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### **Original Research Article**

# Pharmacovigilance study in medicine department in a tertiary care hospital

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#### **ABSTRACT**

**Background:** Adverse drug reactions (ADRs) are major worldwide public health problem. Proper reporting of an ADR is very important as it reduces number of deaths due to ADR and extra financial burden on patients. The aim of the study was to assess the pattern of ADR reporting in outpatients and inpatients of medicine department and to assess their causality, severity and preventability.

**Methods:** This was a prospective observational study done from April 2013 to June 2014 or in 100 consecutive study subjects (which ever happen first) with ADRs in department of medicine. The clinical pattern, spectrum of ADRs reported and assessment of ADRs in terms of causality, severity and preventability .The causality, severity and preventability assessment was done on the basis of applying various scales for each of them.

**Results:** A total of 153 suspected ADRs were reported and evaluated from 100 patients. Dermatological system (28%) was most commonly involved. Drug class most commonly associated was Antimicrobials (51%). 68% ADRs were classified as "Probable" in view of causality, while 68% were found to be "Moderate" in case of severity. In 65% of the cases the ADRs was "Probably Preventable". In majority of the cases the suspected drug was withdrawn and alternate therapy was instituted. Most patients recovered from the ADR.70% of these ADR was Type A.

**Conclusions:** Awareness about ADR reporting is still poor amongst healthcare professionals in India. Conducting regular training programmes can improve the number of ADR reporting.

**Keywords:** Adverse drug reactions, Causality, Health care professionals, Pharmacovigilance Preventability, Under reporting

#### INTRODUCTION

Adverse drug reaction (ADR) is a major worldwide public health problem. It is almost an unavoidable consequence of drug therapy, as no drug is free from unwanted effects. ADR is one of the leading causes of death worldwide.

In developed countries around 3% to 5% of hospital admissions are expected to be due to adverse drug reaction and about 10% of hospitalized patients experience a serious adverse drug reactions.<sup>1</sup>

In India there is a very limited data. An overall incidence of fatal ADRs is 1.8%. Minimum of one ADR has been reported to occur in 8% to 18% of hospitalized patients.

Pharmacovigilance as defined by the World Health Organization (WHO) is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drugrelated problems.

Detection and assessment of ADRs is of great importance for patient safety profile, as more than 60% of approved drugs are associated with some type of adverse effects that are not detected prior to their approval for clinical use.<sup>4</sup>

Most of the developed countries have set up an ADR monitoring system at the national level.

Furthermore, reviewing data from different medical, geographic and social population enhances the ability to

form the basis of new signals which helps in setting up a sound ADR reporting system in the country. [5]

ADR in patients can itself present as those that are responsible for hospital admission and those that occur already in admitted patients.

Hospital based ADR monitoring centres can provide very useful information on drug usage. Management of ADR further adds up financially to an already burdened health care system which is usually preventable.

ADRs reporting are done by various methods but the most commonly applied method is Spontaneous Reporting System (SRS) by Health care professionals (HCP). The main drawback of SRS by HCP is very less number of reporting and also selective reporting. This can lead to false conclusion about drug risk. <sup>8,9</sup>

Therefore, including patients as reporters of ADR may increase its early detection and reporting and provide useful added source of information as patients are found to perceive ADRs more rapidly and clearly, than HCP. In Indian scenario the whole concept of ADR reporting is still in scarce.

ADRs are of great concern to the general population, HCP, and regulatory bodies. <sup>10</sup>

Not much of an attention has been given so far and only a handful of original studies have been done in this regard. India rates as low as less than 1% in Pharmacovigilance reporting when compared to other developed countries reporting of 5% or more. 12

We have very few pharmacovigilance centers at present and lots of hard work is needed, to collect ADR reports which may form the basis of safety surveillance of millions of therapeutically active substances either alone or in combinations.

There is a need of establishing ADR monitoring centre at every tertiary care hospital.

#### **METHODS**

This prospective observational study was conducted after obtaining an approval from institutional ethics committee, subjects with suspected ADRs as Outpatients and inpatients in Department of Medicine, Basaveshwar Teaching and General Hospital, Gulbarga were included in the study only after getting their written informed consent. Study period was of 15 months from April 2013 to June 2014 or first 100 consecutive patients which ever happened first.

Before initiation of the study, a training programme on pharmacovigilance was conducted in medicine department for healthcare professionals. Data of spontaneously reported ADRs by healthcare professionals were collected through the ADR reporting form, made available in medicine OPD and wards. All suspected adverse drug reactions that were due to the medications taken by the patients as outpatients and inpatients and age 13 years and more were included in the study. While the use of alternatives medicines like Homeopathy, Unani, Sidda, Ayurveda, over dosage, excess consumption, mentally retarded patients along with patients who were drug addicts and unconscious patients were all excluded from the study.

For each patient with suspected ADR, a detailed history was taken and any untoward event was labelled as adverse drug reaction after discussion with the treating physician.

A through scrutiny of data was done to assess pattern, extent, severity and duration of the reactions, to detect any predisposing or underlying disease/pathological factors, and to assess any other organ/ system involvement as a part of the drug reaction.

The causality of the reactions was assessed by WHO UMC scale, severity of ADR using Adapted Hartwig scale and preventability assessed by using Modified Schumock and Thornton scale. Follow up was done to assess the clinical progress of the cases.

Average cost per patient was calculated by total amount spent on treating ADRs divided by total the number of patients suspected with ADR. For calculating the cost due to ADR per patient included laboratory investigation, specific drugs used to treat ADR and other supportive therapy were all calculated per unit per patient.

#### Statistical analysis

The data was analysed using descriptive statistics namely mean and standard deviation for quantitative variables SPSS V13 statistical software was used to generate graphs and tables wherever necessary.

#### **RESULTS**

A total of 153 suspected ADRs were reported and evaluated from 100 patients. Dermatological system (28%) was most commonly involved. Drug class most commonly associated was Antimicrobials (51%). 68% ADRs were classified as "Probable" in view of causality, while 68% were found to be "Moderate" in case of severity. In 65% of the cases the ADRs was "Probably Preventable". In majority of the cases the suspected drug was withdrawn and alternate therapy was instituted. Most patients recovered from the ADR.70% of these ADR was Type A.

#### **DISCUSSION**

During the study period total no of the patients with suspected ADRs were 100. Among those ADRs

encountered in male patients were (N=61) when compared to female patients (N=39). This result was in consistence with the earlier documented study. <sup>13</sup>

As far as age and gender distribution of the patients who encountered adverse drug reactions (ADRs) during the study period were concern, in both males and females maximum ADRs were encountered in age group of 41-60 years (41%) followed by 26-40 years (39%)in males, in

females age group 41-60 years (41%) followed by 26-40 years (34%). However the incidence of ADRs has not increased consistently with age. This observation was in contradiction with the observations of the earlier studies where higher incidences of ADRs have been observed with increasing in age suggesting that increasing age is a risk factor for occurrence of ADRs. <sup>14-16</sup> However the contradicting result of the present study could be due to lesser number of geriatric patients in the study.

Table 1: Type of patients.

Type of patients	Male n	Male %	Female n	Female %	Total n	Total %
Outpatient	35	57	17	44	52	52
Inpatient	26	43	22	56	48	48
Total	61	100	39	100	100	100

Table 2: If outpatient than (Adverse drug reaction was the cause for admission).

Outpatient than	Male n	Male %	Female n	Female %	Total n	Total %
Admitted	19	54	5	29	24	46
Not admitted	16	46	12	71	28	54
Total	35	100	17	100	52	100

**Table 3: Presenting complains.** 

Complains	Male n	Male %	Female n	Female %	Total n	Total %	
Skin rash	12	13	16	26	23	15	
Itching	10	11	14	22	20	13	
Vomiting	3	3	3	5	3	2	
Diarrhoea	12	13	5	8	14	9	
Gastric bleeding	4	4	2	3	6	4	
Abdominal pain	8	9	2	3	10	8	
Constipation	1	1	1	2	1	1	
Cough	1	1	2	3	3	2	
Sweating	6	7	2	3	8	5	
Drowsiness	6	7	2	3	8	5	
Weakness	6	7	2	3	8	5	
Seizure	1	1	1	2	2	1	
Abnormal lab findings	2	2	4	6	6	4	
Peripheral neuropathy	1	1	1	2	2	1	
Sedation	3	4	0	0	3	2	
Headache	1	1	1	2	2	1	
Discolouration of sclera	5	5	0	0	5	3	
Hypotension	1	1	2	3	3	2	
Palpitations	1	1	1	2	2	1	
Breathlessness	2	2	1	2	3	2	
Abdominal fullness	1	1	1	2	2	1	
Joint pain	1	1	1	2	2	1	
Weight gain	1	1	0	0	1	1	

Table 1 shows type of patients who develop ADRs, either were outpatients or inpatients. Total 52 patients were outpatients who developed ADRs. While remaining 48

patients were inpatients who developed ADRs. This result was in consistence with the earlier documented study. 18

Table 4: Organ systems involve.

Organ system involve	Male n	Male %	Female n	Female %	Total n	Total %
Skin	17	19	26	42	43	28
Gastrointestinal	25	27	12	19	37	24
Cardiovascular	7	8	5	8	12	8
Central nervous	6	7	2	3	8	5
Hypoglycaemic	18	19	6	10	24	16
Musculoskeletal	2	2	1	2	3	2
Metabolic	1	1	3	5	4	3
Hepatobiliary	6	7	0	0	6	4
Respiratory	1	1	2	3	3	2
Others	8	9	5	8	13	8
Total	91	100	62	100	153	100

Table 5: If reported by health care professionals.

Health care professionals	n	0/0
Senior doctors/Physicians	5	5
Post graduates	61	61
Interns	20	20
Nursing staffs	10	10
Medical students	4	4
Total	100	100

Table 6: Cause of ADR.

Single drug	76	76%
Suspected drug	24	24%
combinations/drug interaction		
Total	100	100%

Table 2 shows that out of 52 outpatients who developed ADRs 24 of them were admitted (46%) while remaining (n=28, 54%) were not admitted as ADRs in those patients were not serious. So from the table above we can say that ADR related hospital admission and ADRs during the hospital stay is significantly high. This result was in consistence with the earlier documented study. 17-19

Table 3 shows presenting complain in each patient due to suspected ADRs and Table 4 shows how those presenting complains has been kept under various organ system classification with gender distribution. The most common presenting complains is skin rash and itching followed by diarrhoea. The commonest organ system involved in ADRs were skin accounting for (n=43, 28%) of total ADRs which is consistent with previous studies that dermatological manifestation of ADR are common.<sup>20,21</sup>

This is followed by involvement of gastrointestinal symptoms (n=37, 24%).

We classified ADRs encountered based on Thompsons and Rawlins classification into Type A and Type B ADRs. It was observed that out of 100 cases 70 cases showed Type A ADRs while remaining 30 cases showed Type B ADRs. This pattern of different type of ADRs observed during the present study were similar to the observations of the earlier studies which had also reported higher incidences of Type A ADRs. <sup>22,23</sup>

We also studied type of prescription involved in ADRs. In the present study majority of the cases who encountered ADR took doctor's prescription (n=92, 92%) while remaining cases (n=8, 8%) took self-prescription on the basis of their previous visit and previous exposure to drug and due to lack of time to go to a doctor.

We also studied type of reporting of ADRs. In the present study all cases (n=100, 100%) of suspected ADRs were reported by health care professionals. There was no spontaneous reporting by the patients.

Table 5 shows maximum reporting of ADRs among the health care professionals were from post graduates (n=61, 61%) and medical students contributed the least (n=4, 4%). This was further correlated by chart review of the patients especially inpatients. The pattern of reporting of the present study were similar to the observation of the previous studies were the active participation of health care professionals can really increase the ADRs reporting. <sup>13,20,24</sup>

Table 6 shows total no of cases (n=76) were suspected ADRs is due to one drug. While remaining 24 cases,

ADR was due to fixed dose combinations or suspected drug interactions.

Table 7 shows that in 76 cases single drug was the cause of ADR. Majority of ADRs were caused due to antimicrobials (n=33, 43%) Amoxicillin + Clavulanic

acid followed by Ceftriaxone which were consistent with previous studies probably because they are most commonly prescribed drugs in our hospital setting. <sup>21,25</sup>

Table 7: 76 cases who had adverse drug reaction with only one drug.

Class of drugs	Male n	Male %	Female n	Female %	Total n	Total %
Antibacterial	17	41	16	45	33	43
Antitubercular	3	7	3	9	6	7
Cardiovascular	5	13	3	9	8	10
Antiepileptics	4	10	1	2	5	7
NSAID's	2	5	3	9	5	7
Diuretics	2	5	3	9	5	7
Brochodilators	1	2	0	0	1	1
Corticosteroids	2	5	1	2	3	4
Hypogylcaemics	3	7	2	6	5	7
Others*	2	5	3	9	5	7
Total	41	100	35	100	76	100

<sup>\*</sup> Drugs were Ondansetron, Ferrous fumarate, Tramadol, Diazepam and Promethazine.

Table 8: ADR due to drug combinations/suspected drug interactions.

Drug combinations/Drug interactions	No of cases	Presenting complains
Isoniazid + Rifampicin + Pyrazinamide	2	Jaundice
Paracetamol + Diclofenac	2	Upper git bleeding
Zidovudine+ Lamivudine+ Nevirapine	1	Pallor
Zidovudine+ Lamivudine+ Nevirapine	1	Headache and insomnia
Zidovudine+ Lamivudine+Efavirenz	1	Jaundice
Glimepiride+Insulin	3	Sweating, drowsiness
Glipizide+Insulin	1	Sweating, drowsiness and weakness
Sitagliptin+Glimepiride	1	Sweating, drowsiness and weakness
Aspirin and clopidogrel	1	Haematuria
Aspirin and clopidogrel	1	Upper git bleeding
Aspirin and clopidogrel	1	Black tarry stools and abdominal pain
Valproate + Atorvastatin	1	Jaundice
Azithromycin +Paracetamol	1	diarrhoea
Diazepam +Alcohol	1	sedation
Ramipril+ Spironolactone	1	palpitations
Ramipril + Aspirin	1	hypertension
Methylprednisolone + Levofloxacin	1	hyperglycaemia
Hydrocortisone + Levofloxacin	1	hyperglycaemia
Norfloxacin + Metronidazole	1	Itching all over the body
Furosemide+ Spironolactone	1	Hyponatremia
Total no of cases	24	

Table 8 shows remaining 24 cases were the cause of suspected ADRs was either fixed dose combinations or suspected drug interactions.

We also studied the final outcome of the suspected drug as a whole. Out of total 100 cases in 52 cases the suspected drug was withdrawn and alternate therapy was implemented. This observation of the present study result were similar to the observation of the past studies. <sup>13,17</sup>

Treatment of ADRs as a whole was also studied. Out of 100 cases total of (n=72, 72%) cases required

symptomatic treatment This observation of the present study were similar to the observation of the past studies. <sup>13,17</sup>

Table 9: Final Outcome of the suspected ADRs.

Outcome	Male n	Male %	Female n	Female %	Total n	Total %
Recovered	40	66	27	69	67	67
Recovering	12	20	7	18	19	19
Continue	4	6	1	3	5	5
Loss to follow up	5	8	4	10	9	9
Deaths	0	0	0	0	0	0
Others	0	0	0	0	0	0
Total	61	100	39	100	100	100

Table 10: WHO UMC causality assessment criteria.

WHO UMC causality	Male n	Male %	Female n	Female %	Total n	Total %
Certain	6	10	4	10	10	10
Probable	41	67	27	69	68	68
Possible	14	23	8	21	22	22
Unlikely	0	0	0	0	0	0
Conditional	0	0	0	0	0	0
Unassessable	0	0	0	0	0	0
Total	61	100	39	100	100	100

Table 11: Adapted Hartwig severity scale.

Adapted Hartwig severity	Male n	Male %	Female n	Female %	Total n	Total %
Mild	14	22	5	13	19	19
Moderate	40	65	28	72	68	68
Severe	7	13	6	15	13	13
Total	61	100	39	100	100	100

Table 12: Schumock and Thornton preventability assessment criteria.

Schumock and Thornton	Male n	Male %	Female n	Female %	Total n	Total %
Definitely preventable	5	8	5	13	10	10
Probable preventable	37	61	28	72	65	65
Not preventable	19	31	6	15	25	25
Total	61	100	39	100	100	100

Table 9 shows outcome due to ADRs in which total of (n=67, 67%) cases recovered. The result of the present study were similar to the results of the past studies. <sup>13,17,26</sup>

Table 10 shows WHO UMC causality assessment criteria which shows total majority of the reported ADRs were evaluated as being probable, (n=68, 68%). The result of

the present study were similar to the results of the past studies. 19,27

Table 11 shows assessment of severity of ADR based on Adapted Hartwig severity scale which shows total majority of ADRs (n=68 ,68%) were categorized as moderately severe which were similar to the findings of previous studies.<sup>28</sup>

Table 12 summarizes about the preventability of suspected ADRs as assessed by Modified Schumock And Thornton Criteria, it revealed that total (n=65, 65%) of ADRs were probably preventable which was in accordance with previous studies.<sup>28</sup>

Total cost incurred during the management of ADRs is Rs 92650.30 which was almost approximately close to the observations in the past studies. Here for 48 inpatients the mean cost for the management of these cases were Rs 368.48 which was approximately similar to the observation of the past studies. Patients who visited the OPD but were not admitted, the mean cost incurred by them were Rs 145.50. Remaining 24 cases who were admitted due to Adr. The mean cost incurred by them was Rs 2943.35.

#### CONCLUSION

Hospital based ADR monitoring and reporting programmes aim to identify and quantify the risks associated with the use of the drugs.

This information may be useful in identifying and minimizing the preventable ADRs while enhancing the knowledge of the prescribers to deal with ADRs more efficiently.

Pharmacovigilance programmes have been introduced in India but it still appears to be in its primitive stage.

The total cost of Rs 92650.30 incurred in the management of total no of ADRs encountered during the study underlines the fact that ADRs pose an extra financial burden to the patients.

Regular training programmes by the way of workshop and seminars must be carried out for health care professionals to increase the awareness about ADR reporting.

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Institutional Ethics Committee

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