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Original Research Article

A pharmacovigilance study of adverse drug reactions in a tertiary care hospital in Haryana

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ABSTRACT

Background: Adverse drug reaction (ADR) is an inevitable risk associated with all the prescribed medicines. They vary in severity & duration in any population. Thus, ADRs are monitored and assessed on a large scale in our country by the Pharmacovigilance programme of India through adverse drug reaction monitoring centres. This study was taken to assess the pattern of ADR reported in a tertiary care hospital in Haryana.
Methods: This study was conducted in the Kalpana Chawla Government Medical College, Karnal, Haryana from January 2018 to June 2019. ADRs were collected from different departments and were analysed according to gender, age, department wise distribution, drugs class involved and ADR that was reported.
Results: A total of 233 ADRs were reported in the above mentioned period. Females were affected more than males, maximum number reported in the age group of 21-60 years. The maximum number of ADRs reported was from Dermatology department. Antimicrobials were the class of drugs that were responsible for the maximum number of ADRs reported. Skin manifestations of various types were the most reported ADRs.
Conclusions: By keeping a careful and timely watch majority of the ADRS can be prevented by early intervention. There is also a need to ensure timely check on the drugs supplied by the various pharmaceutical companies who get the contract for government supply. This will be a step towards improving patient safety.

Keywords: Adverse drug reactions, Pharmacovigilance programme of India, Adverse drug reaction monitoring centres, Causality assessment

INTRODUCTION

An adverse drug reaction (ADR) may be defined as "any harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen or withdrawal of the product".[1] ADRs vary in severity and duration, and can be, appreciably, unpleasant and harmful.[2] The need for the monitoring of ADRs arose as Clinical Trials focused on the safety and efficacy of the therapeutic substance on the selected population. Many aspects of the drug thus remained unexplored.[3] The process of identifying and preventing ADRs is associated with postmarketed drugs i.e. pharmacovigilance, which is extremely important to protect patient health, economic burden associated with ADRs and circulation of large number of over-the-counter and counterfeit drugs in the market.[4]

The history of pharmacovigilance started 169 years ago, on January 29, 1848, when a young girl (Hannah Greener) of England died after receiving chloroform anesthetic before removal of an infected toenail. However, the reason of death could not be ascertained.[5] One of the first reported cases of ADRs was that of

aplastic anemia caused by chloramphenicol in the 1950s.[6] However the thalidomide tragedy in the 1960s was the one which alarmed the world of how toxic the effects of drugs can be and this led to the first international efforts to focus on drug safety in 1961 by WHO.[7,8]

In the middle of the 20th century 1964, there was a launch of yellow card in the UK, which was meant for spontaneous reporting of drug toxicity.[9] In 1968, the World Health Organization (WHO) promulgated the "Programme for International Drug Monitoring", a pilot project with the ulterior motive to centralize world data on ADR. The main objective of this "WHO Programme" was to identify the earliest possible pharmacovigilance (PV) signals. The term PV was proposed in the mid-70s by a French group of pharmacologists and toxicologist. As per their description PV was the assessment of the risks of side effects potentially associated with drug treatment.[10]

In India, a formal ADR monitoring system was started in 1986 with 12 regional centers. In 1997, India became the member of WHO Programme for International Drug Monitoring managed by the Uppsala Monitoring Centre (UMC), Sweden. At inception, 6 regional centers were set up in Mumbai, New Delhi, Kolkata, Lucknow, Pondicherry, and Chandigarh for ADR monitoring in the country.[11] To further enhance the ADR reporting system in India, the Health ministry launched a programme called Pharmacovigilance Programme of India (PvPI) under Central Drugs Standard Control Organisation (CDSCO) in the year 2010. Under the aegis of this program multiple adverse drug reaction monitoring centres (AMC) were established in India all the medical colleges approved by Medical Council of India (MCI).[12,13] The PvPI programme is coordinated by the Indian Pharmacopoeia Commission (IPC) which is located at Ghaziabad to publish official documents, by adding new and updating existing monographs in the form of Indian Pharmacopoeia which results in improving quality of medicine.[13] Over 200 ADR monitoring centres (AMCs) in the country are now acknowledged to monitor and report ADRs.[14] The national ADR reports are sent to the UMCs individual case safety reports (ICSR) database system, VigiBase and is also responsible for generating possible signals and alerts.[15]

The spontaneous reporting systems, which is the method adopted in all the AMCs is the most common method of PV. It has thus played a major role in the detection of signals of new, rare and serious ADRs of drugs and making it easier for physicians, patients and pharmacists to report suspected ADRs to the PV centre.[16,17]

Thus an attempt was made to analyze pattern of all the ADR reports that were submitted in tertiary care teaching hospital in Northern Haryana.

METHODS

A retrospective analysis was done of ADRs that were submitted in the ADR monitoring centre established in the Department of Pharmacology of Kalpana Chawla Government Medical College, Haryana from January 2018 to June 2019.

The reports were collected by faculty and other staff of Department of Pharmacology by visit to the respective indoor and outdoor departments following initial communication received via telephonic call or Whatsapp or text message at the AMC. Detailed information regarding the suspected ADR was collected using the PvPI, ADR reporting form version 2.1.

On the basis of collected data, incidence rate was calculated and the ADRs were classified on the basis of age, sex and most common class of drugs causing them.

Assessment of severity was done using the modified Hartwig and Siegel's criteria which classifies severity of ADR as mild, moderate or severe and causality assessment was done using the "WHO causality assessment scale'', classified as certain, probable, possible, unlikely, unclassified and unclassifiable. Descriptive statistic was used to summarize and analyze the available data on nature and the frequency of various ADRs.

RESULTS

A total of 233 ADRs were submitted from the various departments of Kalpana Chawla Government Medical College in the period of from January 2018 to June 2019.

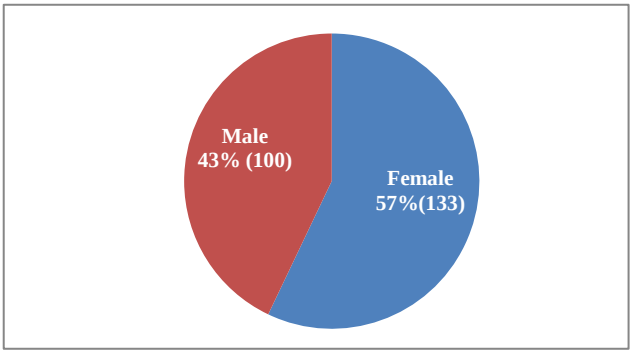

Figure 1: Gender wise distribution of ADRs.

Table 1: Age wise distribution of ADRs.

S. no	Age group (in years)	Number of ADRs	Percentage of total ADRs (%)
1	0-10	14	6
2	11-20	27	11.6
3	21-60	177	75.8
7	>60	15	6.4
Total		233	100

It was shown that out of these 233 ADRs collected, more were present in females (133, 53%) than in males (100, 43%) (Figure 1). It was clearly depicted that maximum number reported in the age group of 21-60 years (177, 75.8%) (Table 1).

Table 2: Department wise distribution of ADRs.

S. no	Department	Number of ADRs	Percentage of total ADRs (%)
1	Anaesthesia	1	0.4
2	Dental	8	3.4
3	Dermatology	60	25.8
4	ENT	3	1.3
5	Eye	1	0.4
6	Medicine	33	14.2
7	Obstetrics and gynaecology	24	10.3
8	Orthopaedics	26	11.2
9	Paediatrics	12	5.2
10	Psychiatry	11	4.7
11	Surgery	54	23.2
Total		233	100%

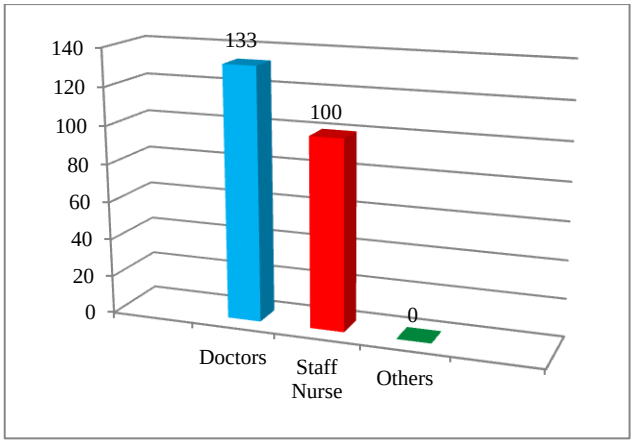

Figure 2: Distribution of reporters of ADR.

Department of dermatology had the maximum reported cases of ADRs during the period (60, 25.8%) followed by surgery department (54, 23.2%) (Table 2). Doctors (133) contributed maximum in the reporting of ADRs followed by the Staff nurse (100). There was no report from the patients directly (Figure 2).

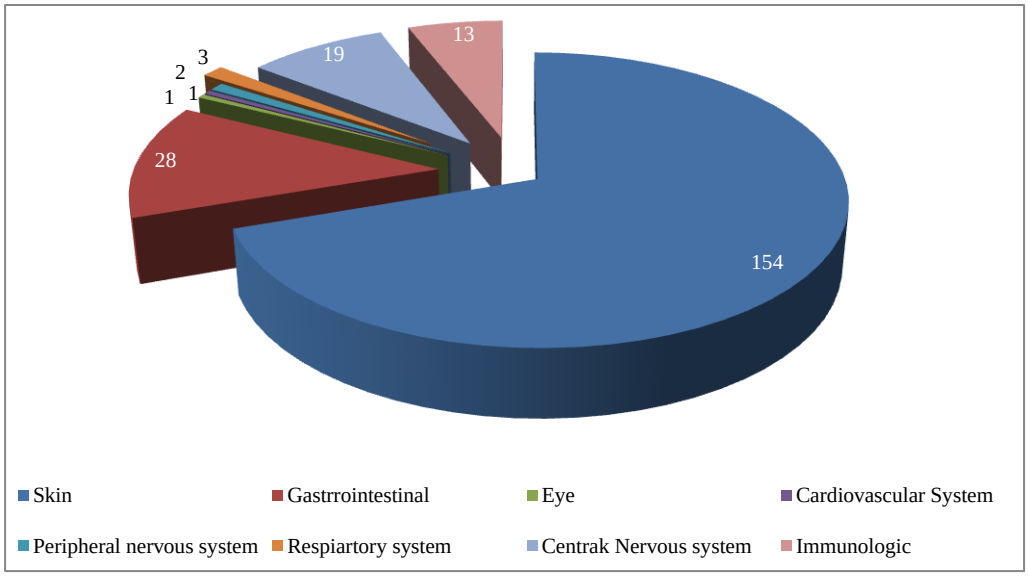

Figure 3: Organ system wise distribution of ADR.

Table 3: Distribution of ADRs amongst various classes of drugs.

S. no	Drug class	Number of ADRs	Percentage of total ADRs (%)
1	Antibiotics and antitubercular	105	45.1
2	Antihelminthics, antiprotozoal and antimalarials	14	6
3	Drugs for cough, bronchial asthma and antihistaminics	5	2.1
4	Antipsychotics	9	3.9
5	Antifungals	4	1.7
6	Antiepileptics	9	3.9
7	IV fluids, nutritional and supplements	20	8.6
8	NSAIDS, opioids and others analgesics	46	19.7
9	Miscellaneous	21	9.1
Total		233	100

Table 4: System wise involvement due to ADRs.

Organ system	ADR	Number	Organ system	ADR	Number
Skin	Rash/urticaria	80	**Central nervous system**	Restlessness	07
	Dermatitis	42		Headache	01
	FDE	16		Tremor	01
	TEN	01		Dizziness	06
	Erythema	06		Psychosis	01
	Exanthema	01		Vertigo	01
	Lichenoid-eruptions	02		Seizure	01
	Pemphigus vulgaris	01		Nocturnal enuresis	01
	Psoriatic erythema	01	**Immunological**	Chills and rigors	06
	Echymosis	01		Drug hypersensitivity	01
	AGEP (acute generalized exanthematous pustulosis)	01		Flare of infection	01
	Dryness of skin	01		Angioedema	13
	DRESS (drug rash with eosinophilia and systemic symptoms)	01	**Endocrine**	Amenorrhea inhibited orgasm	02 01
Gastrointestinal	Vomiting	10	**Musculoskeletal**	Periorbital edema	01
	Diarrhea	02	**Ophthalmology**	Congestion in the eye	01
	Bitter taste	01	**Peripheral nervous system**	Tingling and paresthesia	02
	Gastritis	04	**Respiratory**	Cough/dyspnoea	02
	Oral ulcer	04		Respiratory distress	01
	Nausea	07	**Cardiovascular**	Hypotension	01

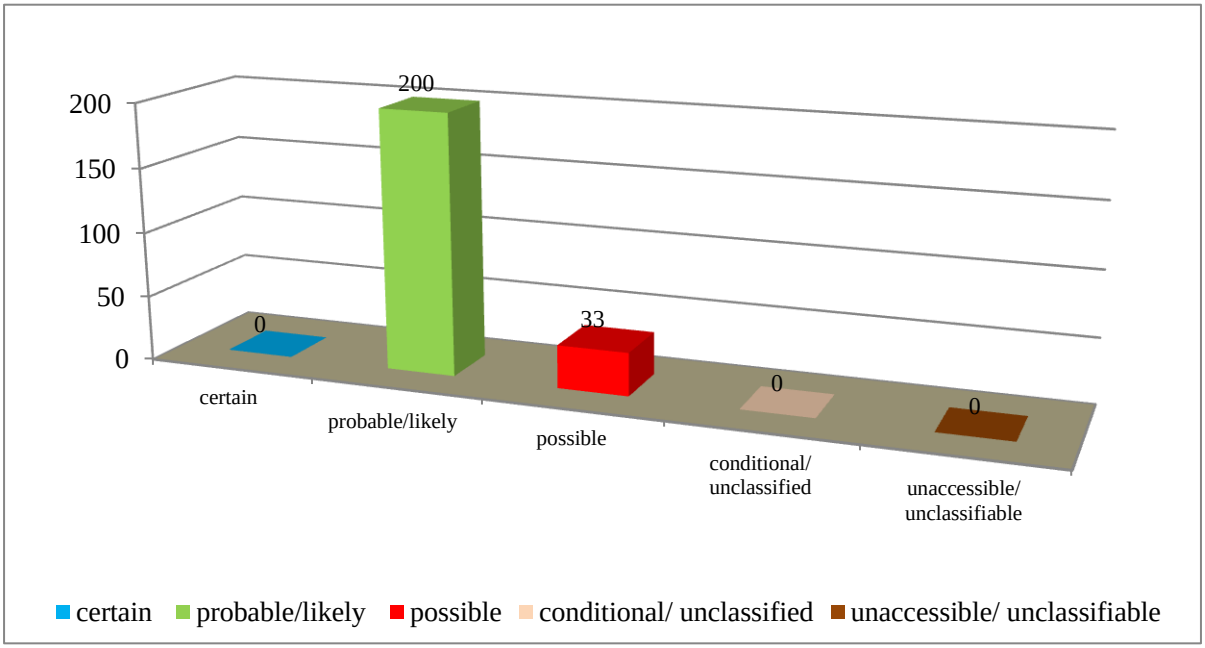

Figure 4: Causality assessment of ADRs.

It is evident that the organ system that was maximally affected was skin (154, 70%) followed by the gastrointestinal (28, 13%) (Figure 3). Table 3 depicts that ADRs among different class were highest for antibiotics and anti-tubercular (105, 45.1%) followed NSAIDS, opioids and others analgesics (46, 19.7%).

Rash/urticaria (80) was the most common manifestation of ADRs followed by dermatitis (42) and angioedema accounting for 13 cases (Table 4). Figure 4 shows according to WHO analysis of ADRs most of the ADRs were probable (200) followed by possible (33). Out of the 233 ADRs reported 195 were moderate followed by 35 mild, while there 3 cases which were severe (Figure 5).

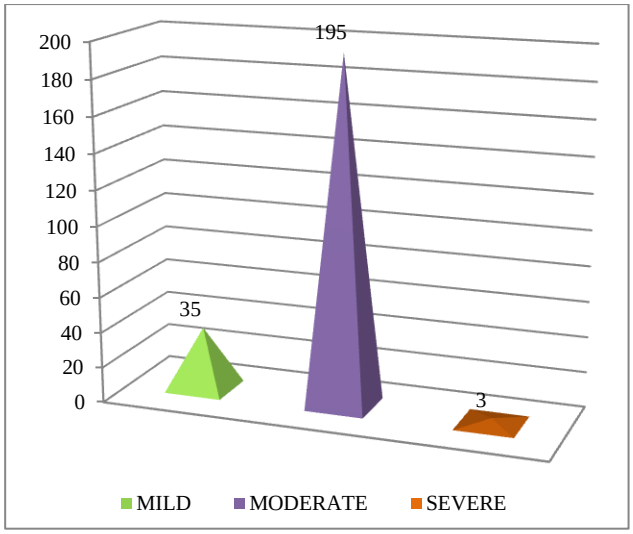

Figure 5: Assessment of severity of ADRs.

DISCUSSION

ADRs are collected from the AMCs and other authorized centre and this information is further conveyed to drug regulatory authorities like PvPI for any significant step on the drugs to improve the patient safety and welfare, and it is the responsibility of all healthcare professionals to support the PvPI in promoting safe use of medicine.[18]

A retrospective analysis of the ADRs that had been reported in the period of January 2018 to June 2019 to the department of Pharmacology, Kalpana Chawla Government Medical College was done. With During this period 233 ADRs were reported. Although ADRs were observed in both the genders but there was more of female preponderance. A study conducted by Sharma et al also showed similar disribution.[19]

In the present study, mainly the adult population showed maximum predilection. 177 (75.8%) cases out of the 233 reported in the age group of 21-60 years. Behera et al conducted a study in which they had divided the age group in three groups with one one group less than 18 years, another 18-60 years and last one more than 60 years. Maximun number of ADRs (78.99%) were reported in 18-60 years which forms the maximum group visiting the Hospital. These results are in conformity with our study.[20] Bhattacharjee et al too demonstrated that Highest incidence (78.95%) of ADRs was observed between 12-59 years of age.[21] These results are also in concordance with our study.

In the present study, dermatology department had the maximum number of ADRs reported (60, 25%), followed by Medicine department (33, 14. 2%). Lihite et al studied the pattern of ADR reporting in a tertiary care hospital in the north east and had similar findings with almost 63% of the ADRs being reported from the Dermatology department.[22]

Doctors contributed maximum to the reporting of the ADRs with 133 ADRs out of the 233 total ADRs reported, followed by the staff nurses who reported 100 ADRs with no patients participating in the reporting of ADRs. In another study conducted by Singh et al 82.32% ADRs were attributed to Doctors while nursing staff reported 21.98% of the total with 4.31% of the ADRs being reported by patients.[23]

Jose et al had documented that skin (23.5%) was the most commonly affected organ system which almost matched in the study conducted by us.[24] However in our study 70% i.e. 154 out of the total ADRs affected skin. Lobo et al. in Brazil also deduced that skin was the most common organ system affected by ADRs (34.5%). [25]

Majority of the ADRs that occurred were due to Antimicrobials and Anti-tubercular therapy (45.1%) followed by Analgesics (NSAIDS, opioids and others analgesics- 19.7%). Jhajj et al results were vis a vis our study where Antimicrobial agents, including those used for anti-tuberculosis therapy, were responsible for 47.3% of the events.[26] A study conducted by Adhikari et al too showed antimicrobials accounted for the 63.76 of ADRs followed by drugs acting on alimentary tract and metabolism 7.32%), nervous system drugs 15.33%.[27] Another study by Rehan et al also showed similar results with maximum number of ADRs occurring due to antimicrobials.[28] Akhideno et al in a study on a pattern of ADR reporting in Nigeria concluded that NSAIDs were the second most common class causing ADRs which are consistent with the findings of present study.[29] One reason that can be held accountable is the excessive prescribing of these classes of drugs.[30,31]

As already mentioned that skin was the most commonly affected system and rash was the most common manifestation followed by Dermatitis. However, no two studies were similar in reporting the incidence for identical skin manifestation. In a study Khan et al the most frequently encountered symptoms were mild rash, urticaria almost in line with the present study.[32] In a another study conducted by Bhabhor et al, the maximum incidence of skin ADRs were also maculopapular rash.[33] Dermatological ADRs are easily identifiable and easily discernable.[34]

Causality assessment was done using WHO-UMC criteria ADRs.[35] Causality assessment of ADRs found in our study revealed that the chance of drug involvement in producing the different ADRs as probable for 200 (85%) cases and possible in 33 (15%). Our findings were consistent with the study conducted by Badyal et al. which showed the similar results.[36] Results of different studies were in concordance with this study.[37] Polypharmacy could be one inductive reason for this trend.[36,20]

Severity assessment of ADRs was done by Modified Hartwig and Siegel scale. Most of the ADRs were

assessed as moderate in severity followed by mild and severe. Studies conducted by Kumar et al also bear the same results.[38,39]

CONCLUSION

Thus ADRs are an unavoidable risk associated with the medicine. The pattern of ADR reporting in our institute will help us to keep a check on the class of drugs causing them so that we can ensure the quality of drug supplied in our pharmacy. Additionally, patients must be educated regarding reporting of ADRs. This will go a long way in the reduction of ADRs that could have otherwise been avoided.

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