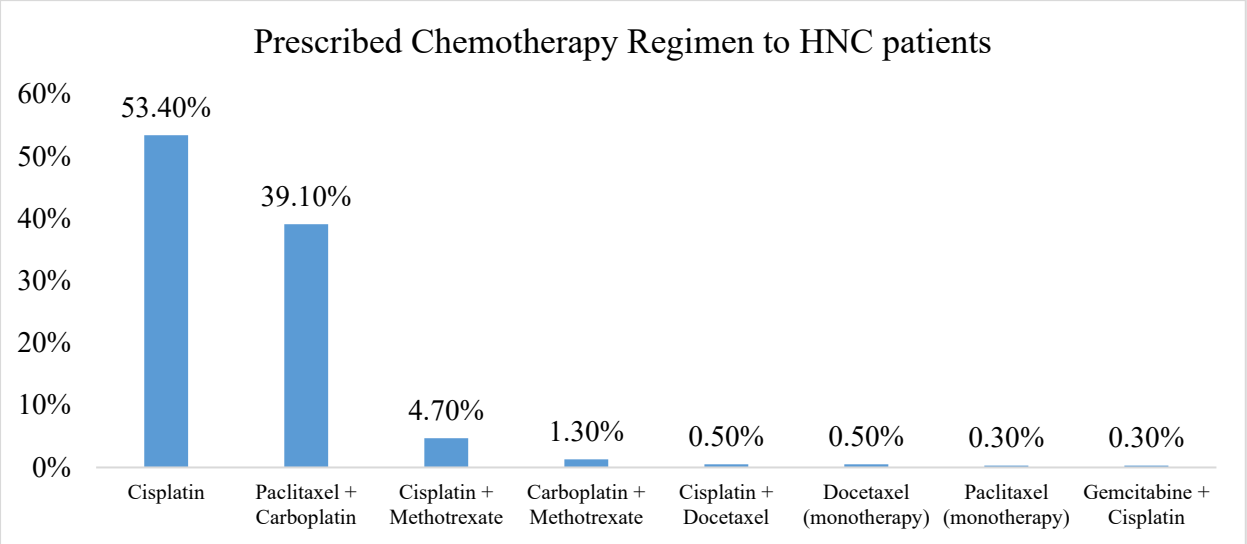



[Figure 2. Gender wise distribution of HNC patients]

**Anatomical distribution of head and neck cancer:** The most commonly affected anatomical site among HNC patient was oral cavity (76.17%, n=294) followed by oropharynx (13.99%, n=54), hypopharynx (6.22%, n=24) and laryngeal cancer (1.30%, n=5), while combined site involvement and other sites such as maxilla and nasopharynx were less frequent.

**Chemotherapy regimens:** Platinum-based chemotherapy found as most prescribed regimen. Majority of patients were prescribed with Cisplatin monotherapy **(**53.37%, n=206) followed by paclitaxel with carboplatin (39.12%, n=151), cisplatin with methotrexate (4.7%, n=18), carboplatin with methotrexate (1.30%, n=5, cisplatin with

docetaxel (0.5%, n=2), docetaxel monotherapy (0.52%, n=2), paclitaxel monotherapy (0.3%, n=1) and gemcitabine with cisplatin (0.3%, n=1). [Figure 3]




[Figure 3. Prescribed Chemotherapy Regimen to HNC patients]

**Adverse Drug Reactions:**

Among the 386 patients receiving chemotherapy, 355 patients (91.97%) experienced at least one adverse drug reaction, while 31 patients (8.03%) did not report any ADR. The reported adverse drug reactions were categorized according to the affected organ system and type of reaction.

**Incidence of ADRs by chemotherapy regimen**

In Cisplatin monotherapy 196 patients out of 206 experienced ADR (95.14%) followed by Paclitaxel with Carboplatin (140 out of 151, 92.71%), Cisplatin with Methotrexate (15 out of 18, 83.33%). However, only 20% patients received Carboplatin with Methotrexate (1 out of 5), and 50% patients received Docetaxel (monotherapy) and Cisplatin + Docetaxel (1 out of 2) experienced ADR. Paclitaxel monotherapy was received by only patient, who had ADR. However, no such ADR reported in Gemcitabine with Cisplatin regimen.

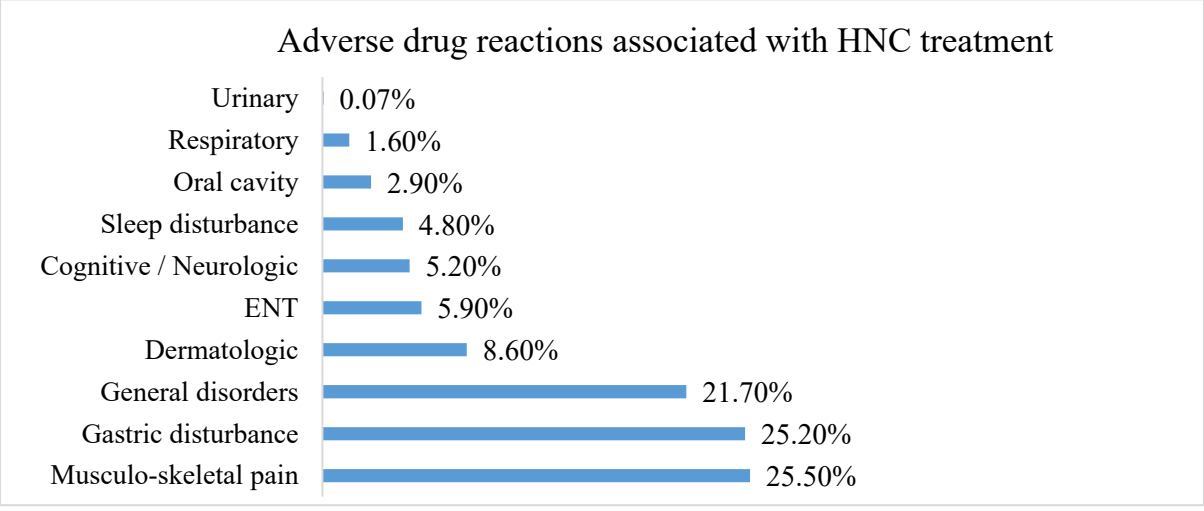
[Table 1. Incidence of ADRs by chemotherapy regimen]

| Chemotherapy regimen | Patients receiving regimen (n) | Patients experiencing ADR (n) | ADR incidence (%) |
|---|---|---|---|
| Cisplatin | 206 | 196 | 95.14% |
| Paclitaxel + Carboplatin | 151 | 140 | 92.71% |
| Cisplatin + Methotrexate | 18 | 15 | 83.33% |

| | | | |
|---|---|---|---|
| Carboplatin + Methotrexate | 5 | 1 | 20% |
| Docetaxel (monotherapy) | 2 | 1 | 50% |
| Cisplatin + Docetaxel | 2 | 1 | 50% |
| Paclitaxel (monotherapy) | 1 | 1 | 100% |
| Gemcitabine + Cisplatin | 1 | 0 | 0% |

The distribution of ADRs across different organ systems is presented below:

***System-wise distribution of ADRs:*** System-wise percentages represent the proportion of patients who experienced at least one ADR within the respective organ system, and individual patients could contribute to more than one category. System-wise analysis illustrated in Figure 4, which showed that musculo-skeletal pain–related ADRs were the most frequently reported (385 events, 25.5%), followed closely by gastrointestinal disturbances (380 events, 25.2%). General disorders accounted for 327 events (21.7%), while dermatological reactions constituted 129 events (8.6%). ADRs related to ENT (89 events, 5.9%) and cognitive/neurological system (79 events, 5.2%) were observed less frequently. Sleep disturbances (72 events, 4.8%) and oral cavity–related reactions (44 events, 2.9%) were also reported. Respiratory ADRs were relatively uncommon (24 events, 1.6%), while urinary ADR was rare (1 event, 0.07%).




[Figure 4. System wise adverse drug reactions associated with HNC treatment; N=355]

***System-wise individual ADRs:*** The specific adverse drug reactions observed within each organ system were further analyzed and depicted in Table 2. Percentages were calculated with reference to the total number of patients who experienced at least one adverse drug reaction as the denominator (n=355). Among gastric

disturbances, constipation (46.2%, n=164) was the most frequently reported ADR, followed by nausea (19.7%, n=70), vomiting (15.2%, n=54) and stomach pain (13.0%, n=46). Among general disorders, change in body weight (44.2%, n=157) was the most common ADR, followed by dizziness and fatigue (33.5%, n=119) and fever (13.5%, n=48). Alopecia was the predominant dermatological ADR, reported in 36.1% of patients (n = 128). Musculo-skeletal and pain-related ADRs included body pain (29.6%, n=105), headache (25.4%, n=90), pain at the site of administration (22.3%, n=79), and joint pain (18.3%, n=65). Sleep disturbance in the form of insomnia was reported in 20.3% of patients (n=72). Oral cavity–related ADRs mainly included mouth ulcers (12.4%, n=44) and difficulty in eating (5.6%, n=20). Neurological ADRs included tremor (17.7%, n=63) and lack of concentration (4.2%, n=15). Respiratory ADRs included shortness of breath (3.9%, n=14) and cough (2.8%, n=10).

[Table 2. System-wise distribution of commonly reported ADRs among patients experiencing ADRs (n = 355)]

| **Type** | **Adverse Events** | **n** | **%** |
|---|---|---|---|
| Gastric Disturbance | Constipation | 164 | 46.2 |
| | Nausea | 70 | 19.7 |
| | Vomiting | 54 | 15.2 |
| | Stomach Pain | 46 | 13.0 |
| Musculo-skeletal / Pain | Body Pain | 105 | 29.6 |
| | Headache | 90 | 25.4 |
| | Pain at Site of Administration | 79 | 22.3 |
| | Joint Pain | 65 | 18.3 |
| General Disorders | Change in Body Weight | 157 | 44.2 |
| | Dizziness and Fatigue | 119 | 33.5 |
| | Fever | 48 | 13.5 |
| Dermatologic | Alopecia (Hair Loss) | 128 | 36.1 |
| Cognitive / Neurologic | Tremor | 63 | 17.7 |
| | Lack of Concentration | 15 | 4.2 |
| Sleep Disturbance | Insomnia | 72 | 20.3 |
| Oral Cavity | Mouth Ulcer | 44 | 12.4 |
| | Difficulty in Eating | 20 | 5.6 |

| | | | |
|---|---|---|---|
| Respiratory | Shortness of Breath | 14 | 3.9 |
| | Cough | 10 | 2.8 |

**Chemotherapy regimen wise ADR Assessment:**

Adverse drug reactions were further analyzed based on chemotherapy regimen administered. Across all chemotherapy regimens, the majority of ADRs were classified as probable by both WHO–UMC causality assessment and Naranjo's algorithm. Most ADRs were of moderate severity according to the Modified Hartwig and Siegel scale, with no severe reactions reported. Preventability assessment revealed that a substantial proportion of ADRs were either definitely or probably preventable, although a considerable number remained not preventable across regimens. Regimen-wise analysis showed that, out of total 1508 ADR, majority of ADR events were associated with cisplatin-monotherapy (812 events, 53.8%), followed by paclitaxel plus carboplatin (601 events, 39.8%). Other regimens contributed comparatively fewer ADR events, including cisplatin plus methotrexate (65 events, 4.3%), carboplatin plus methotrexate (17 events, 1.1%), docetaxel monotherapy (8 events, 0.5%), cisplatin plus docetaxel (4 events, 0.3%), and paclitaxel monotherapy (1 event, 0.07%). No ADR events were observed in the single patient who received gemcitabine plus cisplatin during the study period. [Table 3]

[Table 3. Chemotherapy regimen-wise ADR assessment]

| **Chemotherapy regimen** | **Total ADR events (n)** | **WHO–UMC Causality Scale** | | **Naranjo's Algorithm** | **Modified Hartwig and Siegel Severity Scale** | | **Modified Schumock and Thornton Preventability Scale** | | |
|---|---|---|---|---|---|---|---|---|---|
| | | **Probable** | **Possible** | **Probable** | **Mild** | **Moderate** | **Definitely preventable** | **Probably preventable** | **Not preventable** |
| **Cisplatin** | 812 | 555 (68.3%) | 257 (31.7%) | 519 (63.9%) | 320 (39.4%) | 492 (60.6%) | 274 (33.7%) | 198 (24.4%) | 340 (41.9%) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | (53.84%) | | | | | | | | |
| **Paclitaxel + Carboplatin** | 601 (39.85%) | 416 (69.2%) | 185 (30.8%) | 406 (67.6%) | 253 (42.1%) | 348 (57.9%) | 205 (34.1%) | 167 (27.8%) | 229 (38.1%) |
| **Cisplatin + Methotrexate** | 65 (4.31%) | 46 (70.8%) | 19 (29.2%) | 44 (67.7%) | 27 (41.5%) | 38 (58.5%) | 34 (52.3%) | 25 (38.5%) | 6 (9.2%) |
| **Carboplatin + Methotrexate** | 17 (1.13%) | 11 (64.7%) | 6 (35.3%) | 10 (58.8%) | 7 (41.2%) | 10 (58.8%) | 5 (29.4%) | 7 (41.2%) | 5 (29.4%) |
| **Docetaxel** | 8 (0.53%) | 5 (62.5%) | 3 (37.5%) | 4 (50.0%) | 3 (37.5%) | 5 (62.5%) | 3 (37.5%) | 3 (37.5%) | 2 (25.0%) |
| **Cisplatin + Docetaxel** | 4 (0.27%) | 3 (75.0%) | 1 (25.0%) | 3 (75.0%) | 2 (50.0%) | 2 (50.0%) | 1 (25.0%) | 2 (50.0%) | 1 (25.0%) |
| **Paclitaxel** | 1 (0.07%) | 1 (100%) | 0 | 1 (100%) | 0 | 1 (100%) | 0 | 1 (100%) | 0 |
| **Gemcitabine + Cisplatin** | 0 (0%) | — | — | — | — | — | — | — | — |

**Drug specific ADR Assessment:**

***Cisplatin:*** Cisplatin monotherapy accounted for a total of 812 ADR events. According to the WHO–UMC causality assessment scale, the majority of ADRs were classified as probable/likely, followed by possible reactions. Similar findings were observed with Naranjo's algorithm, where most ADRs were categorized as probable. Based on the Modified Hartwig and Siegel severity scale, most ADRs were of moderate severity, followed by mild reactions, with no severe ADRs reported. Preventability assessment showed that a proportion of ADRs were definitely preventable, some were probably preventable, while the remaining were not preventable.

***Paclitaxel + Carboplatin:*** The paclitaxel plus carboplatin regimen accounted for 601 ADR events. Causality assessment using the WHO–UMC scale showed that the majority of ADRs were probable, with the remaining classified as possible. Similar results were observed using Naranjo's algorithm. Severity evaluation demonstrated

that most ADRs were moderate, followed by mild reactions. Preventability assessment indicated that ADRs were distributed across definitely preventable, probably preventable, and not preventable categories.

***Cisplatin + Methotrexate:*** The cisplatin plus methotrexate regimen was associated with 65 ADR events. Most ADRs were categorized as probable according to both WHO–UMC and Naranjo causality assessments. Severity analysis indicated that moderate ADRs predominated, followed by mild reactions. Preventability evaluation revealed that several ADRs were definitely or probably preventable, while a smaller proportion were not preventable.

***Carboplatin + Methotrexate:*** A total of 17 ADR events were recorded with the carboplatin plus methotrexate regimen. Most ADRs were classified as probable in causality assessment, while severity evaluation showed that ADRs were mainly moderate, followed by mild reactions. Preventability analysis indicated that ADRs were distributed among definitely preventable, probably preventable, and not preventable categories.

***Docetaxel (Monotherapy):*** The docetaxel monotherapy regimen accounted for 8 ADR events. Causality assessment primarily categorized ADRs as probable, while severity evaluation showed that most reactions were moderate, followed by mild ADRs. Preventability assessment indicated that ADRs were distributed across definitely preventable, probably preventable, and not preventable categories.

***Cisplatin + Docetaxel:*** The cisplatin plus docetaxel regimen produced 4 ADR events. The majority of these ADRs were categorized as probable based on causality assessment. Severity evaluation indicated that ADRs were mild to moderate, and preventability analysis showed a distribution across preventable and non-preventable categories.

***Paclitaxel (Monotherapy):*** Only one ADR event was reported with paclitaxel monotherapy, which was classified as probable according to causality assessment and moderate in severity, and was considered probably preventable.

**DISCUSSION:**

Chemotherapy remains an integral component in management of head and neck cancer; however, its therapeutic benefits are often accompanied by a wide spectrum of adverse drug reactions due to the non-selective action of cytotoxic agents on rapidly dividing cells. Monitoring these adverse reactions is therefore essential to ensure treatment safety, improve patient adherence and optimize therapeutic outcomes.[3-6] The present prospective observational study provides insight into the pattern, severity and preventability of chemotherapy-induced adverse drug reactions among head and neck cancer patients treated at a tertiary care hospital in Central Gujarat. The

findings highlight a substantial burden of treatment-related toxicities, with a high proportion of patients experiencing ADRs during chemotherapy. These observations highlights importance of systematic pharmacovigilance and continuous monitoring of chemotherapy-related adverse effects in routine oncology practice.

The present study provides a comprehensive evaluation of adverse drug reactions (ADRs) associated with chemotherapy in head and neck cancer (HNC) patients treated at a tertiary care hospital in the Anand region of Central Gujarat. A high proportion of patients (92.23%) experienced at least one ADR, highlighting the substantial burden of chemotherapy-related toxicities in this population. This finding is consistent with previous pharmacovigilance studies conducted in oncology settings, which have reported a high incidence of ADRs due to narrow therapeutic index and cytotoxic nature of anticancer drugs.

In present study, majority of patients belonged to middle-aged and elderly groups, with a clear male predominance. This demographic pattern aligns with known epidemiology of head and neck cancer in India, where higher exposure to risk factors such as, tobacco and alcohol use among males contributes to increased disease prevalence. The oral cavity was most commonly affected anatomical site, which is in consistent with Indian studies reporting oral cancer as predominant subtype of HNC.

The high burden of ADRs observed in present study can be attributed to several interrelated factors. Age plays an important role, as a large proportion of patients were above 50 years. Advancing age is associated with reduced physiological reserves, altered drug metabolism, decreased renal and hepatic function as well as increased vulnerability to drug-induced toxicities. These factors may contribute to the higher incidence of ADRs in older patients.

Gender differences may also influence ADR occurrence. Although, male patients predominated in study population, female patients are often reported to be more susceptible to certain ADRs due to differences in body composition, hormonal status and drug pharmacokinetics. The demographic distribution of patients in the present study showed that the majority of head and neck cancer patients belonged to the 51–60 years age group, with a clear predominance of male patients. This observation is consistent with the epidemiological pattern of head and neck cancers reported in India and other developing countries, where the disease is more common among middle-aged and older adults.[18,19] The higher incidence among males may be attributed to greater exposure to established risk factors such as tobacco consumption, alcohol use, and betel nut chewing, which are widely prevalent among men in many parts of India.[20] Several epidemiological studies have also reported a similar

male predominance and age distribution among head and neck cancer patients, emphasizing the strong association between lifestyle-related risk factors and the development of these malignancies.[18–20]

In present study, oral cavity was found as most commonly affected anatomical site among head and neck cancer patients. This finding is consistent with several epidemiological study conducted in India, where oral cavity cancers constitute the largest proportion of head and neck malignancies.[21] The high prevalence of oral cavity cancers in the Indian population has been strongly associated with widespread use of tobacco in various forms, including smoking, chewing tobacco, and betel nut consumption. These habits are well-established risk factors for the development of oral squamous cell carcinoma and contribute significantly to the overall burden of head and neck cancers in the region.

Previous hospital-based and population-based studies conducted in India have similarly reported oral cavity as predominant site of head and neck malignancies, followed by cancers of the oropharynx and hypopharynx.[22–24] The predominance of oral cavity cancers in present study may therefore reflect regional lifestyle patterns, particularly high prevalence of tobacco chewing, betel nut consumption and other smokeless tobacco products in Indian population.[20,24]

Additionally, musculo-skeletal pain-related reactions and gastrointestinal disturbances were most frequently reported categories of adverse drug reactions among patients receiving chemotherapy. Chemotherapy-induced toxicities commonly affect rapidly proliferating tissues such as the gastrointestinal epithelium and may also produce systemic symptoms including fatigue, musculo-skeletal discomfort, and generalized weakness. Gastrointestinal toxicities such as nausea, vomiting, and constipation are among the most frequently reported adverse effects associated with platinum-based chemotherapy regimens, particularly cisplatin, due to their effects on the gastrointestinal mucosa and stimulation of the central emetic pathways.[25]

Similar patterns of chemotherapy-related adverse reactions have been reported in previous pharmacovigilance and oncology studies, where gastrointestinal symptoms and generalized systemic reactions constituted a substantial proportion of ADRs among cancer patients receiving cytotoxic therapy.[26,27] These findings support observation that, chemotherapy-related toxicities are largely predictable based on the pharmacological properties of anticancer drugs and their effects on normal tissues with high cellular turnover. In addition to gastrointestinal reactions, general disorders such as fatigue, body pain, and changes in body weight were also frequently observed in the present study. Such symptoms are commonly reported among cancer patients undergoing chemotherapy

and may arise from multiple factors including treatment-related metabolic changes, inflammatory responses, and the underlying disease burden.[27,28]

In present study, constipation, change in body weight, alopecia, dizziness/fatigue, and body pain were among the most frequently reported individual adverse drug reactions in patients receiving chemotherapy. Gastrointestinal reactions such as constipation, nausea, and vomiting are well-recognized complications of cytotoxic chemotherapy and are frequently associated with platinum-based regimens used in the treatment of head and neck cancers.[29] Cisplatin, one of most commonly prescribed agents in present study, is known to cause significant gastrointestinal toxicity due to its stimulatory effects on the chemoreceptor trigger zone and its direct irritant action on gastrointestinal mucosa.[25,29]

Alopecia, also observed as dermatological adverse effect in present study. It is a common toxicity associated with several anticancer drugs, including taxanes and platinum-based compounds. This occurs due to effect of cytotoxic agents on rapidly dividing hair follicle cells leading to temporary hair loss during treatment.[30] Although alopecia is generally reversible after completion of chemotherapy, still it can significantly affect the psychological well-being and quality of life of patients undergoing cancer treatment.[30,31]

In addition, fatigue, body pain and other generalized symptoms were frequently reported in present study. Cancer-related fatigue is one of the most common and distressing symptoms experienced by patients undergoing chemotherapy and may result from treatment-related metabolic changes, inflammatory processes, and overall burden of malignancy.[31,32] Similar findings have been reported in previous studies evaluating chemotherapy-related adverse drug reactions, where systemic symptoms such as, fatigue and musculo-skeletal discomfort were frequently observed among oncology patients receiving cytotoxic therapy.[27,32]

In present study, cisplatin-based chemotherapy accounted for highest proportion of adverse drug reaction events, followed by paclitaxel with carboplatin regimen. This observation is consistent with well-established toxicity profile of platinum-based chemotherapy agents commonly used in treatment of head and neck cancers. Cisplatin is widely recognized for its broad spectrum of adverse effects, including gastrointestinal disturbances, nephrotoxicity, neurotoxicity and generalized systemic symptoms. These toxicities arise primarily from the drug's mechanism of action, which involves DNA cross-linking and disruption of rapidly dividing cells, thereby affecting both malignant and normal tissues.[33]

Several studies evaluating chemotherapy-related toxicities in oncology patients have similarly reported a high frequency of ADRs associated with cisplatin-based regimens. Clinical investigations have demonstrated that,

while cisplatin remains one of the most effective agents for treatment of head and neck malignancies, its use is frequently accompanied by treatment-related adverse effects that require careful monitoring and supportive management.[34] In addition, combination chemotherapy regimens involving paclitaxel and carboplatin are also associated with significant toxicities such as fatigue, peripheral neuropathy, gastrointestinal disturbances, and hematological abnormalities due to the additive pharmacological effects of the two agents.[35] Despite the occurrence of multiple ADRs, platinum-based chemotherapy continues to play a crucial role in the management of head and neck cancers because of its proven therapeutic efficacy. Therefore, close monitoring of patients receiving these regimens through active pharmacovigilance is essential to identify adverse reactions early and minimize treatment-related complications.[33–35]

Causality assessment of adverse drug reactions using the WHO–UMC causality assessment scale and Naranjo's algorithm revealed that the majority of ADRs were categorized as probable, followed by possible reactions. This finding indicates a strong temporal relationship between the administration of chemotherapy agents and the occurrence of adverse reactions, which is consistent with the predictable toxicity profiles of cytotoxic drugs used in cancer treatment. Similar observations have been reported in pharmacovigilance studies involving oncology patients, where most chemotherapy-related ADRs were classified as probable due to the well-documented adverse effect profiles of anticancer drugs.[14,15]

Severity assessment using Modified Hartwig and Siegel severity scale demonstrated that, most ADRs in present study were moderate in severity, followed by mild reactions, while no severe ADRs were reported. Moderate ADRs typically require symptomatic treatment, dose modification, or temporary interruption of therapy but are generally manageable with appropriate supportive care. Comparable findings have been reported in several oncology pharmacovigilance studies where majority of chemotherapy-induced ADRs were categorized as moderate in severity, reflects need for clinical intervention to improve patient safety.[17]

The evaluation of ADR preventability using the Modified Schumock and Thornton preventability scale revealed that a considerable proportion of ADRs were either definitely or probably preventable. This highlights importance of proactive monitoring, timely identification of early symptoms and appropriate supportive interventions in minimizing treatment-related toxicities. Implementation of structured pharmacovigilance programs and regular ADR monitoring in oncology practice can therefore, play a crucial role in improving patient safety and optimizing chemotherapy outcomes.[16]

The findings of present study emphasize the important role of pharmacovigilance in oncology practice. Cancer patients receiving chemotherapy are particularly vulnerable to adverse drug reactions due to the narrow therapeutic index of anticancer drugs. Continuous monitoring and systematic reporting of ADRs are therefore essential for ensuring patient safety and improving quality of cancer care. Active pharmacovigilance programs facilitate early detection of treatment-related toxicities, enable timely clinical interventions, and contribute to safer and more rational use of anticancer drugs.[36]

In addition, effective pharmacovigilance systems can provide valuable real-world evidence regarding the safety profile of chemotherapy regimens used in routine clinical practice. Such information is particularly important in developing countries, where regional variations in patient characteristics, treatment patterns, and healthcare resources may influence the occurrence and management of ADRs.[37] The present study therefore contributes important regional data on chemotherapy-related adverse drug reactions among head and neck cancer patients in Central Gujarat and highlights the need for continued surveillance of treatment-related toxicities in oncology settings.

Despite providing valuable insights into chemotherapy-induced adverse drug reactions, the present study has certain limitations. First, the study was conducted at a single tertiary care center, which may limit the generalizability of the findings to other healthcare settings. Second, the number of patients receiving some chemotherapy regimens was relatively small, which restricts the ability to draw definitive conclusions regarding regimen-specific toxicity profiles. In addition, the study primarily focused on ADRs occurring during the treatment period and did not evaluate long-term or delayed adverse effects of chemotherapy.

Future multicenter studies with larger sample sizes and longer follow-up periods are recommended to further evaluate chemotherapy-related adverse drug reactions in head and neck cancer patients. Such studies may also explore potential strategies for improving ADR prevention, optimizing chemotherapy regimens, and enhancing pharmacovigilance practices in oncology care.

**CONCLUSION:**

The present prospective observational study highlights the substantial burden of chemotherapy-induced adverse drug reactions among patients with head and neck cancer receiving treatment at a tertiary care hospital. A high proportion of patients experienced ADRs during chemotherapy, with gastrointestinal disturbances, musculo-skeletal pain-related reactions, and general systemic symptoms being the most commonly observed. Cisplatin-based chemotherapy regimens were associated with the highest number of ADR events. Most ADRs were

categorized as probable in causality assessment and were moderate in severity, while a considerable proportion were found to be preventable. These findings emphasize the importance of active pharmacovigilance, early detection of adverse reactions, and appropriate supportive care to minimize treatment-related toxicities and improve the safety and effectiveness of chemotherapy in cancer patients.

**CONFLICT OF INTEREST:** None

**ACKNOWLEDGEMENT:** We would like to acknowledge the oncology consultants, nursing staff and pharmacy personnel of Shree Krishna Hospital as well as all participating patients and their families for their cooperation and willingness to contribute to this research.

**AUTHOR'S CONTRIBUTION:** Kruti Sharma: Conceptualization, Methodology, Investigation, Visualization, Writing Original draft, Writing-review and editing. Nilesh Patel: Conceptualization, Methodology, Visualization, Writing-review-editing and project administration. Nirav Asarawala: Conceptualization, Methodology, Visualization, Writing-review-editing and project administration.

**FUNDING:** None

**ETHICAL APPROVAL:** The study protocol was reviewed and approved by the Institutional Ethics Committee of Shree Krishna Hospital (IEC/BU/148/Faculty/31/342/2023).

**REFERENCES:**

1. Elkashty OA, Ashry R, Tran SD. Head and neck cancer management and cancer stem cells implication. Saudi Dent J. 2019 Oct;31(4):395-416.
2. Bagal S, Budukh A, Thakur JS, Dora T, Qayyumi B, Khanna D, Fernandes D, Chakravarti P, Singh R, Patil S, Dikshit R, Chaturvedi P. Head and neck cancer burden in India: an analysis from published data of 37 population-based cancer registries. Ecancermedicalscience. 2023 Sep 21;17:1603.
3. Muhamed AN, Tesema BB, Hiruy EG, Shiferaw SM, Aycheh DT, Abate MD. Nutritional Status and Its Determinants among Adult Cancer Patients Undergoing Chemotherapy Treatment at Hawassa University Comprehensive Specialized Hospital, Hawassa, Southern Ethiopia. J Nutr Metab. 2022 Sep 28;2022:8740272.
4. https://www.who.int/docs/default-source/medicines/safety-of-medicines--adverse-drug-reactions-jun18.pdf?sfvrsn=4fcaf40_2

5. Kalaiselvan V, Thota P, Singh GN. Pharmacovigilance Programme of India: Recent developments and future perspectives. Indian J Pharmacol. 2016 Nov-Dec;48(6):624-628.
6. Pandit, S., Verma, M., & Mishra, P. S. (2020). A prospective study of adverse drug reactions associated with chemotherapy in patients of carcinoma head and neck in Government Cancer Hospital Indore, India. *International Journal of Basic & Clinical Pharmacology*, *9*(6), 897–901.
7. Chopra D, Rehan HS, Sharma V, Mishra R. Chemotherapy-induced adverse drug reactions in oncology patients: A prospective observational survey. Indian J Med Paediatr Oncol. 2016 Jan-Mar;37(1):42-6.
8. Chauhan SM, Abdul MMA, Dolat AS, Gandhar RJ. A retrospective analysis of reporting of adverse drug reactions to oncology drugs: an experience from a national center of clinical excellence. *Int J Curr Pharm Rev Res*. 2025;17(3):1424-31.
9. Sharma K, Jasuja S, Jain M, Singh Y. Assessment of adverse drug reactions in oral cancer patients receiving chemotherapy treatment at tertiary care centres in North-Western India. Scr Med. 2023;54(1):45-51.
10. Goyal YN, Solanki KC, Mistry RA, Joshi ND, Singh AP, Gajera MV. Pattern of adverse drug reactions due to cancer chemotherapy in a tertiary care teaching hospital in Gujarat. *Int J Sci Res*. 2014;3(1), 333-335.
11. Central Drugs Standard Control Organization. Suspected Adverse Drug Reaction Reporting Form. New Delhi: CDSCO; 2022. Available from: https://cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2018/UploadPvPI/ADRnewReporting_Form_1.4.pdf
12. https://healthcare-bulletin.co.uk/article/a-prospective-observational-study-on-adverse-drug-reactions-in-elderly-patients-receiving-polypharmacy-in-a-tertiary-care-hospital-3199/
13. http://www.who-umc.org/
14. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239-45.
15. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm. 1992;27(6):538.
16. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992;49(9):2229-32.

17. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394–424.
18. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209–249.
19. Gupta B, Johnson NW. Systematic review and meta-analysis of association of smokeless tobacco and oral cancer in South Asia and the Pacific. *PLoS One.* 2014;9(11):e113385.
20. Francis DL, et al. Head and neck cancer rates in India: an analysis of epidemiological trends. *Oral Oncology.* 2024.
21. Sankaranarayanan R, Ramadas K, Amarasinghe H, et al. Oral cancer: prevention, early detection and treatment. *Lancet Oncology.* 2015;16(3):e116–e125.
22. Mehrotra R, Yadav S. Oral squamous cell carcinoma: etiology, pathogenesis and prognostic value of genomic alterations. *Indian Journal of Cancer.* 2006;43(2):60–66.
23. Gupta B, Johnson NW, Kumar N. Global epidemiology of head and neck cancers: a continuing challenge. *Oncology.* 2016;91(1):13–23.
24. Jordan K, Schmoll HJ, Aapro MS. Comparative activity of antiemetic drugs. *Cancer Chemotherapy and Pharmacology.* 2007;60(2):143-154.
25. Venkatesan P, et al. Monitoring of adverse drug reactions in cancer patients receiving chemotherapy. *Indian Journal of Pharmacology.* 2018;50(2):89-95.
26. Kirthi C, et al. Adverse drug reactions in oncology patients receiving chemotherapy. *Journal of Pharmacology and Pharmacotherapeutics.* 2014;5(3):199-203.
27. Nurgali K, Jagoe RT, Abalo R. Adverse effects of cancer chemotherapy: anything new to improve tolerance and reduce sequelae? *Frontiers in Pharmacology.* 2018;9:245.
28. Hesketh PJ. Chemotherapy-induced nausea and vomiting. *New England Journal of Medicine.* 2008;358(23):2482–2494.
29. Trueb RM. Chemotherapy-induced alopecia. *Seminars in Cutaneous Medicine and Surgery.* 2009;28(1):11–14.
30. Hofman M, Ryan JL, Figueroa-Moseley CD, Jean-Pierre P, Morrow GR. Cancer-related fatigue: the scale of the problem. *Oncologist.* 2007;12:4–10.

31. Stone P, Hardy J, Huddart R, A'Hern R, Richards M. Fatigue in patients with cancer. *European Journal of Cancer.* 2000;36(7):843–849.
32. Dasari S, Tchounwou PB. Cisplatin in cancer therapy: molecular mechanisms of action. *European Journal of Pharmacology.* 2014;740:364–378.
33. Pignon JP, le Maître A, Maillard E, Bourhis J. Meta-analysis of chemotherapy in head and neck cancer. *Lancet.* 2009;373(9658):169–180.
34. Markman M. Toxicities of the taxanes: neuropathy and other adverse effects. *Cancer Chemotherapy and Pharmacology.* 2003;52:S15–S19.
35. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. *Lancet.* 2000;356(9237):1255–1259.
36. Pirmohamed M, Breckenridge AM, Kitteringham NR, Park BK. Adverse drug reactions. *BMJ.* 1998;316(7140):1295–1298.