

## Original Research

# A pharmacovigilance study in the department of medicine of a university teaching hospital

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### ABSTRACT\*

The aim of the present study was to monitor adverse drug reactions (ADRs) in the Medicine out patient department (OPD) of a University Teaching Hospital.

Method: A prospective evaluation of the ADRs reported in the Department of Medicine of our University Teaching Hospital over a period of 4-months was conducted.

Results: During the study period, a total of 600 patients visited the Medicine OPD and 122 ADRs were reported. Out of 122 reports that were identified, a higher percentage of ADRs in males (52.4%) was observed as compared to females (47.5%). Of the 122 ADRs, 50 were found to be mild (41.0%), 49 moderate (40.2%), and 23 severe (18.2%). A total of 71 (58.0%) ADRs were observed in patients receiving 4 or more medications concurrently. Conversely 46 (37.7%) ADRs were detected in patients using 3 or less medicines. The largest number of reports were associated with antihypertensive therapy (39.3%), followed by antimicrobials (31.1%) and antidiabetics (10.7%). Amongst the organ systems affected, gastrointestinal ADRs constituted a major component (24.7%) followed by skin reactions (22.2%). On causality assessment, nearly 29.5% ADRs were considered as probable, 33.6% possible and 6.6% could not be categorised and were placed under unassessable.

Conclusion: The present work is the maiden pharmacovigilance study conducted at our university teaching hospital. The data presented here will be useful in future, long term and more extensive ADR monitoring in the hospital and in

promotion of rational prescribing and drug use in the hospital.

**Keywords:** Adverse Drug Reaction Reporting Systems. India.

### RESUMEN

El objetivo del presente estudio fue monitorizar las reacciones adversas medicamentosas (RAM) en el departamento de consultas externas (DCE) de un Hospital Universitario.

Método: Se realizó una evaluación prospectiva de las RAM comunicada en el Departamento de Medicina e nuestro Hospital Universitario durante un periodo de 4 meses.

Resultados: Durante el periodo de estudio, 600 pacientes visitaron el DCE y en 122 se comunicaron RAM. De las 122 comunicaciones, se observó un mayor porcentaje de hombres (52,4%) que de mujeres (47,5%). De las 122 RAM, 50 fueron leves (41,0%), 49 moderadas (40,2%) y 23 graves (18,2%). 71 RAM (58,0%) se observaron en pacientes con 4 o más medicamentos simultáneos. Mientras que 46 (37,7%) RAM se observaron en pacientes con 3 o menos medicamentos. El mayor número de comunicaciones estaba asociado a tratamientos antihipertensivos (39,3%), seguidos de antimicrobianos (31,1%) y antidiabéticos (10,7%). Entre los órganos y sistemas afectados, el gastrointestinal constituía el mayor (24,7%) seguido de las reacciones cutáneas (22,2%). En el análisis de causalidad, casi el 29,5% de las RAM se consideraron como probables, el 33,6% como posibles y el 6,6% no pudieron clasificarse por ser invalorables.

Conclusión: El presente trabajo es el principal estudio de farmacovigilancia realizado en nuestro hospital universitario. Los datos aquí presentados serán útiles para la monitorización futura y más intensa de RAM en el hospital y para promover la prescripción y el uso racionales en el hospital

**Palabras clave:** Sistemas de comunicación de reacciones adversas. India.

(English)

### INTRODUCTION

According to WHO'S definition an Adverse Drug Reaction (ADR) is a response to a drug that is

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noxious and unintended, and occurs at doses normally used in human for the prophylaxis, diagnosis, and treatment of disease, or for modification of physiological function.<sup>1,2</sup>

Lazarous et al.<sup>3</sup> estimated that ADRs were the fourth to sixth largest cause of death in the United States. There are few recent reports on epidemiology of ADRs.<sup>4</sup> In United Kingdom most of the studies were performed in the previous two decades and were restricted to specific areas such as monitoring of ADRs in geriatric patients.<sup>5-12</sup> The largest UK study was based on retrospective review of case reports and gave poor documentation.<sup>13</sup>

The detection of adverse drug reactions (ADRs) has become increasingly significant because of introduction of a large number of potent toxic chemicals as drugs in the last two or three decades. WHO has intervened seriously in the matter and established an international adverse drug reactions monitoring centre at Uppsala, Sweden which is collaborating with national monitoring centres in around 70 countries.<sup>14</sup>

In India there are very few active ADRs monitoring centres and a lot of effort is required in order to collect ADR data which may generate from safety surveillance of billions of therapeutically active substances either alone or in combinations.

We performed a prospective analysis of ADRs caused by medicines prescribed in the department of medicine in the Majeedia Hospital, attached to Hamdard University, situated in south Delhi locality to define prevalence and to assess causality of these reactions.

## METHODS

ADR monitoring at our university teaching hospital was done from December 2003 to March 2004. Patients attending Medicine out patient department (OPD) irrespective of age and sex were included in the study. Patients taking more than ten prescription drugs at a time were not included in the study. All mentally retarded, drug addicts, unconscious and patients unable to respond to verbal questions were also excluded from the study.

An informed consent was taken from the patients for participating in the study. The study was initiated after the approval of the study protocol by Hamdard University Institutional Review Board.

The adverse drug reactions experienced by the patients were documented on ADR monitoring form designed on the basis of WHO guidelines.<sup>15</sup> The form includes data like age, sex, demographic details, past medical history, present drug treatment, description of adverse drug reaction, its assessment and treatment for the drug reaction.

Monitoring was done by following two methods: Intensive ADR monitoring of patients in Medicine OPD by a registered pharmacist and voluntary reporting of ADRs by physician.

Causality assessment of adverse events was done according to the causality categories recommended by the WHO Uppsala Monitoring Center.<sup>13</sup>

## RESULTS

During the 4 months study period, a total of 600 patients visited the Medicine OPD (Table 1). A total of 122 ADRs were reported in 600 patients. The gender distribution among the patients who experienced ADRs was comparative with males having experienced more number of ADRs as compared to the females (64 versus 58). The frequency of ADRs was maximum (43.4%) in patients with age group of 25-50 years; next susceptible age group was that of elderly patients (more than 50 years) with 40.1% of ADRs. The number of ADRs in less than 25 years age was lowest (14.7%).

Age (years)	Men	Women	Total
0-10	1 (2.90%)	0	1 (0.17%)
11-20	51 (15.04%)	22 (8.43%)	73 (12.16%)
21-30	90 (26.55%)	67 (25.67%)	157 (26.17%)
31-40	64 (18.88%)	63 (24.14%)	127 (21.17%)
41-50	65 (19.17%)	50 (19.16%)	115 (19.17%)
51-60	43 (12.68%)	37 (14.18%)	80 (13.33%)
61-70	20 (5.90%)	16 (6.13%)	36 (6.00%)
71-80	4 (1.18%)	6 (2.30%)	10 (1.67%)
81-90	1 (0.29%)	0	1 (0.17%)
Total	339 (56.50%)	261 (43.50%)	600 (100%)

As expected polypharmacy had a major influence on the occurrence of ADRs with a total of 71 (58.0%) ADRs observed in patients receiving 4 or more medications concurrently (Table 2). Conversely, 46 (37.7%) ADRs were detected in patients on 3 or less medicines. The frequency of ADRs associated with different routes of administration was as follows: oral (n = 110), parenteral (n = 11) and topical (n = 1).

Number of medicines	Number of ADRs	Percentage (%) of ADR
1	15	12.29
2	20	16.39
3	11	9.02
4	19	15.57
5	29	23.77
6	12	9.84
7	11	9.02
Unspecified	5	4.10

The gastrointestinal side effects (e.g. gastritis, dysphasia etc.) were at the top with 24.7% followed by skin and subcutaneous disorders (22.2%). Other main groups were metabolic and nutritional disorders (8.3%), CNS and neurological disorders (7.4%). The detailed description of organ systems affected by ADRs is shown in Table 3.

Out of a total number of 122 ADRs, 6 (4.9%) were classified as certain, e.g. hypersensitivity reaction with intravenous contrast medium, skin reaction with cefotaxime injection, itching and dermatitis with etophylline tablets and hypoglycemia with glibenclamide tablets. Thirty six ADRs (29.5%) were considered probable e.g. dry cough with enalapril

and dysphasia with furosemide tablets. Forty one (33.6%) were classified as possible e.g. loss of appetite and pain in abdomen with antitubercular medicines and breathlessness with nimesulide and

metoprolol. Eight ADRs (6.6%) could not be categorized and were placed under unassessable category e.g. itching with antitubercular drugs, mental depression with metoprolol, (Table 4).

S. No.	Organ system affected by ADR	No. of ADRs	Percentage of ADRs
1	Blood and lymphatic system disorders	4	3.3
2	Immune system disorders	2	1.6
3	Endocrine system disorders	5	4.2
4	Metabolism and nutritional disorders	10	8.3
5	CNS and Neurological disorders	9	7.4
6	Eye disorders	1	0.8
7	Ear and labyrinth disorders	1	0.8
8	Cardiac disorders	5	4.1
9	Vascular disorders	7	5.7
10	Respiratory system disorder	11	9.1
11	Gastrointestinal disorders	30	24.7
12	Skin and subcutaneous disorders	27	22.2
13	Hepato-biliary disorders	1	0.8
14	Musculoskeletal, connective tissue and bone disorders	1	0.8
15	Reproductive system disorders	1	0.8
16	General disorders and administration site condition	7	5.7

Of the 122 ADRs, 50 (41.0%) were found to be mild e.g. cold extremities with atenolol, 49 (40.2%) moderate e.g. dry cough with ramipril and 23 (18.2%) severe e.g. subcutaneous bleeding with carbimazole. Most of the severe ADRs were associated with antitubercular, oral hypoglycemic drugs, insulin and heparin. These were reported more commonly with injectables as compared to oral medications. Ten serious and the life threatening ADRs were also reported e.g. hepatitis with antitubercular medicines and anaphylactic reactions with iopromide (i.v. contrast medium). Drug induced morbidity is an important cause of hospitalization and is associated with significant mortality. Most of the ADRs observed in our study were either mild or moderate (Table 5).

Probability scale	Number of ADRs
Certain	6
Probable	36
Possible	41
Unlikely	26
Conditional	5
Unassessable	8
Total	122

Group	No. of ADRs	Percentage of ADRs
Mild	50	41.0%
Moderate	49	40.2%
Severe	23	18.2%
Total	122	100%

Distribution of ADRs across therapeutic classes was as follows: antihypertensives (39.3%), antimicrobials (31.1%), antidiabetics (10.7%) and NSAIDs (6.7%). Among the individual drugs, ramipril was associated with maximum cases of ADRs (6.6%) followed by amlodipine (5.7%) and atenolol (4.1%). In case of fixed dose drug combinations, isoniazid + rifampicin + ethambutol +

pyrazinamide combination was responsible for 13.1% ADRs.

## DISCUSSION

Number of drug related visits to the OPD was 5.1 % whereas 3.1% ADRs led to the hospitalization of patients. One reason for the above occurrence could be the concomitant disease conditions in these patients and thus more susceptibility of patients to the adverse effects of medicines.

Although male population had more prevalence of ADRs, the difference was negligible with respect to female population. Previous studies report that the occurrence of ADRs is more common in women.<sup>16-17</sup> In our study the majority of ADRs were in 25-50 years age group. The reasons that could be attributed are that the patients of this age group suffered from hypertension and diabetes due to modern sedentary lifestyle. Increased stress in daily life make this age group more prone to hypertension and diabetes. So this age group used more number of medicines and frequently visited the medicine OPD for their regular check-up and complained for drug related adverse events, though most of these adverse events were mild and easily tolerated.

Majority of the ADRs were associated with oral administration of medicines followed by parenteral route. Most of the ADRs with injectable medications were severe. The one topical reaction observed was erythema (localized skin redness) on application of benzyl nicotinate and heparin sodium cream. Gastrointestinal ADRs were most commonly observed with oral medications.

The incidence of adverse drug events is not directly proportional to the number of drugs being taken but increases remarkably as number of drugs rises. Polypharmacy needs to be discouraged for a good number of ADRs results from drug-drug interactions. The Boston Collaborative group (1972)

reported 36% ADRs, 6.9% of which were attributed to drug interactions in a cohort of 10,000 patients. Advancing age, improved economical status has been correlated with an increased use of prescription drugs.<sup>19</sup> Patients also cannot identify correctly 60% of their medicines, 40% of patients received drugs prescribed by two or more physicians, increasing the possibility of drug–drug interactions, 12% patients take drugs prescribed for someone else and 60% patients consider their drugs completely safe. These factors must also contribute to the occurrence of drug–induced illness and might be responsible, at least in part, for the frequency of admission to hospitals of patients with adverse reaction to drugs.<sup>18</sup>

Both hypertensive and diabetic patients are predisposed to ADRs and they are at inevitable risk of bad effects of drugs due to sub-optimal functionality of their organ systems. This necessitates careful organ function analysis prior to prescription writing of any medication. One of the essential reasons of wide prevalence of ADRs in

hypertensive and diabetic patients is that they are elderly and are often on multiple drug therapy.

In our study, we found gastrointestinal side effects (e.g. gastritis, dysphagia etc.) at the top followed by skin and subcutaneous disorders. Next main groups are metabolic, nutritional, CNS and neurological disorders. Neurological ADRs were at the top of the list of ADRs in previous studies<sup>19,20</sup> and gastrointestinal ADRs were reported amongst the top three groups of ADRs.<sup>19</sup>

## CONCLUSION

The present work is the maiden pharmacovigilance study conducted at our university teaching hospital. It has provided base line information about the prevalence of ADRs and their distribution amongst different age groups, genders, organ systems affected and therapeutic classes of medicines. The data presented here will be useful in future, long term and more extensive ADR monitoring in the hospital and will be useful in framing policies towards rational use of drugs.

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