

## A Hospital Based Observational Assessment of the Pattern of Adverse Drug Reactions with Chemotherapeutic Drugs

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Received: 18-02-2023 / Revised: 14-03-2023 / Accepted: 15-04-2023

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Conflict of interest: Nil

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### Abstract:

**Aim:** The aim of the study was to assess the pattern of adverse reactions to chemotherapeutic agents commonly prescribed.

**Material & Methods:** This was an observational, non-interventional and retrospective study conducted at the ADR monitoring centre (AMC) which was coordinated by the Department of Pharmacology Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India. Suspected ADR forms reported at the AMC of this hospital during the duration of 2 years were collected. During the study.

**Results:** Among the 200 patients included in the study, 110 (55%) were females and 90 (45%) were males. Majority of the cases were seen in the age group of 51-60 years (26%). 140 (70%) patients were married. Most of them (82%) had never smoked, while some (14%) were ex-smokers and a few others (4%) were current smokers. Most common ADRs were skin rashes (24%), followed by jaundice, urticaria and fixed drug eruptions. Maximum number of ADRs was suspected to be caused by Anti Tubercular drugs (32%), followed by anticancer drugs (14%), fluoroquinolones (13%), anti-fungal (10%), cephalosporins (8%), antiamoebic (5%) and vancomycin (4%). Least number of ADRs were suspected to be caused by macrolides, doxycycline, antimalarial, sulphonamides, dapsone, anti-HIV drugs, permethrin and aminoglycosides.

**Conclusion:** ADRs due to antibiotics and anticancer drugs is a significant health problem.

**Keywords:** Pharmacovigilance, Cutaneous manifestation of adverse drug reaction, Chemotherapeutic drugs, Antimicrobial drugs, Anticancer drugs, Retrospective study

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### Introduction

Adverse drug reactions (ADRs) constitute a major clinical problem in terms of human suffering and increased healthcare costs. [1] An adverse drug reaction (ADR) is any undesirable effect of a drug beyond its anticipated therapeutic effects occurring

during clinical use. World Health Organization (WHO) defines an ADR as “any response to a drug which is noxious, unintended and occurs at doses used in man for prophylaxis, diagnosis or therapy.” [2] Adverse drug reactions are important causes of mortality and

morbidity in both hospitalized and ambulatory patients. In many countries ADRs rank among the top 10 leading causes of mortality. [3]

The drugs commonly associated with ADRs are antiepileptics, antineoplastics, antibiotics, anticoagulants, and nonsteroidal anti-inflammatory drugs. Among them, antineoplastic drugs are one of the most toxic drugs used in therapeutics. [4] Although the recent advancement of anticancer agents has increased survival rates, cancer and the treatment can debilitate the patient both physically and psychologically. The most common ADRs associated with anticancer treatment are alopecia, bone marrow suppression, nausea and vomiting, infection, pain, myelosuppression, haemorrhagic cystitis, mucositis, increased toxicity with impaired renal function, cardiac toxicity, hot flushes, electrolyte imbalance, deep vein thrombosis etc. In addition to the adverse effects, some patients also develop depression, anxiety, sexual dysfunction leading to poor quality of life. The common drugs causing ADRs are taxanes, platinum compounds, alkylating agents, anticancer antibiotics etc. [5-7]

Lack of awareness among healthcare professionals, fear of litigations on the part of the prescriber, lack of time to report, insufficient hospital staffs are main causes of under-reporting of ADRs. [6] The ADR reporting rate in India is less than 1% compared to the worldwide rate of 5%. [8] Variations in ADRs are likely to exist worldwide because of varied patterns of prescribing practices and trends of hospitals, genetic and epidemiological variations of the population. [9]

Hence, it is necessary to recognise the pattern of ADRs related to anticancer drugs to improve the quality of life and also to reduce cost of ADR related hospitalisation among cancer patients. Thus, the aim of the study was to assess the pattern of adverse reactions to

chemotherapeutic agents commonly prescribed.

### Material & Methods

This was an observational, non-interventional and retrospective study conducted at the ADR monitoring centre (AMC) which was coordinated by the Department of Pharmacology Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India. Suspected ADR forms reported at the AMC of this hospital during the duration of 2 years were collected. A total of 200 cancer patients of both sexes and all ages who developed at least one ADR during or after the treatment with anticancer drugs were included. During the study

### Inclusion Criteria

- Only those suspected ADR forms involving at least one chemotherapeutic drug (antimicrobial or anticancer drug) with at least one dose.
- Suspected ADR forms involving chemotherapeutic agent alone or in combination with any other drug.
- Patients with all age groups, both inpatients and outpatients.
- Pregnant and lactating mothers.

### Exclusion Criteria

- Incomplete ADR forms and patients with open medications were excluded from the study.

ADR reporting form designed by Centre for Drug Standard Control Organisation (CDSCO) was used to collect the data regarding ADRs. ADR forms were evaluated and analyzed under these headings: gender wise distribution, age wise distribution, department wise distribution of ADRs, frequency of ADRs with different chemotherapeutic agents, type of ADRs and causality association of ADRs was done according to WHO UMC causality scale 8 and diagnosis, suspected drugs causing ADRs, treatment details, description of the event, onset and ablation

of adverse event, type of ADRs, system affected by the ADRs, outcome of the ADRs, relevant laboratory investigations were recorded.

### Statistical Analysis

The data collected were analysed using SPSS, IBM Corporation, version 21.0. The

data was incorporated in the MS excel sheet and frequencies and percentages were determined for each variable and data in numbers was converted to percentages to achieve readily comparable information.

### Results

**Table 1: Demographic details of patients**

<b>Gender</b>	<b>N%</b>
Male	90 (45)
Female	110 (55)
<b>Age groups</b>	
0-10 years	24 (12)
11-20 years	20 (10)
21-30 years	16 (8)
31-40 years	24 (12)
41-50 years	32 (16)
51-60 years	52 (26)
61-70 years	20 (10)
71-80 years	12 (6)
<b>Marital Status</b>	
Married	140 (70)
Unmarried	60 (30)
<b>Smoking</b>	
Never	164 (82)
Ex-smoker	28 (14)
Current smoker	8 (4)

Among the 200 patients included in the study, 110 (55%) were females and 90 (45%) were males. Majority of the cases were seen in the age group of 51-60 years (26%). 140 (70%) patients were married. Most of them (82%) had never smoked, while some (14%) were ex-smokers and a few others (4%) were current smokers.

**Table 2: ADRs with suspected drugs**

<b>Type of ADR</b>	<b>N</b>	<b>%</b>
Skin rashes	48	24
Jaundice	18	9
Fixed drug eruptions	16	8
Anaphylactic reactions	12	6
Psychosis	8	4
Nausea and vomiting	8	4
Diarrhea	8	4
Ototoxicity	6	3
Pruritus	5	2.5
Discoloration of skin and nails	5	2.5
Hyperpigmentation	4	2
Breathlessness	4	2
Body ache	5	2.5
Swelling on lips	3	1.5

Nephrotoxicity	3	1.5
Dizziness	4	2
Bullous eruptions	2	1
Photo dermatitis	3	1.5
Fever	3	1.5
Gastritis	3	1.5
Others	32	16

Most common ADRs were skin rashes (24%), followed by jaundice, urticaria and fixed drug eruptions.

**Table 3: Class wise distribution of suspected drugs**

Suspected drugs	N%
ATT	64 (32)
Anticancer	28 (13)
FQs	26 (13)
Antifungal	20 (10)
Cephalosporins	16 (8)
Anti-amoebic	10 (5)
Vancomycin	8 (4)
Doxycycline	6 (3)
Macrolides	6 (3)
Anti-malarial	4 (2)
Dapsone	3 (1.5)
Sulfonamides	3 (1.5)
Permethrin	2 (1)
Aminoglycosides	2 (1)
Anti-HIV	2 (1)

Maximum number of ADRs was suspected to be caused by Anti Tubercular drugs (32%), followed by anticancer drugs (14%), fluoroquinolones (13%), anti-fungal (10%), cephalosporins (8%), anti-amoebic (5%) and vancomycin (4%). Least number of ADRs were suspected to be caused by macrolides, doxycycline, antimalarial, sulphonamides, dapsone, anti-HIV drugs, permethrin and aminoglycosides.

### Discussion

Drugs are primarily used for the diagnosis, prevention, treatment of various diseases. But it is sometimes observed, that these drugs have been proved fatal. This could be due to variable person-to-person responses towards a drug. Even at therapeutic doses, people develop adverse effects. [9] Adverse drug reactions (ADRs)

are one of the leading causes of repeated hospitalization and they adversely affects the quality of life. [10] According to epidemiological studies, ADRs are the fourth to sixth leading cause of death with an incidence of about 7%. [11] Impact of ADRs on patients includes deterioration of quality of life, increased hospitalisation, economic burden to health management and increased mortality rate. The estimated cost to treat ADRs is 1.7% of total budget of hospital. [12] As ADRs are inevitable, so ADR monitoring has become an important tool to detect uncommon and occasionally serious ADRs, ensuring patient safety. Although the recent advancement of anticancer agents has increased survival rates, cancer and the treatment can debilitate the patient both physically and psychologically. The most common ADRs associated with anticancer

treatment are alopecia, bone marrow suppression, nausea and vomiting, infection, pain etc. In addition to the adverse effects, some patients also develop depression, anxiety, sexual dysfunction leading to poor quality of life. The common drugs causing ADRs are taxanes, platinum compounds, alkylating agents, anticancer antibiotics etc. [13,14]

Among the 200 patients included in the study, 110 (55%) were females and 90 (45%) were males. Majority of the cases were seen in the age group of 51-60 years (26%). The results of our study are in accordance with another study conducted by Arulappan et al in which ADRs were higher in adults as compared to pediatrics and geriatrics age group. [15] Probably adult patients were more prone to ADRs to chemotherapeutic drugs due to age related pharmacokinetic and pharmacodynamic changes and presence of co morbid conditions and intake of multiple drugs in addition. Most common ADRs were skin rashes (24%), followed by jaundice, urticaria and fixed drug eruptions. Skin rashes were the most common ADR reported in our study which is parallel with another studies conducted by Arualeppan et al and Jayanthi et al. [15,16] Most of the ADRs were probable in our study which is in accordance with the studies conducted by Arulappan et al, Reema et al in which most of the ADRs were probable in nature. [15,17] Maximum number of ADRs was suspected to be caused by Anti Tubercular drugs (32%), followed by anticancer drugs (14%), fluoroquinolones (13%), anti-fungal (10%), cephalosporins (8%), antiamebic (5%) and vancomycin (4%). Least number of ADRs were suspected to be caused by macrolides, doxycycline, antimalarial, sulphonamides, dapson, anti-HIV drugs, permethrin and aminoglycosides. In other studies, also, antibiotics were maximally responsible for most of the ADRs. [15,17] One study by Jayanthi et al shows that  $\beta$  lactams were responsible for maximum ADRs. [16]

## Conclusion

ADRs due to antibiotics and anticancer agents are a significant health problem during the management of the infections and tumors. Skin and mucous membrane are frequently involved with ADR due to these agents. This study helped health care professional in determining the different patterns of ADRs with chemotherapeutic agents.

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