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Prevalence Pattern of Adverse Drug Reaction with Causality Assessment to Chemotherapy in a Tertiary Hospital, Nepal

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ABSTRACT

Introduction: Chemotherapy drugs have a small margin between effective and harmful dosages, adverse drug reactions (ADRs) become a serious issue in cancer therapy. This study aimed to investigate the frequency, severity and causality of chemotherapy-induced ADRs in a tertiary care hospital setting.

Objectives: To assess prevalence pattern and causality outcome of ADRs to chemotherapeutic agents.

Methodology: A hospital-based observational cross-sectional study was conducted among 200 cancer patients under systemic anticancer medication (SACT) at Birat Medical College Teaching Hospital from May to October 2024. The causality of adverse drug reactions (ADRs) was assessed using Naranjo's Causality Assessment Scale, while the severity of ADRs was evaluated using the Hartwig and Siegel Severity Assessment Scale. Data analysis was performed using SPSS version 26, employing descriptive statistics. Chi-square or Fisher's Exact Test was used to determine associations between independent variables and causality of ADRs. A p-value < 0.05 was considered statistically significant.

Results: Among the 200 participants, the mean age was 55.05 ± 14.11 years; breast cancer 44(22%) was the most prevalent malignancy. The most commonly reported adverse drug reactions (ADRs) were anorexia (28; 14%) and taste changes (22; 11%). Causality assessment revealed that most ADRs were classified as possible or likely, with a few being definite. Most reactions were of mild to moderate in severity. A statistically significant association was found between age category and in causality of ADRs (p=0.039).

Conclusions: Chemotherapy-related ADRs are quite frequent; often presenting as mild to moderate gastrointestinal symptoms. The significant association between age and ADRs underscores the need for closer monitoring of elderly patients, emphasizing the importance of strengthening and enhancing local pharmacovigilance systems in Nepal.

Introduction

Cancer remains one of the most lethal diseases affecting worldwide, with treatment modalities including surgery, radiotherapy, chemotherapy, immunotherapy, monoclonal antibody therapy, and others.[1] Among these, antineoplastic drugs play a critical role in cancer management due to their proven efficacy. However, their use is often limited by their high toxicity and narrow therapeutic window.[2]

Adverse drug reactions (ADRs) represent a major global concern, contributing substantially to morbidity and mortality and posing a significant challenge in cancer therapy.[3] Anticancer agents, in particular, are well known for their high potential

to cause ADRs.[4,5] Unfortunately, many of these reactions remain underreported, leading to an underestimation of their clinical impact. Hence, comprehensive evaluation of ADRs considering their causality, probability, and severity is essential to optimize patient safety and treatment outcomes.[6]

Several methods have been developed to assess the causality of ADRs, including those proposed by the Adverse Drug Reaction Advisory Committee (ADRAC), the World Health Organization–Uppsala Monitoring Centre (WHO-UMC), the Jones algorithm, the Yale algorithm, and the Naranjo algorithm.[7,8,9] Among these, the Naranjo algorithm is one of the most widely used tools due to its simplicity, reproducibility, and applicability across diverse clinical settings. Therefore, this study employs the Naranjo algorithm to systematically assess the causality of ADRs associated with anticancer drugs.

Although chemotherapy use in Nepal is increasing, there is a lack of systematic research evaluating the incidence, causality, and severity of adverse drug reactions (ADRs) associated with anticancer treatments. To fulfill this gap, the frequency and patterns of ADRs are to be documented to improve Nepal's pharmacovigilance system and create a more complete ADR reporting database

The objectives of this study are to examine the pattern of ADRs associated with chemotherapeutic agents and to assess the causality and severity among the cancer patients receiving different chemotherapy regimens in Nepal.

Methodology

A hospital-based observational cross-sectional study was conducted in Birat Medical College Teaching Hospital at department of Pharmacology over a period of six months from (May–October 2024). Ethical approval for the study was obtained from the Institutional Review Committee (IRC) of BMCTH.

The study population were patients undergoing systemic anticancer treatment (SACT) during the study period. A consecutive sampling technique was used to enlist patients. Every patient was included only once in the study, follow-up visits were not noted as discrete entries to avoid data duplication. All participant under SACT at the age between 18 and 80 years old were included in the study. Elderly patients over 80 years and children under 17, and the Patients with terminal end-stage cancer getting palliative or terminal treatment were excluded from the study. Participants were explained about the study objectives before data collection and obtained their voluntary written informed consent, along with consent from their attendants.

Using Cochran's formula for cross-sectional studies, the sample size was calculated as:

$n = Z^2 PQ/d^2$.

Where:

• p: 46.1% (from Tamang R. et al.)[10] is the prevalence of ADR causality.

• q = 1 – p

• Z = 1.96 (95% confidence interval)

• d = 0.05 (acceptable error margin)

$n = (1.96)^2 \times 0.461 \times (1-0.461) /(0.05)^2 = 382$

Since we have finite population, so we use sample size for finite population (n')

= n / [1+{(n-1) / N}]

Where, N is the finite population =400, n' is the new adjusted sample size

= 382 / [1+ {(382-1)/400}] = 382/1+0.9525= 382/1.9525 = 195.6 =196

Hence, the ultimate number of patients was 196. To enhance the reliability of findings and to compensate for potential non-response or incomplete data, the sample size was rounded up to 200 participants. Every eligible cancer patient who had ADRs while undergoing chemotherapy was regarded a study unit.

Data were collected using a structured and pretested questionnaire created on the basis of standard pharmacovigilance reporting templates recommended by the World Health Organization (WHO). The questionnaire includes demographic information, medical background, cancer diagnosis, drugs treatment, and detail information about ADRs.

Prior to the main study, the questionnaire was pretested on a small sample of patients (n = 10) to ensure clarity, relevance, and consistency. Based on intern doctor and research team input, necessary modification was implemented in the questionnaire.

Data collecting was carried out through a combination of patients record review and face-to-face interviews with patients and, when necessary, their family members. Interviews were conducted during the same treatment visit wherever feasible to lower recollection bias. Chemotherapy prescriptions were reviewed from the day care ward and interviewed patients and their attendants in the local language about the occurrence of adverse drug reactions (ADRs) during and after each chemotherapy cycle.

All the data collection activities were performed by intern doctors and the researchers themselves who underwent training to ensure uniform understanding about ADR definitions, reporting criteria, and data recording procedures. Supervised data collection, regular cross-checking of results, and consensus conversations with each other helped to minimize inter-observer variation.

After the data collection was finished, the causality of ADRs associated with various anticancer medication was assessed using Naranjo's Causality Assessment Scale.[11] The Naranjo ADR Probability Scale consists of ten questions each answered as either Yes, No, or "Do not know." Each response is assigned a point value (−1, 0, +1, or +2), and the total score classifies ADRs as probable, possible, definite and doubtful in relation to the suspected medications." Similarly, the severity of ADRs was assessed with the Hartwig and Siegel Assessment Scale.[12]

Results

Table 1: Sociodemographic and clinical characteristics of cancer patients (n=200)

Variables		Frequency	Percent (%)
Gender	Male	82	49.00
	Female	118	51.00
Age groups	Below 30 years	10	5.00
	30-39 years	13	6.50
	40-49 years	37	18.50
	50-59 years	61	30.50
	60-69 years	47	23.50
	70-79 years	27	13.50
	80 years and above	5	2.50
	Mean age (days)	55.05±14.11	
Comorbidities	None	67	33.30
	Diabetes mellitus (DM)	32	15.90
	Hypertension (HTN)	36	17.90
	Thyroid disorder	12	6.00
	Other	24	11.90
	Both HTN & DM	24	11.90
	Both HTN & thyroid disorder	5	2.50
Occupation	Unemployed	16	8.00
	Business	35	17.40
	Farmer	57	28.40
	Housewife	39	19.40
	Teacher	36	17.90
	Service	10	5.00
	Other	7	3.50
Types of Cancers	Lungs Ca	29	14.50
	Breast Ca	44	22.00
	Ovary Ca	15	7.50
	Nasopharyngeal Ca	22	11.00
	Pancreas Ca	16	8.00
	Urinary Bladder Ca	6	3.00
	Colon Ca	18	9.00
	Rectum Ca	4	2.00
	Stomach Ca	4	2.00
	Cervical ca	13	6.50
	Gallbladder Ca	4	2.00
	ALL (Acute Lymphoblastic leukemia)	7	3.50
	NHL (Non-Hodgkin's lymphoma)	3	1.50
	Marginal lymphoma	9	4.50
	Others (prostate, liver, oropharyngeal)	6	3.00

The study included 200 patients undergoing chemotherapy. Of these, 82 (41%) were male and 118 (59%) were female. The mean age of participants was 55.05 ± 14.11 years, with the largest proportion (30.5%) aged 50–59 years, followed by 23.5% in their 60s and 18.5% in their 40s. Breast cancer was the most common malignancy, affecting 44 patients (22%), followed by lung cancer in 29 (14.5%), nasopharyngeal cancer in 22 (11%), and colon cancer in 18 (9%). Less common cancers included gallbladder cancer, acute lymphoblastic leukemia, and various lymphomas. Regarding comorbidities, 67 patients (33.3%) had no additional illnesses, while hypertension 36, (17.9%) and diabetes mellitus 32, (15.9%) were the most prevalent. In terms of occupation, the majority were farmers 57, (28.4%), followed by teachers 36, (17.9%), business professionals 35, (17.4%), and service workers 10, (5%) (Table 1).

Table 2: Chemotherapeutic agents' distribution (single or in combination)

Chemotherapeutic agents	Frequency	Percentage (%)
Carboplatin + Paclitaxel	25	12.40
Gemcitabine + Carboplatin	34	16.90
Cyclophosphamide + Doxorubicin	16	8.00
Trastuzumab + Carboplatin	16	8.00
Docetaxel + 5Fluro	12	6.00
Cisplatin	6	3.00
Vincristine + bleomycin + decarbazine	8	4.00
Oxaliplatin	6	3.00
Oxaliplatin + Gemcitabine	10	5.00
Etoposide + Cisplatin	6	3.00
Carboplatin	6	3.00
Oxaliplatin + 5Fluro + Leucovorin	22	11.00
Oxaliplatin + 5-Fluro + Leucovorin + pegast	2	1.00
Oxaliplatin + Doxorubicin	2	1.00
Paclitaxel	6	3.00
Rituximab	4	2.00
Rituximab + Bendamustin	3	1.00
Cyclophosphamide + Doxorubicin + Vincristine	6	3.00
Azacytidine	3	1.00
Vincristine	3	1.00
Paclitaxel+ Gemcitabine	4	2.00

The most frequently used chemotherapy regimens were Gemcitabine + Carboplatin (34, 16.9%), Carboplatin + Paclitaxel (25, 12.4%), and Oxaliplatin + 5-Fluorouracil + Leucovorin (22, 11%), together accounting for over 40% of all treatments. Overall, combination therapies dominated, indicating a preference for multi-agent regimens over single-agent therapy (Table 2).

Gastrointestinal and sensory disturbances were the most common adverse drug reactions (ADRs). Anorexia occurred in 28 patients (14%) and taste changes in 22 (11%), followed

by diarrhea in 17 (8.5%). Rare ADRs included headache and leukoplakia 2, (1% each), and thrombocytopenia and dizziness 1, (0.5% each) (Table 3).

Table 3: Prevalence patterns of ADRs (n=200)

Adverse drugs reactions	Frequency (n)	Percentage (%)
Nausea and vomiting	12	6.00%
Anorexia	28	14.00%
Vomiting	7	3.50%
Taste changes	22	11.00%
Alopecia	6	3.00%
Constipation	6	3.00%
Fatigue	6	3.00%
Stomach pain	10	5.00%
Nausea	5	2.50%
Anemia	5	2.50%
Thrombocytopenia	1	0.50%
Dizziness	1	0.50%
Fever	13	6.50%
Dyspnea	3	1.50%
Diarrhea	17	8.50%
Insomnia	3	1.50%
Neutropenia	13	6.50%
Infection	11	5.50%
Headache	2	1.00%
Leucopenia	6	3.00%
Leukoplakia	2	1.00%
Neuropathy	10	5.00%
Mucositis	11	5.50%

Causality assessment using Naranjo's algorithm classified most ADRs as probable, followed by possible, with relatively few definite reactions. Anorexia and taste changes had the highest proportion of probable causality 18, (64.3% and 16, (72.7%), respectively. Definite ADRs were uncommon, noted mainly in taste changes 2, (9.1%), stomach discomfort 1, (10%), diarrhea 2, (11.8%), and infection 1, (9.1%) (Table 4).

Table 4: The Causality assessment by Naranjo's algorithm scale (n=200)

Adverse drugs reaction (ADRs)	Possible, n(%)	Probable, n(%)	Definite, n(%)	Total
Nausea and vomiting	5(41.67%)	7(58.33%)	0	12
Anorexia	8(28.57%)	18(64.29%)	2(7.14%)	28
Vomiting	1(14.29%)	6(85.71%)	0	7
Taste changes	4(18.18%)	16(72.73%)	2(9.09%)	22
Alopecia	3(50%)	3(50%)	0	6
Constipation	1(16.67%)	5(83.33%)	0	6
Fatigue	4(66.67%)	2(33.33%)	0	6
stomach pain	5(50%)	4(40%)	1(10%)	10
Nausea	2(40%)	3(60%)	0	5
Anemia	3(60%)	2(40%)	0	5
Dizziness	1(100%)	0	0	1
fever	10(76.92%)	3(23.08%)	0	13
Dyspnea	1(33.33%)	2(66.67%)	0	3
Diarrhea	10(58.82%)	5(29.41%)	2(11.76%)	17
Insomnia	3(100%)	0	0	3
Neutropenia	1(7.69%)	12(92.31%)	0	13
Infection	0	10(90.91%)	1(9.09%)	11
Headache	1(50%)	1(50%)	0	2
leucopenia	0	6(100%)	0	6
leukoplakia	0	2(100%)	0	2
Neuropathy	2(20%)	6(60%)	2(20%)	10
Mucositis	7(63.64%)	4(36.36%)	0	11
Thrombocytopenia	1(100%)	0	0	1

Severity assessment based on Hartwig's scale indicated that most ADRs were mild to moderate. Mild ADRs predominated, particularly in taste changes 17(77.27%), vomiting 7(100%), anorexia 13(46.43%), and neutropenia 8(61.54%). Severe ADRs were less frequent, including anorexia 2(7.14%), anemia 1(20%), diarrhea 2(11.76%), dyspnea 2(66.67%), infection 3(27.27%) and mucositis 3(27.27%). Overall, the findings show that most ADRs were manageable, though some required medical intervention or modification of therapy.

Data were analyzed in SPSS version 26 using descriptive statistics, chi-square/Fisher's exact test were used to assess associations between independent variables (age, sex, occupation, comorbidities) and ADRs causality. A significant association was found between age and ADR causality ($p = 0.039$), whereas gender, comorbidities, and occupation did not show significant correlations ($p = 0.693$) (Table 5).

Table 5: Association between socio-demographic and Causality of ADRs (n=200)

Variables		Causality of ADRs			p-value
		Probable n(%)	Definite n(%)	Definite n(%)	
Gender	Female	37(31.4%)	74(62.7)	7(5.9)	0.177
	Male	36(43.9%)	43(52.4%)	3(3.7%)	
Age groups	Below 30 years	6(60%)	4(40%)	0	0.039
	30-39 years	3(23.1%)	7(53.8)	3(23.1%)	
	40-49 years	10(27%)	23(62.2%)	4(10.8%)	
	50-59 years	23(37.7%)	38(62.3%)	0	
	60-69 years	19(40.4%)	26(55.3%)	2(4.3%)	
	70+	12(37.5%)	19(59.4%)	1(3.1%)	
Occupation	Unemployed	16(45.7%)	17(48.6)	2(5.7%)	0.693
	Business	20(35.1%)	33(57.9%)	4(7%)	
	Farmer	10(25.6%)	26(66.7%)	3(7.7%)	
	Housewife	4(40%)	6(60%)	0	
	Teacher	11(30.6%)	24(66.7%)	1(2.8%)	
	Service	8(50%)	8(50%)	0	
	Other	4(57.1%)	3(42.9%)	0	
Comorbidities	None	22(32.8%)	43(64.2%)	2(3%)	0.084
	Diabetes	14(43.8%)	17(53.1%)	1(3.1%)	
	Hypertension	10(27.8%)	24(66.7%)	2(5.6%)	
	Thyroid disorder (TD)	3(25%)	6(50%)	3(25%)	
	Both HTN & TD	3(60%)	2(40%)	0	
	Both HTN & DM	8(33.3%)	14(58.3%)	2(8.3%)	
	Other	13(54.2)	11(45.8%)	0	

Discussion

The present study explored the pattern of adverse drug reactions (ADRs) among cancer patients receiving various chemotherapeutic agents. In our study population, 82 men (49%) and 118 women (51%) showed ADRs, indicating a nearly equal distribution across genders. While the rate among women was somewhat more, the difference was slight and statistically insignificant. This suggest that in this environment, both men and women were equally vulnerable to the toxic effects of chemotherapy. The average age of study participants was 55.05 ± 14.11 years, this highlights that most of the patients were middle-aged and older adults' groups. Patients in their 50s had a higher ADR frequency followed by those in their 60s, reflecting the fact that cancer incidence itself tends to rise with advancing age. Several previous studies have indicated that female patients often experience more ADRs than males, which has been related to biological and physiological causes, differences in body composition, hormonal state, and the pharmacokinetic processing of medications.[13,14] However, the almost equal distribution in our study implies that gender might not be a major predictor of ADRs risk in this people. ADRs in the 50–59 age group could be related to age-related physiological changes, including decreased organ function, modified metabolism, and reduced drugs clearance. These factors, combined with the higher prevalence of comorbidities in older adults, likely increase susceptibility to chemotherapy-induced toxicities. Such findings reinforce the need for cautious dosing and continuous monitoring to elderly cancer patients.[15,16]

Combination chemotherapy is the foundation of cancer treatment because it reduces the likelihood of drug resistance and enhances overall anti-cancer activity compared to single-drug therapy.[17,18] In our study, combination regimens accounted for over 40% of all treatment protocols, aligning with international guidelines that recommend multi-agent chemotherapy for common solid tumors such as breast, lung, and colorectal cancers. This reflects a worldwide tendency toward evidence-based, multi-drug treatments shown to increase survival rates in diseases including metastatic breast cancer and advanced pancreatic adenocarcinoma.[19,20] Therefore, a major challenge is still striking a balance between safety and effectiveness, highlighting the need for close surveillance and prompt treatment of adverse drug events.

This study shows a broad spectrum of ADRs, the most often reported were anorexia (14%), taste changes (11%), and diarrhea (8.5%). The frequency of taste changes was significantly less 22(11%) than in some earlier studies, which indicated rates between 45% and 84%. Variation may come from variations in patient

groups, chemotherapy regimens, or data collection techniques.[21] Our study depended on clinician-verified interviews; while other utilized self-reported surveys that captures more subjective symptoms. Anorexia became a notably significant ADR because of its influence on weight loss, malnutrition, and decreased treatment tolerance, which could compromise both quality of life and therapeutic continuation.[22] Diarrhea was another often-seen adverse response consistent with chemotherapy-induced mucosal damage impacting quickly dividing intestinal cells.[23] The overall pattern of ADRs observed dominated by gastrointestinal and metabolic toxicities is comparable to findings from other studies, which also rank diarrhea, nausea, vomiting, and loss of appetite among the most prevalent reactions in oncology patients.[22]

The findings of causality in this study are consistent with other Nepalese studies among chemotherapy patients, where 47.1% of ADRs were probable and 46.1% were possible, as well as with Sharma et al. (2022), who reported 58.68% probable and 40.99% possible ADRs.[10, 24] This pattern suggests that "possible" ADRs are relatively common, potentially due to limited polypharmacy and overlapping symptom profiles, whereas "definite" causality is rare.[25]

According to the Hartwig and Siegel severity scale, most ADRs in this study were mild to moderate. This pattern is consistent with previous studies conducted in Nepal and worldwide oncology research.[26] Severe ADRs were rare which include mucositis, dyspnea, and infections while the majority of ADRs are tolerable, some need immediate clinical care and may require modification in chemotherapy regimens.[10,24,26]

Statistical analysis revealed a significant association between age and ADR causality ($p = 0.039$), suggesting that the likelihood of developing a drug-related adverse event increases with advancing age. This finding is in line with previous studies highlighting age as a critical risk factor due to physiological frailty and altered pharmacodynamics in older patients.[27] Conversely, no significant associations were observed with gender, occupation, or comorbidities. ADRs risk is multifactorial and not solely determined by demographic variables. These insights emphasize the need for age-sensitive treatment planning, personalized dosing, and active pharmacovigilance systems to minimize the impact of chemotherapy-induced toxicities in cancer care.[25]

Conclusion

This study found that adverse drug reactions (ADRs) were common among patients undergoing chemotherapy, with gastrointestinal and sensory disturbances particularly anorexia (14%) and taste changes (11%) being the most prevalent. Most ADRs were assessed as probable by Naranjo's causality scale and were mild to moderate in severity. A significant association between age and ADRs causality ($p = 0.039$) indicated that older patients were more prone to treatment-related toxicities. The overall ADR pattern was comparable to international studies, highlighting gastrointestinal effects as the most frequent. These findings emphasize the need for age-sensitive chemotherapy protocols, continuous patient monitoring, and strengthened pharmacovigilance systems to ensure early detection and effective management of ADRs.

Limitations of the Study

This single-center, cross-sectional study may limit the generalizability of findings and unable to show delayed or prolonged toxicity. ADRs identification was based on clinical judgment using validated scales, which introduces some degree of subjectivity. Additionally, pharmacogenomic testing, which could explain inter-individual variability in ADR risk, was not available. Future multicenter longitudinal studies incorporating larger sample sizes and genetic testing could provide more comprehensive predictors of ADR severity.

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References

1. Warr DG. Chemotherapy- and cancer-related nausea and vomiting. Curr Oncol. 2008;15(Suppl 1): S4-S9. DOI: 10.3747/co.2008.171 PMID: 18231647 PMCID: PMC2216421

2. Gandhi TK, Bartel SB, Shulman LN, Verrier D, Burdick E, Cleary A, et al. Medication safety in ambulatory chemotherapy setting. Cancer. 2005;104(11):2477-2483. DOI: 10.1002/cncr.21442 PMID: 16245353

3. Baniasadi S, Fahimi F, Shalviri G. Developing an adverse drug reaction reporting system at a teaching hospital. Basic Clin Pharmacol Toxicol. 2008;102(4):408-11. DOI: 10.1111/j.1742-7843.2008.00217.x PMID: 18312492

4. Routledge PA, O'mahony M, Woodhouse K. Adverse drug reactions in elderly patients. Br J Clin Pharmacol. 2004;57(2):121-6. DOI: 10.1046/j.1365-2125.2003.01875.x PMID: 14748810 PMCID: PMC1884428

5. Sievers TD, Lagan MA, Bartel SB, Rasco C, Blanding PJ. Variations in administration of cyclophosphamide and mesna in the treatment of childhood malignancies. J Pediatr Oncol Nurs. 2001; 18: 37-45. DOI: 10.1177/104345420101800105 PMID: 11172408

6. Al Meslamani AZ. Underreporting of adverse drug events: a look into the extent, causes, and potential solutions. Expert Opinion on Drug Safety. 2023 May 4;22(5):351-4. DOI: 10.1080/14740338.2023.2224558
PMID: 37300402

7. Kramer MS, Hutchinson TA. The Yale algorithm. Special workshop: clinical. Drug Inf J 1984; 18: 283-291. DOI: 10.1177/009286158401800315
PMID: 10268557

8. World Health Organization. The use of the WHO-UMC system for standardized case causality assessment. Uppsala: The Uppsala Monitoring Centre. 2005 Jul 13;1. Available from: http://www.who-umc.org/Graphics/24734.pdf.

9. 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 Aug;30(2):239-45. DOI: 10.1038/clpt.1981.154. PMID: 7249508. DOI: 10.1038/clpt.1981.154
PMID: 7249508

10. Tamang R, Bharati L, Khatiwada AP, Ozaki A, Shrestha S. Pattern of Adverse Drug Reactions Associated with the Use of Anticancer Drugs in an Oncology-Based Hospital of Nepal. JMA J. 2022 Oct 17;5(4):416-426. DOI: 10.31662/jmaj.2021-0015
PMID: 36407064 PMCID: PMC9646287

11. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992 Sep;49(9):2229-32. DOI: 10.1093/ajhp/49.9.2229

12. Karch FE, Lasagna L. Adverse drug reactions. A critical review. JAMA. 1975 Dec 22;234(12):1236-41. DOI: 10.1001/jama.1975.03260250028021
PMID: 1242749

13. Zopf Y, Rabe C, Neubert A, Gassmann KG, Rascher W, Hahn EG, et al. Women encounter ADRs more often than do men. Eur J Clin Pharmacol. 2008 Oct;64(10):999-1004. DOI: 10.1007/s00228-008-0494-6
PMID: 18604529

14. Özdemir BC, Gerard CL, Espinosa da Silva C. Sex and Gender Differences in Anticancer Treatment Toxicity: A Call for Revisiting Drug Dosing in Oncology. Endocrinology. 2022 Jun 1;163(6): bqac058. DOI: 10.1210/endocr/bqac058
PMID: 35560216 PMCID: PMC9113364

15. Balducci L, Extermann M. Management of cancer in the older person: a practical approach. Oncologist. 2000;5(3):224-37. DOI: 10.1634/theoncologist.5-3-224
PMID: 10884501

16. Ozols RF, Bundy BN, Greer BE, Fowler JM, Clarke-Pearson D, Burger RA, et al. Gynecologic Oncology Group. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2003 Sep 1;21(17):3194-200. DOI: 10.1200/JCO.2003.02.153
PMID: 12860964

17. Yardley DA. Drug resistance and the role of combination chemotherapy in improving patient outcomes. Int J Breast Cancer. 2013; 2013:137414. DOI: 10.1155/2013/137414
PMID: 23864953 PMCID: PMC3707274

18. Pritchard JR, Lauffenburger DA, Hemann MT. Understanding resistance to combination chemotherapy. Drug Resist Updat. 2012 Oct;15(5-6):249-57. DOI: 10.1016/j.drup.2012.10.003
PMID: 23164555 PMCID: PMC3975170

19. Lewis A, Nagrial A. Systematic Review of Single-Agent vs. Multi-Agent Chemotherapy for Advanced Pancreatic Adenocarcinoma in Elderly vs. Younger Patients. Cancers (Basel). 2023 Apr 13;15(8):2289. DOI: 10.3390/cancers15082289
PMID: 37190218 PMCID: PMC10136963

20. Bayat Mokhtari R, Homayouni TS, Baluch N, Morgatskaya E, Kumar S, Das B, et al. Combination therapy in combating cancer. Oncotarget. 2017 Jun 6;8(23):38022-38043. DOI: 10.18632/oncotarget.16723
PMID: 28410237 PMCID: PMC5514969

21. Belqaid K, Orrevall Y, McGreevy J, Månsson-Brahme E, Wismer W, Tishelman C, et al. Self-reported taste and smell alterations in patients under investigation for lung cancer. Acta Oncol. 2014 Oct;53(10):1405-12. DOI: 10.3109/0284186X.2014.895035
PMID: 24702121 PMCID: PMC4220986

22. Arends J, Baracos V, Bertz H, Bozzetti F, Calder PC, Deutz NEP et al. ESPEN expert group recommendations for action against cancer-related malnutrition. Clin Nutr. 2017 Oct;36(5):1187-1196. DOI: 10.1016/j.clnu.2017.06.017
PMID: 28689670

23. Tewari KS, Colombo N, Monk BJ, Dubot C, Cáceres MV, Hasegawa K, et al. Pembrolizumab or Placebo Plus Chemotherapy with or Without Bevacizumab for Persistent, Recurrent, or Metastatic Cervical Cancer: Subgroup Analyses From the KEYNOTE-826 Randomized Clinical Trial. JAMA Oncol. 2024 Feb 1;10(2):185-192. DOI: 10.1001/jamaoncol.2023.5410
PMID: 38095881 PMCID: PMC10722390

24. Jiang H, Lin Y, Ren W, Fang Z, Liu Y, Tan X, et al. Adverse drug reactions and correlations with drug-drug interactions: A retrospective study of reports from 2011 to 2020. Front Pharmacol. 2022 Aug 22; 13:923939. DOI: 10.3389/fphar.2022.923939
PMID: 36133826 PMCID: PMC9483724

25. Beijer HJ, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. Pharm World Sci. 2002 Apr;24(2):46-54. DOI: 10.1023/A:1015570104121
PMID: 12061133

26. Woo SD, Yoon J, Doo GE, Park Y, Lee Y, Lee SH, et al. Common causes and characteristics of adverse drug reactions in older adults: a retrospective study. BMC Pharmacol Toxicol. 2020 Dec 10;21(1):87. DOI: 10.1186/s40360-020-00464-9
PMID: 33303036 PMCID: PMC7727226

27. Shrmeka MS, Semman MF, Moges BT, Dereja FN, Garedo AW. Chemotherapy-related adverse drug reaction and associated factors among adult cancer patient attending Jimma medical center oncology unit, Southwest Ethiopia. PLoS One. 2025 May 16;20(5): e0321785. DOI: 10.1371/journal.pone.0321785
PMID: 40378362 PMCID: PMC12084033