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Original Research Article

A retrospective analysis of adverse drug reaction reported in a tertiary care hospital

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ABSTRACT

Background: The adverse drug reactions (ADRs) reported to pharmacovigilance centre in tertiary care hospital was analysed to find out the incidence and causality.
Methods: This was a retrospective study to analyse the ADR reported at pharmacovigilance centre after ethical clearance from Institutional Ethic Committee (IEC). ADR data were analysed and ADRs were categorized as department-wise, system affected and causative drug. The causality of each ADR was assessed by WHO-UMC scale.
Results: The majority of patients who had suffered from ADRs were between 19-64 years of age (94.2%) and male patients (58.6%) were affected more than female (41.4%). Pulmonary medicine department has reported highest number of ADR followed by dermatology department. Skin (46.5%) was most affected system followed by gastrointestinal (30.45%), CNS (21.26%), respiratory (9.0%) and remaining systems. Rifampicin (13.79%) shows the largest numbers of ADR followed by zidovudine (13.21%), nevirapine (12.64%) and diclofenac sodium (8.0%). The maximum ADRs reported were probable (94.8%) followed by possible (5.2%).
Conclusions: In conclusion, the skin was most affected system followed by gastrointestinal, central nervous and respiratory system. Rifampicin has caused maximum ADRs followed by zidovudine, nevirapine and diclofenac sodium. The causality analyses showed that majority of ADRs were probable (94.8%) while remaining falls in possible (5.2%) category.

Keywords: Adverse drug reaction, Pharmacovigilance, UMC scale

INTRODUCTION

Adverse drug reaction (ADR) as defined by WHO are "any noxious, unintended, undesired effect that occurs at dosage used in human for prophylaxis, diagnosis and therapy".[1] There is need to strengthen the ADR reporting system in India because of underreporting of ADR (<1%) as compared to other countries.[2] This may be due to multiple factor including lack of awareness among health care professionals and poor post marketing surveillance by pharmaceuticals.

ADR reporting is an important component of monitoring and evaluation activity in hospital.[3,4] In November 2004 CDSCO, ministry of health and family welfare government of India launched the National Pharmacovigilance programme (NPP) which was converted to Pharmacovigilance Programme of India (PvPI) in 2010 to monitor the ADRs that include government or private sector.[5] The PvPI aims at safe use of medicine. Thus, it is important to have ADR data of all the drugs, so that necessary measures can be taken in this regard. The present study was planned to analyse ADRs reported in tertiary care hospital.

The objective of the study was to retrospectively analyse ADRs reported to Pharmacovigilance centre in a tertiary care hospital. Analysis was done to find out the incidence and causality of reported ADR.

METHODS

This was a retrospective study. The analysis of ADR reported at Pharmacovigilance centre in tertiary care hospital during last one and half year (from 1-1-2014 to 30-4-2015) was done. The clearance from institutional

ethical committee was taken before the commencement of study. Confidentiality was maintained at all the level.

Completed ADR reporting forms submitted to ADR monitoring centre were analysed. The details filled up in the form were checked for mandatory parameters including patient's detail, type of ADR, drugs causing ADR, etc.

ADRs were analysed and results were categorized as follows:

- Demographic details
- Department-wise
- System affected
- Causative drug
- Causality of ADRs

WHO-UMC scale adopted by PvPI was used for causality assessment.

Results were presented in tabular form, Pie chart and bar diagram.

RESULTS

A total of 174 ADRs were detected, documented and reported during the last one and half year.

The majority of patients who had suffered from ADRs were between 19-64 yrs. of age (94.2%) of total ADRs followed by 0-18 yrs. (5.2%). There was only 0.6% of reporting in the age group more than 65 yrs. The studies also revealed male patient (58.6%) were affected more than female (41.4%) (Table 1).

Table 1: Demographic details.

Gender		
	Total no. 174	**Percentage**
Male	102	58.6
Female	52	41.4
Age distribution		
0-18 yrs	9	5.2
19-64 yrs	164	94.2
65 yrs and above	1	0.6

The analysis showed that Pulmonary medicine department reported highest number of ADRs (31.6%) followed by dermatology department (24.1%). The least number of reporting were from surgery department (0.6 %) (Table 2).

On analysis of system affected the skin was most commonly affected (46.5%) followed by gastrointestinal (GI) tract (30.45%), CNS (21.26%) and respiratory system (9.19%). The involvement of genitourinary and haemopoetic systems was (1.72 % each). The endocrine system (thyroid) was affected in (0.57%) of patients (Table 3).

Table 2: Department wise ADR report.

Departments	No. of ADR (n=174)	Percentage
TB and Chest	55	31.6
Dermatology	42	24.1
ART center	36	20.7
Psychiatric	17	9.8
Medicine	11	6.3
Obs. and Gynec.	5	2.9
Pediatric	5	2.9
Orthopedic	2	1.1
Surgery	1	0.6

Table 3: System wise ADR reports.

Systems	No. of Patient (Total=174)	% of patients
Skin	81	46.55
GIT	53	30.45
CNS	37	21.26
Respiratory System	16	9.19
Genitourinary	3	1.72
Anemia	3	1.72
Endocrine	1	0.57

The details of ADR related to each system are mentioned in Table 4.

In our study the rifampicin shows the largest number of ADRs (13.79%) of total followed by zidovudine (13.21%) then nevirapine (12.64%). Diclofenac sodium also shows significant no. of ADR (8.0%) (Table 5).

The maximum ADRs reported were probable (94.8%). This was followed by possible (5.2%). No ADR was reported from any other category of WHO-UMC scale (Table 6). [5]

DISCUSSION

In this study, the Patient suffering from ADRs were between 19-64 years of age in which males (58.6%) were more affected than females (41.4%). In contrast to A. P Gor's study which showed that the sex of the patients did not affect the incidence rate of ADR, our study showed a higher prevalence among males.[5]

Patidar et al observed that the occurrence of ADRs was (45.94%) in men and (54.05%) in women.[6] Other studies by Sriram et al, Richa, VR Tandon et al reported that males have greater risk of ADR than females.[12,15] There are various factors like age of patients, gender, number of drug taken, duration of hospital admission, genetic factors, ethnicity, dietary, and environmental factors affecting the ADR incidence.

Table 4: Clinical feature wise ADR reports.

System	ADR	Drug	No. of patient
Skin	Multiple Scaly Plaque like lesion	Losartan, Atenolol	2
	Angioedema	Iron Sucrose, Diclofenac Sodium, Ibuprofen, Ceftriaxone, Artemether, Amoxicillin + Clavulanic acid	11
	Hyperpigmented patches	Cotrimoxazole	1
	Multiple Erythromatous Maculopapular Rash	Nevirapine, Cotrimoxazole, Cefoperazone, Azithromycin, Ibuprofen, Phenytoin Sodium, Multivitamin Tablets Isoniazid, Isoniazid+ Rifampicin, Diclofenac Sodium + Paracetamol, Zidovudine	43
	Exfoliative Dermatitis	Zidovudine+ Lamivudine+Nevirapine	10
	Urticaria (itching)	Dilofenac Sodium, Amoxicillin, Navirapine, Abacavir, Topiramate	13
	Steven Johnson Syndrome (Cutaneous ulceration Epidermal Necrosis)	Lamotrigine	1
GIT	Gastritis ((Gastric Intolerance, Vomiting Nausea, Abdominal Pain and Decrease appetite)	Zidovudine, Nevirapine, Lorazepam, Capreomycin, Levofloxacin, Pyrizinamide	52
	Jaundice	AKT (Cat. I)	1
CNS	Excessive Sedation (Drowsiness)	Mirtazepine, Olanzepine	6
	Chills and Rigor	Chloramphenicol	2
	Peripheral Neuropathy (Tingling Numbness)	Stavudine, Stavudine +Nevirapine + Lamivudine, Stavudine +Nevirapine + Lamivudine + Zidovudine	5
	Dizziness	Pregabaline, Phenytoin Sodium, Mirtazepine	4
	Restlessness (Anxiety)	Pregabaline, Desvenlafaxine, Quetiapine	4
	Headache	Desvenlafaxine, Etiozolam, Azithromycin	5
	Tonic Posturing	Amoxicillin + Clavulanic acid	1
	Insomnia induced psychosis	Isoniazid	1
	Decrease Hearing	Capreomycin	1
	Tonic Convulsion	Tetanus	1
	Fever	Rifampicin, AKT, Abacavir, Nevirapine, Isoniazid	7
Respiratory	Dry Cough (Throat pain, Hemoptosis)	Rifampicin, Isoniazid, Nimesulide	4
	Angioedema	Iron Sucrose, Diclofenac sodium, Ibuprofen, Ceftriaxone, Artemether, Amoxicillin + Clavulanic acid	11
Endocrine	Hypothyroidism	AKT (Cat. IV)	1
Genitourinary	Candidiasis. Paracystitis, cystitis	Rifampicin, Tenovir Pyrizinamide	3
Misc	Anaemia	Ziduvadine	3

The present study revealed a predominance of adult over paediatric populations. Most of the patients (94.1%) were between 19-64 years of age group. The reason for the high morbidity in adult population may be because of multi drug therapy or other disease like hypertension, diabetes, asthma or other chronic diseases. Our finding similar with the finding of Patidar et al, Murphy et al.[6,8] The most common category associated with ADRs was skin (46.55%). This finding is consistent with the study by Coelho et al, Fredy et al, Rajesh et al, but it differs from reports of Suh et al where gastrointestinal manifestations had the highest rate, which was second highest in our study (30.45%).[9-11,13] Sriram et al, Rajesh et al Murphy et al, Gor AP, Desai SV, Brennan TA, Leape LL et al, Fredy et al, Leone et al, reported that other antibiotics are the most common classes causing ADRs but in our study patients on anti-tubercular drugs had maximum ADRs.[5,7,12,13] The most common drug causing ADR is rifampicin (13.79%). It is because of anti-tubercular drug used for long duration (minimum 6 months) as compare to other antibiotics, followed by zidovudine (13.21%) and nevirapine (12.64%).

Table 5: Drug wise ADR.

Name of Drug	Frequency of ADR	ADR reported
Antitubercular drugs		
AKT	10	Gastritis, vomiting nausea anorexia
Rifampicin + Isoniazid	3	Gastritis, vomiting, abdominal pain
Rifampicin	24	Gastritis, vomiting, abdominal pain dry cough and fever
Isoniazid	9	Maculopapular rashes with fever, chills, psychosis insomnia weakness
Pyrizinamide	4	Cystitis, weight loss, dyspnoea, anorexia
Antiviral drugs		
Nevirapine	22	Multiple erythromatous patch, maculopapular rashes with fever, erythromatus maculopapular lesions, nausea vomiting headache.
Zidovudine	23	Exfoliative dermatitis, anaemia, xerosis, fixed drug eruptions, acute gastritis, severe vomiting abdominal pain
Acyclovir	1	Skin rash and fever
Abacavir	1	Fever and itching
Tenofovir	1	Paracystitis
Stavudine+Lamivudine	4	Tingling Numbness and Peripheral Neuritis
Stavudine+Lamivudine+Nevirapine	1	Tingling Numbness and Peripheral Neuritis
Antibacterial Agents		
Co-trimoxazole	3	Hyperpigmented patches, erythromatous Patch
Chloramphenicol	2	Chills and rigor
Azithromycin	8	Gastritis, Headache, abdominal pain, Erythromatous maculopapular rashes
Ceftriaxone	1	Angioedema
Capreomycin	2	Decrese hearing, vomiting
Levofloxacin	1	Chest pain, Decrease appetite
Amoxicillin + Clavulanic acid	4	Skin lesion, Angioedema and Tonic posture
Cefoperazine + Sulbactam	1	Erythromatous patch, Rashes
Antimalarial drugs		
Artemether	1	Angioedema
Antihypertensive drugs		
Losartan	1	Multiple Scaly Plaque like lesion
Atenolol	1	Multiple Scaly Plaque like lesion
Analgesic drugs		
Ibuprofen	2	Maculopapular rashes, angioedema and urticaria
Diclofenac Sodium	13	Urticaria, angioedema - itching, tingling, numbness, maculopapular rashes and tightening in chest
Nimesulide	1	Burning micturition,throat pain and Steven Johnson syndrome.
Diclofenac Sodium	1	Maculopapular rashes
Antidepressant and antipsychotic drugs		
Mirtazapine	3	Excessive sedation, vertigo and confusion
Desvenlafaxine	2	Headache, anxiety and restlessness
Olanzapine	4	Drowsiness and weight gain
Quetiapine	1	Anxiety, Restlessness
Etizolam	1	Severe Headache
Lorazepam	1	Nusea, Vomiting and Dizziness
Anticonvulsant drugs		
Divaproex Sodium	3	Gastric intolerance, vomiting, abdominal fullness, giddiness and restlessness
Lamotrigine	1	Steven Johnson syndrome and cutaneous ulceration
Pregabaline	1	Dizziness, restlessness
Topiramate	1	Generalized itching
Phenytoin Sodium	6	Erythromatous maculopapular rashes
Miscellaneous drugs		
Iron Sucrose	2	Angioedema
Multivitamins	1	Rashes, abdominal pain
Tetanus Vaccine	1	Tonic convulsion

This study also shows significant level of ADR by diclofenac sodium (8%) similar to Shrivastava MP et al.[14]

Table 6: Causality of reported ADR (total 174).

UMC-Scale	No. of reports	% of reports
Certain	0	0
Probable/likely	165	94.8
Possible	9	5.2
Unlikely	0	0
Conditional/Unclassified	0	0
Unassessable/Unclassifiable	0	0

In our study, maximum ADRS reported were probable (94.8%) followed by possible (5.2%) No other ADR reported in other category of WHO-UMC System. Definite is least due to rechallenge is not possible. In contrast Sriram et al study showed that 42% were possible and 23% were probable.[12]

CONCLUSION

In conclusion, the skin was most affected system followed by gastrointestinal, central nervous and respiratory system. Rifampicin has caused maximum ADRs followed by zidovudine, nevirapine and diclofenac sodium. The causality analyses showed that majority of ADRs were probable (94.8%) while remaining falls in possible (5.2%) category.

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