Analysis of reporting of adverse drug reactions in a tertiary care hospital: One year survey

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Abstract

Introduction: Adverse drug reactions (ADRs) are inevitable component of drug therapy which negatively affects quality of life, increases physician visits, hospitalizations and even death. It also poses economic burden on health care system.

Aim: To ascertain various ADRs occurring in our hospital; this can generate a notion to inculcate the culture of ADR reporting in view of improving the health safety of patients.

Materials and Methods: A retrospective, record based study, conducted by analyzing ADR forms, reported over a period of 12 months and were further analyzed for demographic details, organ system involved, types of ADRs, suspected drugs, causality, severity, outcome and reporters qualification.

Results: A total of 532 ADR reporting forms were studied in which 563 types of ADRs were seen. Male preponderance (57.1%) was seen with majority of ADRs between 40-59 yrs. of age (33.2%). Gastrointestinal tract (47.24%) was most commonly affected with abdominal pain, diarrhea and nausea. Antibiotics were the most common suspected group of drugs. Majority of ADRs were probable/likely (46.35%) and were of moderate category (56.12%). Most of the patients recovered/resolved (91.35%) from the reaction and majority of reports was from non-health professionals/consumers (53.19%).

Conclusions: Results drawn from this study suggests reinforcing Pharmacovigilance Programme of India as it can help in minimization/prevention of ADRs through early detection. Also, it would be helpful if the system of ADR monitoring is designed in such a way that it encourages health care professionals to report ADRs spontaneously and intensively through a proper communication channel for ensuring patient safety.

Keywords: Adverse drug reaction, Antibiotics, ICSR, IPC, PvPI

Introduction

The evolution of drugs in last decade has given significant benefit to patients but at the same time incidence of Adverse Drug Reaction (ADR) has considerably inflated. ADR as defined by World Health Organization (WHO) is 'a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function'.[1] ADR negatively affects the quality of life, increases physician visits, hospitalizations and even death. It has been observed that drug induced conditions leads to 5% of all hospital admissions and 10–20% of hospitalized patient develops ADRs.[2] The morbidity and mortality associated with ADRs also poses great economic burden on the health care system of country. In many countries, it ranks among top ten leading cause of morbidity and mortality in both ambulatory as well as in hospitalized patients.[3] The risk of ADRs is an intrinsic intimidation to all drug therapy and is influenced by certain factors such as dose, frequency, duration of therapy, drug interactions, genotype and pharmacokinetic profile of special age group patients such as pediatric and geriatric. Due to the soaring prevalence and at times potentially serious repercussion of drug therapy, ADRs may have a dramatic impact in clinical practice and on the health of society.[4] Therefore, ADR reporting is an important component of monitoring and evaluating drug activity in health care sector.[5,6]

Pharmacovigilance an important aspect in this domain aims at making the best use of drugs with the help of high quality data gathered through this reporting system. According to WHO, Pharmacovigilance is defined as 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem'.[7] WHO initially established its Programme for International Drug Monitoring in 1968. In 1978, Uppsala Monitoring Centre (UMC) a WHO collaborating centre was created in order to support this program. In India, in the year 2010 the Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services under the aegis of Ministry of Health and Family Welfare (MoHFW), launched the nationwide Pharmacovigilance Programme of India (PvPI). Indian Pharmacopoeia Commission (IPC), Ghaziabad under the MoHFW has been functioning as the National Coordination Centre (NCC) for PvPI since April 2011. Under this programme, till date 270 ADR Monitoring Centers (AMCs) had been formed in different medical colleges and hospitals covering the entire country. Owing to indefatigable effort by IPC and AMCs, since April 2011 there has been rapid progress in reporting of ADRs by the healthcare professionals[12] and the annual database of PvPI for year 2018-19 accounted for 64, 441 reports [13] Through these data PvPI regularly recommends the drug regulatory authorities and suggests the healthcare professionals for improving the safe use of drugs. However, despite the effort of national and international authorities, under-reporting is still quite common, i.e., only 1% as compared to 5% in

other countries.[14,15] There is a considerable need to create and enhance awareness in community and healthcare professionals about the importance of monitoring of drug outcomes. Awareness regarding the detection, management, prevention, and reporting of ADR is utmost important for improving patient care and to reduce the cost. This study is thus aimed to strengthen the ADR database through retrospective analysis and compilation of the pattern of ADRs and suspected drugs reported to our AMC, which can generate a notion among clinicians of this region to inculcate the culture of ADR reporting in view of improving the health safety of patients. Moreover, the regional data generated from this study can also help in planning the institute/ state health policy.

Materials and Methods

This was a retrospective, record based study and was commenced after obtaining due approval from the Institutional Ethics Committee (1121/IEC/2019). This study was conducted by analyzing the suspected ADR forms which were reported over a period of 12 months (August 2018 to July 2019) from various clinical departments of our institute to its ADR Monitoring Centre i.e., Department of Pharmacology. A total of 532 reported ADRs were evaluated for mandatory parameters including patient's detail, type of ADR, drugs causing ADR, etc. as per Standard Operating Procedure (SOP) of IPC, Ghaziabad and

was further studied retrospectively with the help of Individual Case Safety Reports (ICSRs) and other additional documents such as prescriptions and investigation reports (where necessary). After analysis, results were categorized as follows:
1. Demographic detail of patients
2. Organ system involved
3. Types of ADRs
4. Suspected drugs causing ADRs
5. Causality assessment of ADRs
6. Severity assessment of ADRs
7. Outcome of ADRs
8. Reporters qualification

Results were presented in tabular form, pie chart and bar diagram in appropriate proportions and percentages. This study was done after maintaining strict confidentiality about the particulars of involved patients.

Results

During one year, i.e., from August 2018 to July 2019 a total of 532 ADR reporting forms were collected which were consequently reported in which 563 types of ADRs were seen. The gender distribution showed male preponderance as compared to females. The majority of patients who suffered from ADRs were between 40-59 yrs. of age. (Table 1)

Table 1: Demographic details

Gender distribution	Number of patients (Total=532)	Percentage of patients
Male	304	57.1
Female	228	42.8
Age distribution	Number of patients (Total=532)	Percentage of patients
0-19	41	7.7
20-39	174	32.7
40-59	177	33.2
>60	140	26.3

On analysis of the organ systems, gastrointestinal tract (GIT) was most commonly affected followed by central nervous system (CNS), skin, generalized, cardiovascular system (CVS), respiratory system, and hematological system. From the respective systems the most common types of ADRs were abdominal pain, diarrhea, nausea, headache, dizziness, insomnia, rash, pruritus, fatigue myalgia, palpitation, cough and anemia. (Table 2)

Table 2: Organ System and associated ADRs

Organ systems involved	Types of ADRs	n (%)
Gastrointestinal tract	Abdominal pain (67), Diarrhoea (46), Nausea (46), Dry mouth (41), Constipation (26), Vomiting (16), Dyspepsia (07), Indigestion (04), Anorexia (04), Heartburn (03), Dysguesia (03), Stomatitis (02), Bloating (01)	266(47.24%)
Central nervous system	Headache (42), Dizziness (27), Insomnia (20), Drowsiness (17), Sleepiness (07), Tremor (05), Restlessness (04), Nervousness (02), Vertigo (02), Sweating (02), Mood swings (01)	129(22.91%)
Skin	Rash (41), Pruritus (27), Angioedema (02), Alopecia (01)	71(12.61%)

Generalized	Fatigue (17), Myalgia (14), Blurred vision (09), Weakness (06), Fever (06), Arthralgia (04), Dysuria (03), Hypoglycemia (02), Weight loss (01), Hyperuricemia (01)	63(11.19%)
Cardiovascular system	Palpitation (08), Hypotension (06), Chest pain (03), QTc prolongation (01)	18(3.19%)
Respiratory system	Cough (09), Dyspnoea (05)	14(2.48%)
Hematological System	Anaemia (02)	02(0.35%)

On total 477 drugs were suspected of causing 563 types of ADRs from which 124 drugs were antibiotics and were the most common group of drug associated with ADRs, followed by analgesics, hormones & related drugs, antidepressants, proton pump inhibitors, antihistaminics, miscellaneous drugs, antipsychotics, anticonvulsants, antihypertensives, antiemetics, diuretics, antiamoebics, antituberculars, antianxieties, anticancers, antihelmintics, beta blockers, hypolipidaemics, bronchodilators, antivertigo drugs, antivirals, 5α reductase inhibitors, muscle relaxants, antifibrinolytics, antiplatelets and antigout. From the respective groups, most offending drugs were Amoxicillin+clavulanic acid, Paracetamol, Prednisolone, Escitalopram, Esomeprazole, Levocetrizine, Pregabalin+Nortriptylline, Olanzapine, Levetiracetam, Amlodipine, Ondansetron, Spironolactone+Torasemide, Metronidazole, Bedaquiline, Clonazepam, Cisplatin, Albendazole, Metoprolol, Rozuvastatin, Doxophylline, Betahistine, Tenofovir, Dutasteride, Tizanidine, Tranexamic acid, Clopidogrel and Febuxostat (Table 3)

Table 3: Suspected drugs causing ADRs

Antibiotics (n=124)	Amoxicillin+Clavulanic acid (17), Levofloxacin(16), Ceftriaxone (14), Azithromycin (11), Cefixime (11), Cefpodoxime (07), Cefuroxime (07), Cefoperazone+Sulbactam (06), Ofloxacin (06), Piperacillin+Tazobactam (04), Clarithromycin (04), Ciprofloxacin (03), Amikacin(03), Rifaximin (03), Doxycycline (03), Tetracycline (02), Moxifloxacin (02), Clindamycin (01), Linezolid (01), Faropenam (01), Ceftazidime (01), Moxifloxacin (01)
Analgesics (n=54)	Paracetamol (14), Tramadol (10), Dicyclomine+Mephenamic acid (08), Diclofenac (07), Aceclofenac (06), Piroxicam (04), Etoricoxib (02), Lornoxicam(01), Naproxen(01), Ibuprofen(01)
Hormones & related drugs (n=39)	Prednisolone (14), Thyoxine (08), Hydrocortisone(03), Deflazacort (02), Teneligliptin (02), Dexamethasone(02), Metformin (02), Loteprednol (01), Danazol (01), Medroxyprogesterone (01), Budesonide (01), Glibenclamide (01), Glimepiride(01)
Antidepressants (n=25)	Escitalopram (10), Amitriptyline (06), Sertraline (03), Mirtazapine (03), Paroxetine (02), Duloxetine (01)
Proton Pump Inhibitors (n=24)	Esomeprazole (14), Rabeprazole (10)
Antihistaminics (n=21)	Levocetrizine (07), Fexofenadine (06), Montelukast (05), Hydroxyzine (02), Cetrizine (01)
Miscellaneous drugs (n=19)	Pregabalin+Nortriptylline (05), Naproxem+Domperidone (03), Chlordiazepoxide+Clidinium (03), Calcium citrate (02), Benfotiamine (02), Pantoprazole+Flunarizine (02), Ferrous fumarate (01), Methylcobalamin (01)
Antipsychotics (n=18)	Olanzapine (09), Aripiprazole (04), Quetiapine (02), Flupenthixol (01), Palperidone (01), Clozapine(01)
Anticonvulsants (n=18)	Levetiracetam (11), Phenytoin (03), Lacosamide (01), Carbamazepine (01), Valproic acid (01), Topiramate (01)
Antihypertensives (n=18)	Amlodipine (8), Telmisartan (02), Cilnidipine (02), Nimodipine (02), Olmesartan (01), Carvedilol (01), Losartan (01), Ramipril (01)
Antiemetics (n=15)	Ondansetron (08), Domperidone (06), Granisetron (01)
Diuretics (n=13)	Spironolactone+Torasemide (06), Furosemide (05), Furosemide+Lasilactone (02)
Antiamoebic (n=12)	Metronidazole (08), Ornidazole (04)
Antituberculars (n=11)	Bedaquiline (09), Rifampicin(01), Pyrazinamide(01)
Antianxiety (n=10)	Clonazepam (07), Etizolam (02), Lorazepam (01)
Anticancer (n=10)	Cisplatin (04), Rituximab (02), Gemcitabine (02), Asparaginase (01), Methotrexate(01)
Antihelmintics (n=07)	Albendazole (05), Albendazole+Ivermectin (02)
Beta blockers (n=06)	Metoprolol (03), Labetalol (01), Timolol (01), Propranolol (01)
Hypolipidaemics (n=06)	Rozuvastatin (06)
Bronchodilators (n=05)	Doxophylline (02), Salbutamol (01), Aminophylline (01), Formoterol(01)
Antivertigo (n=04)	Betahistine(03), Cinnarizine+Dimenhydrinate(01)

Antivirals (n=03)	Tenofovir (02), Valacyclovir (01)
5α reductase inhibitors (n=03)	Dutasteride(02), Finasteride (01)
Muscle relaxants (n=03)	Tizanidine (02), Thiocolchicoside (01)
Antifibrinolytic (n=03)	Tranexamic acid (03)
Antiplatelet (n=03)	Clopidogrel (03)
Antigout (n=03)	Febuxostat (03)

The analysis of causality assessment showed that the maximum ADRs reported were probable/likely (46.35%). This was followed by possible (41.03%), unlikely (11.54%) and certain (1.06%). Conditional/Unclassified and Unassessable/Unclassifiable were found to be nil (Fig. 1)
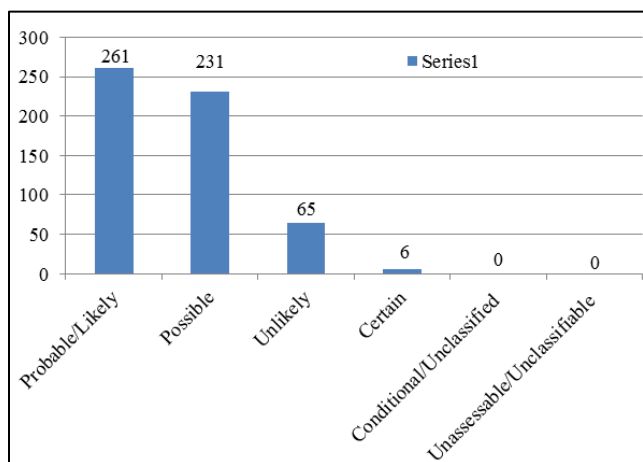
Fig. 1: Causality of reported ADRs

On analysis of severity assessment, it was found 56.12% ADRs belonged to moderate category, 43.33% ADRs belonged to mild category and 0.53% ADRs were of severe category (Fig. 2)
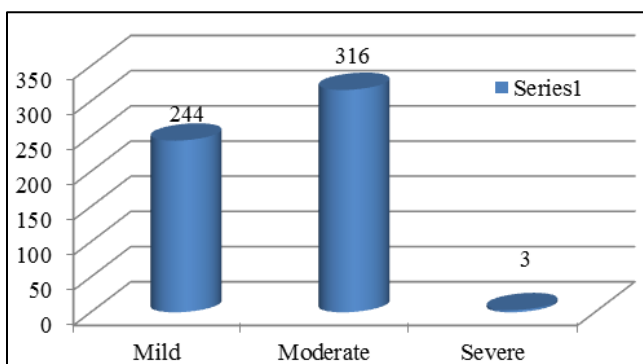

Fig. 2: Severity assessment of ADRs

The outcome of these ADRs was that most of the patients i.e., 91.35% recovered/resolved, 7.7% were recovering /resolving. The outcome of 0.75% cases was unknown and 0.18% case did not recovered/ongoing at the time of report (Fig. 3)
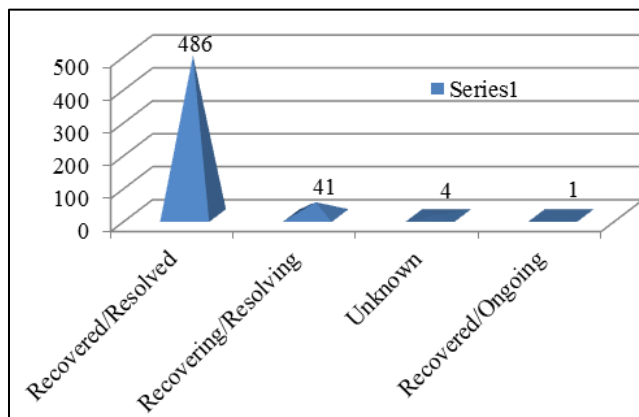

Fig. 3: Outcome of ADRs

The reporter qualification showed that 53.19% reports were from non-health professionals/consumers, 39.66% reports were from other health professionals and 7.14% were from physicians. (Fig. 4)
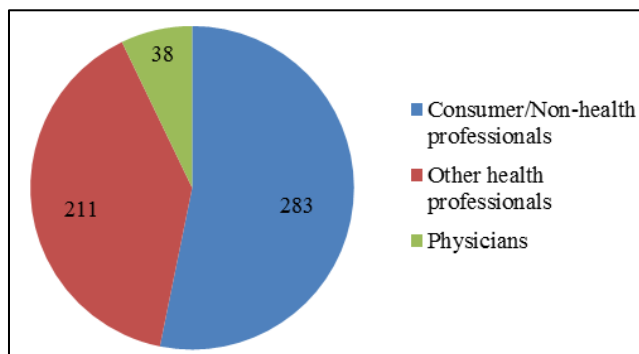

Fig. 4: Reporters qualification

Discussion

In this study, males were more affected with ADRs than females which are in concordance with several other studies.[16-18] However, some studies showed female preponderance which is in contrast to our study.[19,20] Thereby concluding that influence of gender is just an incidental finding and it does not affect number of ADRs reported. The age group most commonly affected was 40-59 years, which may be attributed to the more number of concomitant drugs being taken by this age group in our centre, this was similar in other studies also.[21,22]

The most common organ system affected with ADR was GIT and is consistent with some other studies[23,24] but it differs from reports of Fredy et al where skin manifestations had the highest rate, which was third highest in our study.[25]

The most common suspected drug responsible for ADRs were antibiotics which may be due to the reason that antibiotics were the most commonly prescribed either for prophylactic or curative therapy. The results were consistent with previous studies.[26-28] Analgesics were reported to be the second most common group of drug causing ADRs which in some other studies had been reported to be the most common group of suspected drugs.[18,29]

According to WHO-UMC causality assessment criteria[30] majority of the ADRs were of probable/likely category with the suspected drug, followed by possible, unlikely and certain. These results were similar to some studies but different from the results observed in them.[19,31,32] According to modified Hartwig and Siegel severity scale[33] major part of the ADRs belonged to moderate category, followed by mild and severe category. These patterns of ADRs were consistent with other studies.[34,35] In outcome of the reactions, most of the patients have shown recovery after the withdrawal of offending drug and/or with treatment of ADRs, followed by recovering/resolving, unknown outcomes and only one severe case at the time of respective reports.[24]

The present study showed that major reporting was done by non-health professionals/consumers who were followed by other health professionals and physicians accounted for least number of reports. There are various probable reasons identified for underreporting which in part happens due to the voluntary notification system mainly. Other reasons could be attributed to lack of attitude, time constraint, work overload of healthcare professionals, having misbelief that adverse events that are already known and which have a causal relationship with the offending drug are not to be reported, hesitancy of health professionals to report because they fear litigation and think reporting might go against them. Similar trend and rational has also been stated by other studies.[2,24] However, all the health care professionals extended their support in validating the ADRs.

This study has quite limitations, such as; due to the nature of our study, sensitization of health care professional regarding ADR reporting cannot be done. Due to lack of communication and consequently scanty documentation at the time of reporting we were not able to draw results in parameters such as preventability assessment, action taken due to ADR, management of ADRs, concomitant medications and relevant medical/medication history. In future, fluent communication between AMCs and healthcare professional/ consumers could help in documenting more relevant information which could mitigate these drawbacks.

Conclusion

The present study exhibits an exemplary profile of the ADRs which strongly suggests that it is need of the hour to reinforce the existing Government's Pharmacovigilance Programme of India as it can help in minimization or prevention of ADRs through early detection and effective communication, which can ultimately help each patient to receive optimum therapy. Knowing the importance of this programme, our AMC has been working tirelessly since its recognition by IPC, i.e., December 2012 and has reported 1999 cases to IPC till December 2019. In past various sensitization activities had been conducted/organized by our AMC in form of seminar/workshop for health care professionals and street-shows for consumers/non-health professionals. In addition to this, toll-free number of IPC and contact number of our AMC has been incorporated in the OPD prescription of our institute for better and easy communication which resulted in considerable reporting by non-health professionals/consumers. Much has been done but more is to be done. Hence, it would be more helpful if the system of ADR monitoring is designed in such a way that it encourages clinicians and other health care professionals to report ADRs spontaneously and intensively through a proper communication channel for ensuring patient safety.

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Conflict of interest
None.

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