International Journal of Basic & Clinical Pharmacology
Singh A et al. Int J Basic Clin Pharmacol. 2020 Apr;9(4):625-632
http://www.ijbcp.com
pISSN2319-2003 | eISSN2279-0780

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20201189

Original Research Article

Pattern of adverse drug reactions reported at a tertiary care teaching hospital in northern India

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Received: 28 January 2020
Revised: 09 March 2020
Accepted: 11 March 2020

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ABSTRACT

Background: Adverse drug reactions (ADRs) are among the leading cause of morbidity and mortality in hospital setup. This study was conducted with the aim of understanding the pattern and occurrence of ADRs to minimize their risk and safeguard public health.
Methods: This study is a retrospective analysis of pattern of ADRs reported at ADR monitoring centre (AMC) in a tertiary care hospital. A total of 207 spontaneous ADR reports collected over a period of 18 months were analysed for pattern and type of reactions, demographic profile of patients, organ system affected by ADRs, causative drugs, route of drug administration, severity of reaction, their outcome, management and causality assessment.
Results: Most common age group affected by ADRs was 41-50 years with almost equal involvement of male and female gender. Cutaneous reactions involving skin like rashes and itching were most common ADRs. The most common causative drug for ADRs were antimicrobials agents like Penicillin and Cephalosporin group of antibiotics. Orally administered drugs were most commonly involved in causing ADRs. Most of the ADRs belonged to Type A category, were non-serious and moderate in severity. Most of the patients recovered from the ADRs on stopping the suspected drug. On assessing the causality, most of the ADRs were probable with the suspected drugs.
Conclusions: Most of the patients recover from ADRs with appropriate and timely intervention, but it is important to understand the pattern and occurrence of ADRs for patient safety and this is possible only with an effective and robust pharmacovigilance system.

Keywords: Adverse drug reaction, AMC, Causality assessment, Pharmacovigilance

INTRODUCTION

Medicines are intended for treatment and better outcome but still there are possibilities of occurrence of adverse drug reactions. Adverse drug reaction is defined as "a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of the disease or for the modifications of physiological function."[1] According to various studies, adverse drug reactions are one of the leading causes of morbidity and it accounts for a significant number of hospital admissions in India and worldwide. A study in India reported overall incidence of 9.8% ADRs including 3.4% of total hospital admissions and 3.7% ADRs developed during hospital stay.[2] Hence, understanding the benefit and risk of drug therapy is necessary for which an effective nationwide pharmacovigilance system is essential.

Pharmacovigilance (PV) is defined by the WHO as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem".[3] Pharmacovigilance Programme of India (PvPI) was operationalized in July, 2010 by Ministry of Health and Family Welfare, Government of India. The AIIMS, New Delhi was established as National Coordination Centre (NCC) for PvPI. 22 ADR Monitoring Centres (AMCs) had been set up under this programme. In 2011, NCC was shifted to Indian Pharmacopoeia Commission (IPC), Ghaziabad. During last 7 years PvPI has collaborated with several national health programmes and research institutions and the number of AMCs (ADR Monitoring Centres) has increased to more than 250. In 2017, the Pharmacovigilance Programme of India (PvPI)- Indian Pharmacopoeia Commission (IPC), in Ghaziabad, India, became a WHO Collaborating Centre.[4] Since there exist considerable social and economic consequences of adverse drug reactions, there is a need to engage healthcare professionals and the public at large, in a well-structured programme. The vision of PvPI is to improve patient safety and welfare in Indian population by monitoring drug safety and thereby reducing the risk associated with use of medicines.[5] Our AMC (adverse drug reaction monitoring centre) is designated under PvPI and is working for the safety and welfare of patients by early detection, reporting and monitoring of ADR in hospital setup and by providing its prompt and appropriate management. This is a retrospective study done to analyze the ADR reported at our AMC to know the type and pattern of ADR reported, demographic profile of patients, organ system involved, causative drugs, severity, outcome, management and causality assessment, in view of improving health safety of patients.

METHODS

All the ADR reported in the study duration were included in this study. The ADRs were collected from various departments at our AMC, on the "suspected adverse drug reaction reporting form" from the health care professionals, as prescribed by IPC.[6] Causality for ADRs were assessed according to WHO Uppsala Monitoring Centre (UMC) Causality Assessment Criteria.[7] The Pv associate at our AMC then uploads the reports in Vigiflow software and send it to NCC, IPC Ghaziabad which is further send after analysis to Uppsala Monitoring Centre, Sweden for maintaining ADR database, further analysis and signal detection.[8]

A total of 207 suspected ADR reports were received from various department at our AMC from September 2017 to February 2019. These reports were analysed retrospectively for the demographic profile of patients, type and pattern of ADRs, causative drugs, severity of ADRs, their outcome, management and causality assessment.

This study was done after getting ethical clearance from the Institutional Ethics Committee, strict confidentiality was maintained about the particulars of involved patients during the study. Data analysis was done using descriptive statistical analysis.[9]

RESULTS

The age group most commonly involved with ADRs was in the range of 41-50 years (n=44, 21.25%) followed by 51-60 years (n=39, 18.84%) and then 21-30 years (n=38, 18.35%). The gender distribution was almost equal for both males (n=104, 50.25%) and females (n=103, 49.75%) as shown in Figures 1 and 2.

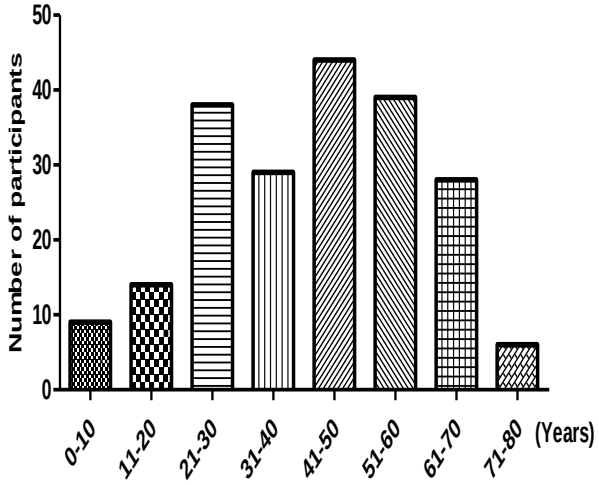

Figure 1: Age distribution.

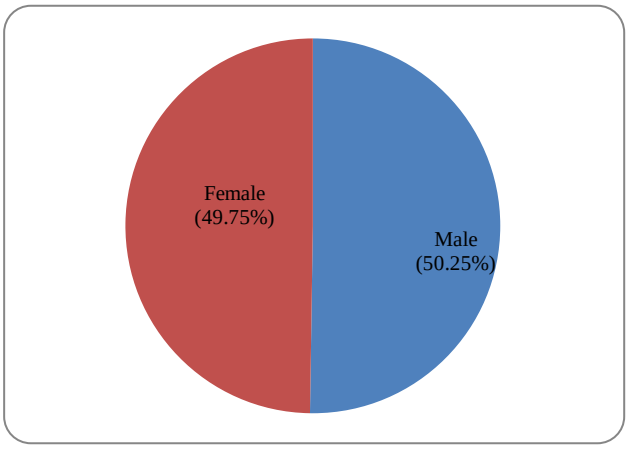

Figure 2: Gender distribution.

Cutaneous ADRs (n=92, 44.44%) involving skin like rashes and itching were the most common ADRs reported by various departments. This is followed by generalized ADRs (n=52, 25.12%) like whole body discomfort, chills and rigors, and then gastrointestinal ADRs (n=20, 9.66%) like vomiting, abdominal pain, and diarrhoea (Table 1).

The drugs involved most commonly with ADRs were Antimicrobial agents (n=62, 29.95%) belonging to Penicillin and Cephalosporin group, followed by drugs acting on central nervous system (n=41, 19.80%) like Antiepileptics and Antidepressants which is then followed by Anti-cancer drugs (n=24, 11.59%) like Paclitaxel and Rituximab (Table 2).

Table 1: Pattern of ADRs involving different organ systems.

ADRs	Value
Cutaneous	(44.44 %)
Skin rashes	61
Itching	16
Skin inflammation	7
Hyperpigmentation	2
Exfoliation	2
Ecchymotic patches	1
Thrombophlebitis	1
Stevens Johnsons syndrome	1
Pimples on face	1
Generalised ADR	52 (25.12%)
Chills and rigors	16
Body discomfort	15
Generalised swelling	9
Dizziness	4
Weakness	3
Lymphadenopathy	1
Muscle cramps	1
Generalised inflammation	1
Giddiness	1
Generalised oedema	1
Gastrointestinal ADRs	20 (9.66%)
Vomiting	5
Abdominal pain	5
Diarrhoea	4
Hepatitis	2
Nausea	1
Loss of appetite	1
Difficulty in eating and drinking	1
Gastritis	1
Central nervous system ADRs	13 (6.28%)
Sleepiness	4
Sedation	2
Tingling	2
Headache	2
Tremors	1
Stiffness	1
Cardiovascular ADRs	12 (5.79%)
Palpitation	11
Hypertension	1
Respiratory system ADRs	10 (4.83%)
Dyspnoea	7
Chest pain	2
Hematological ADRs	4 (1.93%)
Thrombocytopenia	3
Pancytopenia	1
Renal system ADRs-	3 (1.44%)
Hyperuricaemia	2
Uremia	1
Endocrine system ADRs	1 (0.48%)
Gynaecomastia	1

Table 2: Suspected drugs causing ADRs.

ADRs	Value
Antimicrobial agents (antibiotics)	62 (29.95%)
Ceftriaxone	8
Piperacillin+tazobactum	7
Ciprofloxacin	6
Isoniazid+rifampicin	5
Amoxicillin+clavulanic acid	4
Pyrazinamide	3
Aztreonam	2
Tigecycline	2
Meropenem	2
Colistimethate sodium (Colistin)	2
Vancomycin	2
Teicoplanin	2
Linezolid	2
Polymyxin B	2
Cefuroxime	1
Clarithromycin	1
Lamivudine+tenofovir+efavirenz	1
Cefoperazone+sulbactam	1
Cefixime	1
Amphotericin B	1
Ticarcillin+clavulanic acid	1
Imipenem+cilastatin	1
Moxifloxacin	1
Fluconazole	1
Penicillin G	1
Voriconazole	1
Rifampicin	1
Drugs acting on central nervous system	41 (19.80%)
Pregabalin	6
Amitryptiline	4
Valproic acid	4
Gabapentine	4
Notriptyline	4
Oxcarbazepine	3
Phenytoin	3
Tramadol	2
Duloxetine	2
Levetiracetam	2
Cinnarizine	1
Topiramate	1
Vilazodone	1
Pyridostigmine	1
Mirtazapine	1
Buspirone	1
Mannitol	1
Chemotherapeutic agents (anti-cancer drugs)	24 (11.59%)
Paclitaxel	10
Rituximab	5
Oxaliplatin	3
5-Fluoro uracil	1
Carboplatin	1
Docetaxel	1
Etoposide	1
Erlocip	1
Gefitinib	1

Continued.

ADRs	Value
Nutritional supplements and electrolytes	19 (9.17%)
Human albumin	7
KCl	2
Celemin hepa	2
Normal Saline	2
Cobamamide	1
Pyridoxine	1
Evion	1
Folic acid	1
Vitamin D3	1
Ringer lactate	1
Cardiovascular drugs	16 (7.72%)
Amlodipine	4
Metoprolol	4
Rosuvastatin	2
Telmisartan	1
Amiodarone	1
Enalapril	1
Carvedilol	1
Atenolol	1
Ivabradine	1
Gastrointestinal drugs	14 (6.76%)
Domperidone	5
Ondansetrone	2
Metoclopramide	1
Bifilac	1
Raberprazole	1
Furazolidone	1
Dicyclomine	1
Metronidazole	1
Norfloxacin+tinidazole	1
Non-steroidal anti-inflammatory drugs	10 (4.83%)
Etoricoxib	5
Indomethacin	2
Aceclofenac	1
Paracetamol	1
Aspirin	1
Endocrine system drugs	10 (4.83%)
Levothyroxine	2
Ergocalciferol	2
Calcium carbonate	2
Dexamethasone	1
Canagliflozin	1
Megesterol	1
Metformin	1
Renal system drugs	4 (1.93%)
Spironolactone+torasemide	2
Furosemide+amiloride	1
Alfuzosin hydrochloride	1
Haematological system drugs	3 (1.44%)
Vitamin K (Phytomenadione)	1
Clopidogrel	1
Iron-Sucrose	1
Anti-histaminic drugs	3 (1.44%)
Hydroxyzine	1
Monteleukast+fexofenadine	1
Levocetrizine	1
Vaccine	1 (0.48%)
DPT	1

According to Rawlins and Thompson classification 74.87% ADRs (n=155) belonged to type A (augmented or predictable) category and 25.12% ADRs (n=52) belonged to type B (bizarre/unpredictable) category (Figure 3).[10]

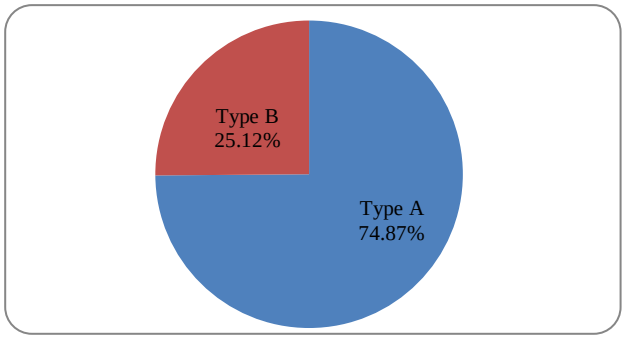

Figure 3: Type of ADRs.

Oral route of drug administration accounts for 57% (n=118) ADRs, I.V. route for 42.51% (n=88) while I.M. route for only one ADR (n=1, 0.48%) out of total cases (Figure 4).

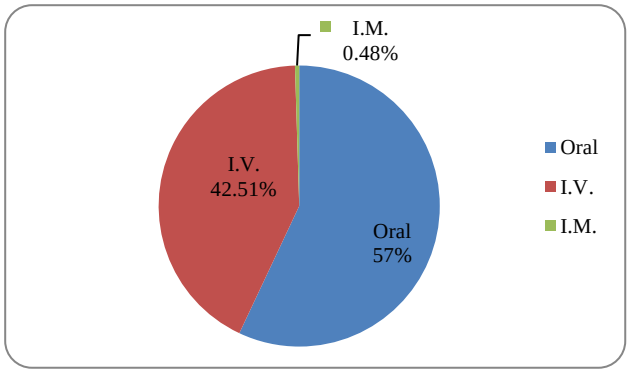

Figure 4: Route of drug administration.

For assessing the severity of ADRs, modified Hartwig and Siegel Scale was used.[11] According to this scale, maximum ADRs belonged to moderate category (n=111, 53.62%), mild category ADRs were 43.96% (n=91) while only 2.41 % ADRs (n=5) were severe (Figure 5).

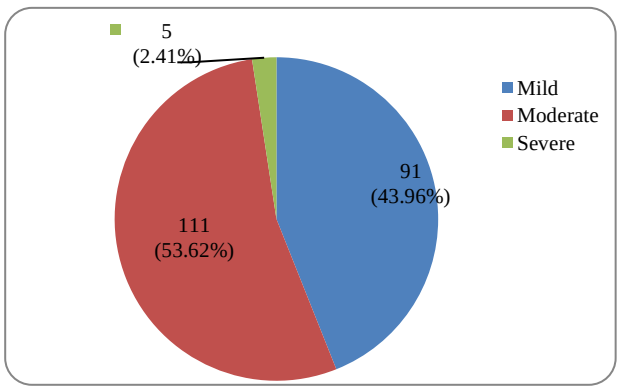

Figure 5: Severity of ADR.

The WHO-UMC Causality Assessment Criteria was used for assessing causality of ADRs. According to this criteria, maximum ADRs (n=195, 94.20%) were probable 2.89% (n=6) were possible, 1.44% (n=3) were certain while 1.44% (n=3) were unlikely with the suspected drug (Figure 6).

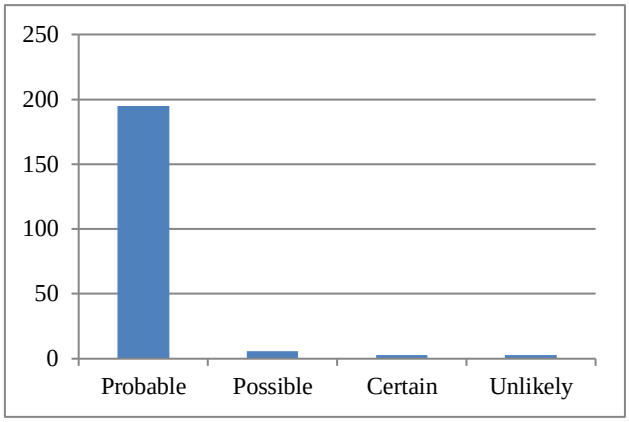

Figure 6: Causality assessment of ADRs.

Most of the ADRs (97.58%, n=202) were non-serious while only 2.41% (n=5) were serious in nature. The patients who recovered from the ADR after taking appropriate steps like stopping the suspected drug were 59.90% (n=124), patients who did not recover at all were 39.61% (n=82) while 0.48% (n=1) one case was fatal which led to death of the patient.

Table 3: Seriousness, outcome, and management of ADRs.

Serious: 5 (2.41%)	Recovered: 124 (59.90%)	Suspected drugs stopped: 117 (56.52%)
	Not-recovered: 82 (39.61%)	Suspected drugs stopped then re-started: 4 (1.93%)
Non-serious: 202 (97.58%)	Fatal (death): 1 (0.48%)	Suspected drugs not stopped: 86 (41.54%)

In 56.52% (n=117) cases, the suspected drug was stopped completely after ADR was noticed in 1.93% (n=4) cases, the suspected drug was restarted after stopping once the symptoms subsided while in 41.54% (n=86) cases the drug was not stopped and was continued after assessing the risk and benefit of the therapy as the ADR was less important than the benefit of the drug therapy for the patient (Table 3).

DISCUSSION

ADRs belong to one of the major causes of morbidity and mortality in hospital setup, but most of the cases remain below the tip of iceberg due to lack of reporting of such cases. This study was done to analyse the ADRs reported

at AMC, retrospectively for the pattern and type of ADRs, causative drugs, demographic profile of patients, type and severity of ADRs and their causality assessment.

A total of 207 suspected ADR reports were received from various departments at our AMC over a period of 18 months, from September 2017 to February 2019. The pattern of gender distribution of these ADRs showed that male and female patients suffering from ADRs were almost equal, male (50.25%) and female (49.75%), which is just coincidental finding as several other studies showed male preponderance[12-14] while few studies showed female preponderance.[15,16] Thus, it is concluded that gender does not influence the ADRs due to drugs. The age group affected most commonly with ADRs were in the age range of 41-50 years (21.25%), as found in other studies also.[17,18] The age group most commonly involved also depends on the type of disease for which the patients are visiting particular hospital setup. As there are diseases which affect a particular age group and so the ADRs caused by such treatments will also affect only that particular age group of patients.

The organ system affected most commonly by ADRs was cutaneous reactions involving skin (44.44%) followed by generalized ADRs (25.12%) involving whole body and further followed by ADRs affecting gastrointestinal system (9.66%). Similar patterns were also found in other studies.[19,20]

The commonest ADRs reported by patients were rashes, itching, whole body discomfort, chills, rigors, vomiting, abdominal pain and diarrhoea which is also similar to other studies.[21]

The drugs most commonly suspected to be causing the ADRs belong to Antimicrobial agents (29.95%). Antibiotics like Penicillin and Cephalosporins were most commonly involved. This is followed by drugs acting on central nervous system (19.80%) like Antiepileptics and Antidepressants which is further followed by Anti-cancer drugs (11.59%) like Paclitaxel and Rituximab. These findings are in agreement to another similar study.[22] Patients given drugs by oral route were most commonly affected by ADRs (57%) in present study followed by I.V. route (42.51%) and I.M. route with only one case (0.48%). According to Rawlins and Thompson classification of ADRs, 74.87% ADRs belonged to Type A category while 25.12% ADRs were of Type B category. Majority of ADRs were non-serious (97.5%) and only 2.41% were serious, which is similar to another study.[22]

Most of the patients recovered from the ADRs (59.90%) while 39.61% patients did not recover at all and only one case (0.48%) was fatal which led to death of the patient. In 56.52% patients, the suspected drug was stopped in 1.93% cases it was restarted again after stopping, when the symptoms of ADR subsided while in 41.54% cases the drug was not stopped at all. According to modified Hartwig and Siegel scale, 53.62% ADRs belonged to moderate category, 43.96% ADRs were of mild category while only 2.41% ADRs were severe. These patterns of ADRs were consistent with other similar studies.[23,24]

The causality of ADRs were assessed according to WHO-UMC causality assessment criteria and it was found that maximum ADRs were probable (94.20%), 2.89% were possible while only 1.44% belonged to both certain and unlikely category. These findings were similar to a study but different from results obtained in other studies.[25,26]

Limitations

There are certain limitations of this study, most common being underreporting of ADRs by health care professionals (HCPs). Although we have conducted many sensitization programmes for increasing awareness among HCPs, but still under reporting remains the most important limitation of spontaneous reporting of ADRs.

Another limitation is short duration of study period because, after this duration our Pv associate was transferred to NCC, Ghaziabad due to some reasons. Lack of patient follow-up is another limitation.

So present results may not be generalized on large scale as the study was confined to our AMC only, still the findings will contribute to the pattern of ADRs reported in tertiary care hospitals.

CONCLUSION

This study concluded that the age group most commonly affected by ADRs was in the age range of 41-50 years with equal frequency in both male and female gender, although these may be incidental findings. Cutaneous reactions like rashes and itching were the most commonly reported ADRs and antimicrobial agents like Penicillin and Cephalosporin group of antibiotics were the most common causative drugs leading to ADRs.

Drugs administered orally were most commonly involved in causing ADRs in this study. Most of the reactions were non-serious and moderate reactions in which the patient recovered from the symptoms of ADRs after stopping the suspected drugs. Only one case was fatal which led to death of the patient. Also, most of the reactions were Type A reactions and were probable with the suspected drugs.

This study apart from its few limitations, stresses on the need of an effective and robust pharmacovigilance system for ADR monitoring and also strongly suggests that ADR reporting concepts need to be enhanced among health care professionals, to safeguard public health.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by Institutional Ethics Committee

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Cite this article as: Singh A, Jain A, Soni M, Shukla P, Lahon J, Verma AK. Pattern of adverse drug reactions reported at a tertiary care teaching hospital in northern India. Int J Basic Clin Pharmacol 2020;9:625-32.