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Original Research Article

Pattern of adverse drug reactions with chemotherapeutic drugs in a tertiary care hospital of North India: a retrospective study

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ABSTRACT

Background: Adverse drug reactions are important causes of mortality and morbidity in the patients. Early detection, evaluation and monitoring of ADRs is essential to improve public health.
Methods: This was an observational, non-interventional and retrospective study conducted at the ADR monitoring centre of a tertiary care hospital of North India. Suspected ADR forms reported over a period of 4 years involving at least one chemotherapeutic drug with at least one dose were analyzed.
Results: A total of 261 chemotherapeutic drugs associated ADRs were analyzed. Out of these, maximum numbers of ADRs were reported by males (54%). Maximum reporting was done by Skin and VD department (37.93%). Causality assessment was probable in maximum number of cases (54%). Most common ADRs were skin rashes (21.46%), followed by jaundice, urticaria and fixed drug eruptions. Maximum ADRs were suspected to be caused by Anti tubercular drugs (31.42%) followed by anticancer drugs (14.56%).
Conclusions: 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

INTRODUCTION

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.[1] So there is a need to study ADRs seriously to create awareness about ADRs among patients and to motivate health care professionals in the hospital to report ADRs to minimize the risk. Early detection, evaluation and monitoring of ADRs are essential to reduce unintended harm to patients and thus improve public health.[2] 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.[3] With continued rise in the number of antineoplastics, the spectrum of ADRs associated with them has also diversified. Antibiotics remain the most commonly prescribed group of drugs by all the clinical specialties due to high prevalence of infectious diseases, particularly in developing countries. However, this group is also most widely misused in the form of self-medication, over-the-counter use and irrationally prescribed many a times.[4-6]

Consequently, leading to worrisome increase in prevalence of resistant pathogen, which have a significant impact on the mortality and morbidity due to infectious diseases and can add unnecessary financial burden to the patient and community at large.[7] 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. There is a need to study ADRs seriously to create awareness among patients and to motivate health care professionals in the hospital to report ADRs to minimize the risk.

METHODS

This was an observational, non-interventional and retrospective study. It was conducted at the ADR monitoring centre (AMC) of a tertiary care hospital of North India. Suspected ADR forms reported at the AMC of this hospital from January 2016 to December 2019 were collected. Only those suspected ADR forms involving at least one chemotherapeutic drug (antimicrobial or anticancer drug) with at least one dose were included in the study. Suspected ADR forms involving chemotherapeutic agent alone or in combination with any other drug were included. Patients with all age groups, both inpatients and outpatients were included. Pregnant and lactating mothers were also included. Incomplete ADR forms and patients with open medications were excluded from the study. 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] The data was incorporated in the MS-excel sheet and data in numbers was converted to percentages to achieve readily comparable information. Aims of this study were to assess the pattern of adverse reactions to chemotherapeutic agents commonly prescribed.

RESULTS

During the study period, a total of 261 chemotherapeutic agents associated ADRs were analyzed. Out of 261 ADRs, 54% of ADRs were reported by males and 46% of ADRs were reported by females. Maximum number of ADRs (43%) was reported by the age group greater than 41 years, followed by 41% by age group 21-40 years. Least number of ADRs (16%) were reported by age group less than 20 years. Maximum number of ADRs were reported by Skin and VD department (37.93%), followed by chest and TB (30.65%), oncology (10.34%), medicine (8.43%) and pediatrics (7.66%). Least number of ADRs were reported by OBG department, surgery, ophthalmology, radiotherapy, psychiatry and orthopedics department (Figure 1). As per WHO UMC scale, causality assessment was probable in 54%, possible in 40% and certain in 6% cases (Figure 2).

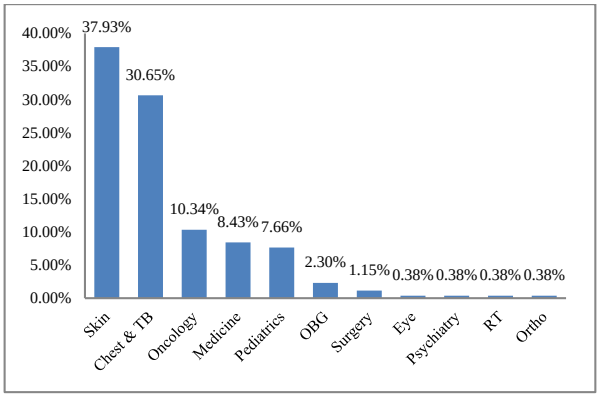

Figure 1: Department wise distribution of ADRs.

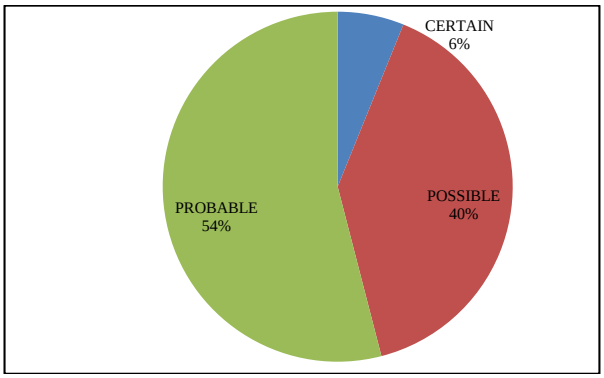

Figure 2: Causality assessment as per WHO UMC scale.

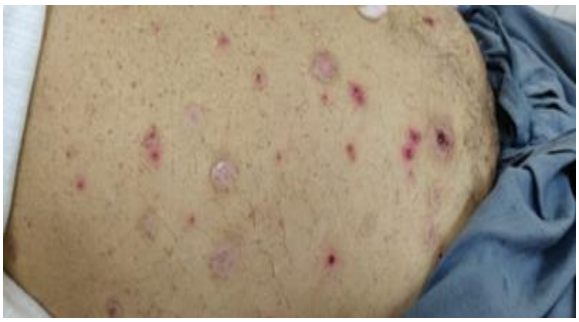

Figure 3: Skin rashes due to cephalosporins.

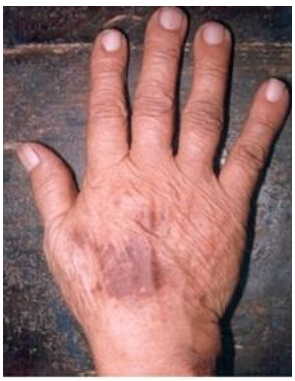

Figure 4: FDE due to metronidazole.

Table 1: List of reported ADRs with suspected drugs.

Type of ADR	N	%
Skin rashes	63	24.1
Jaundice	23	8.8
Fixed drug eruptions	22	8.4
Anaphylactic reactions	16	6.1
Psychosis	10	3.8
Nausea and vomiting	10	3.8
Diarrhea	9	3.4
Ototoxicity	8	3.0
Pruritus	7	2.6
Discoloration of skin and nails	6	2.2
Hyperpigmentation	5	1.9
Breathlessness	5	1.9
Bodyache	7	2.6
Swelling on lips	4	1.5
Nephrotoxicity	4	1.5
Dizziness	5	1.9
Bullous eruptions	3	1.1
Photodermatitis	4	1.5
Fever	4	1.5
Gastritis	4	1.5
Others	42	≤1.1 each

Out of 261 ADRs reported, most common ADRs were skin rashes (24.1%) (Table 1) followed by jaundice (8.8%) and fixed drug eruptions (8.4%) (Figure 4).

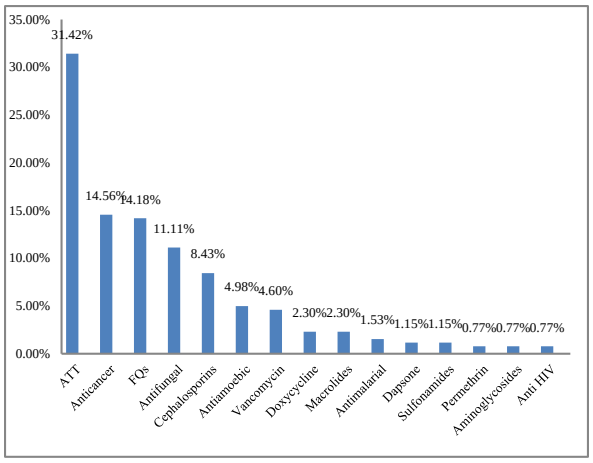

Figure 5: Class wise distribution of suspected drugs.

Least number of ADRs reported were redman syndrome, constipation, mucosal erosions, convulsions, giddiness (1.1% each), anemia, hepatitis, backpain, alopecia, oral ulcers, facial swelling, generalized erythema, acneiform eruptions (0.07% each) and drug induced lupus erythematosus, gum hypertrophy, arrhythmia, dysfunctional uterine bleeding, hand foot syndrome, irregular menstruation, keratoconjuctivitis, leucocytoclastic vasculitis, toxic epidermonecrolysis, steven Johnson syndrome (0.03% each) (Table 1). Maximum number of ADRs was suspected to be caused by Anti Tubercular drugs (31.42%), followed by anticancer drugs (14.56%), fluoroquinolones (14.18%), anti-fungal (11.11%), cephalosporins (8.43%), antiamoebic (4.98%) and vancomycin (4.60%). Least number of ADRs were suspected to be caused by macrolides, doxycycline, antimalarial, sulphonamides, dapsone, anti-HIV drugs, permethrin and aminoglycosides (Figure 5).

DISCUSSION

ADRs are frequently seen with the medicines, therefore assessing and detailed study of each adverse event is an important part of recording and reporting under the pharmacovigilance programme.[1,8] Therefore, describing pattern of the ADR must be kept in mind while reporting of the ADR of the medicines. In this retrospective study a total of 261 ADRs were reported during the study period. In the current study, ADRs were reported maximally from male patients which is similar to other studies conducted elsewhere.[9,10] Adult patients accounted maximum number of ADRs. The results of our study are in accordance with another study conducted by Arulappen et al in which ADRs were higher in adults as compared to pediatrics and geriatrics age group.[9] 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. Maximum number of ADRs was reported from skin and VD department, chest and TB department followed by oncology department. Whereas in other studies conducted by Arualeppan et al and Shamna et al general medicine was the department where maximum ADRs were reported.[9,10] 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.[9,11] Most of the ADRs were probable in our study which is in accordance with the studies conducted by Arulappen et al, Reema et al in which most of the ADRs were probable in nature.[9,12] Maximum numbers of ADRs were reported by use of antitubercular drugs, anticancer drugs and fluoroquinolones. In other studies, also, antibiotics were maximally responsible for most of the ADRs.[9,12] One study by Jayanthi et al shows that β lactams were responsible for maximum ADRs.[11]

Limitations

Limitations of current study were; it was conducted in a single AMC centre, so large numbers of ADRs were not reported and due to voluntary/spontaneous nature of reporting, probably lesser number of ADRs had been reported.

CONCLUSION

ADRs due to antibiotics and anticancer agents is 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.

These ADRs can be easily identified and managed with active vigilance and timely reporting.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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