*ejpmr, 2020,7(3), 352-355*

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

# STUDY OF ADVERSE DRUG REACTIONS PROFILE IN A TERTIARY CARE HOSPITAL: A RETROSPECTIVE OBSERVATIONAL STUDY

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**Article Received on 31/12/2019** **Article Revised on 21/01/2019** **Article Accepted on 11/02/2020**

## ABSTRACT

**Objective:** To study adverse drug reactions (ADRs) profile in a tertiary care hospital and to determine seriousness, predictability, causality, severity and outcome of ADRs. **Method:** A retrospective observational study was conducted in a tertiary care hospital over a period of five years. Recorded data was collected from various department regarding details of patients, drugs, ADRs and entered in a proforma. It was evaluated using appropriate scales. Simple descriptive statistics was used for analysis. **Results:** Total number of ADRs reported in five years were 410. As per criteria 330 ADRs were included and analyzed out of which female patients were 217 (65.76%) and males 113 (34.24%). Majority of patients were in age group of 21 to 50 years (69.7%). Among these reactions 29 (8.78%) were serious and 301 (91.21%) non-serious. Maximum ADRs reported from medicine department 188 (56.9%). Cutaneous ADRs were most frequent 134 (40.6%). Antiretroviral agents were most common drugs causing 80 (24.2%) ADRs. Overall predictability was 69.7%. When causality assessment was done 2 (0.6%) ADRs were certain, 121 (36.7%) probable and 207 (62.7%) possible. Severity assessment showed 129 (39.1%) reactions were mild, 201 (60.9%) moderate and none in severe grade. Outcome was 256 (77.6%) patients had recovered, 69 (21%) were recovering and 2 (0.6%) had not recovered from ADR. **Conclusion:** Most of ADRs in our study was due to polypharmacy. Due to these ADRs there is prolonged hospitalization and increase in economic burden. Hence there is always a need for prevention and periodical monitoring of ADRs.

**KEYWORDS:** Adverse drug reactions, causality assessment, severity.

## INTRODUCTION

Adverse drug reaction (ADR) is defined as 'any noxious change which is suspected to be due to drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug'.[1] Disease prevalence, economic status, culture and ethnicity contribute to different ADR patterns.[2] ADRs are major cause for prolonged hospitalization, increase hospital expense, morbidity and mortality.[3,4]

According to WHO, Pharmacovigilance is defined as 'science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems'.[1] Information about ADRs is mainly received through voluntary reporting systems. Many observational studies have examined the incidence, pattern and severity of ADRs, but most of these have been performed in other countries.[5] According to Pharmacovigilance Programme of India (PvPI) performance report 2017-18 total ADRs reported in 2018 were 81,638. There is increasing trend in the last five years.

Understanding the burden of ADRs, the relevant types and drugs involved is important to create awareness among the health professionals and to facilitate the rational drug use. It also helps to reduce readministration of offending drugs to prevent further morbidity in the patients. Hence this study is undertaken, to evaluate ADRs occurring in patients of our tertiary care hospital.

## METHODS

This retrospective observational study was conducted over a period of five years from January 2014 to December 2018 in a tertiary care hospital, BIMS, Belagavi. Our institution is an approved ADR monitoring center (AMC) under Pharmacovigilance Programme of India (PvPI). After the approval by institutional ethics committee, the recorded data of each patient in various departments was collected based on inclusion and exclusion criteria's and then evaluated. The data regarding demographic details of patients, drugs and adverse drug reactions was entered in a specially designed proforma and later into MS excel sheet.

Inclusion criteria: i) All records of outpatients and inpatients with suspected adverse drug reaction. ii) All age and sex.

Exclusion criteria: i) Patient records without proper documentation regarding information of reporter and patient details, drug and ADR details were excluded.

ADR reports were evaluated for seriousness, predictability, causality, severity and outcome using appropriate scales. Data analysis was carried out with simple descriptive statistics like percentage.

As per the specified criteria for serious ADR by WHO and US Food and Drug Administration (USFDA) and same being adopted by CDSCO in ADR reporting form, is being followed in our study.[6]

Also, the predictability classification of six types as determined by Aronson includes type A to type F.[7] In our study, Type A, C, D, E and F were considered predictable. Type B was considered unpredictable.

Causality was classified into six categories: certain, probable/likely, possible, unlikely, conditional/unclassified, unassessable/unclassifiable based on the WHO-Uppsala Monitoring Center criteria.[8]

Severity of ADRs was determined by using modified Hartwig criteria.[9]

Outcome of reactions was categorized according to CDSCO suspected ADR reporting form as recovered, recovering, not recovered, and recovered with sequelae, fatal or unknown.

## RESULTS

Total numbers of ADRs reported in five years were 410. As per the inclusion criteria 330 reported ADRs were analyzed out of which 217(65.76%) patients were females and 113(34.24%) males. Majority of patients were in the age group 21 to 50 years (69.7%). Among these ADRs 29(8.78%) were serious and 301(91.21%) were non-serious. The most common reason for considering as serious reaction was prolongation of hospitalization in 23(6.96%) cases. 4(1.2%) ADRs were life threatening which included Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), and 2(0.6%) cases needed an intervention to prevent permanent disability like ototoxicity and hearing loss caused by kanamycin and decreased vision due to ethambutol. There were no reports of death or congenital abnormalities.

Maximum ADRs were reported from Medicine department 188(56.9%) followed by ART Centre 80(24.2%) as shown in table 1. Cutaneous ADRs were the most frequent 134(40.6%) followed by cardiovascular ADRs 58(17.6%) and gastrointestinal ADRs 55(16.7%) shown in table 2.

**Table 1: ADRs reported from various departments.**

| Department | Number of ADRs (%) |
|---|---|
| Medicine | 188 (56.9) |
| ART Centre | 80 (24.2) |
| Dermatology | 25 (7.6) |
| TB Chest | 25 (7.6) |
| Emergency | 4 (1.21) |
| Psychiatry | 3 (0.9) |
| Ophthalmology | 2 (0.6) |
| Pediatrics | 1 (0.3) |
| ENT | 1 (0.3) |

**Table 2: Showing system affected.**

| System | Number of ADRs (%) |
|---|---|
| Cutaneous | 134 (41) |
| Cardiovascular | 58 (17.6) |
| Gastrointestinal | 55 (16.7) |
| CNS | 28 (8.5) |
| Hematological | 17 (5.2) |
| Sensory | 15 (4.6) |
| Renal | 10 (3) |
| Respiratory | 4 (1.2) |
| Endocrine | 4 (1.2) |
| Musculoskeletal | 3 (0.9) |

The drugs associated with the ADRs were divided into a few therapeutic classes. Antiretroviral agents were responsible for 80(24.2%) of all the ADRs followed by cardiovascular agents 70(21.2%), antidiabetics 44(13.3%), antimicrobials 39(11.8%), antitubercular 25(7.6%), NSAIDs and steroids 18 each (5.5%) as shown in Fig 1.

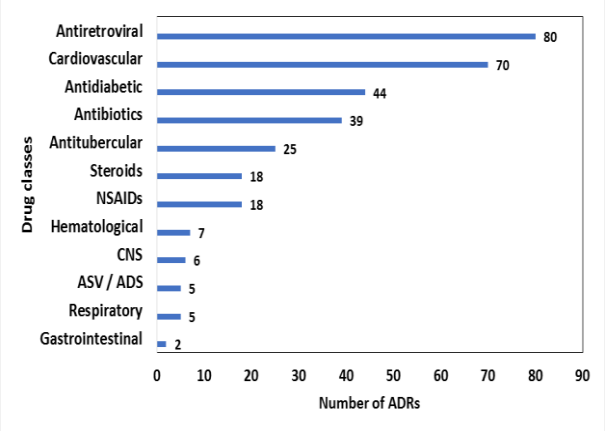


**Figure 1: Drugs classes involved in ADRs.**

Out of 330 ADRs, 165 reactions belonged to type A, 100 were type B, 64 were type C and 1 was type D according to the Aronson classification. Since type A, C and D reactions were considered as predictable, the predictability of ADRs reported in our study period was 69.7%.

Using the WHO-Uppsala Monitoring Center criteria for causality assessment, 2(0.6%) ADRs were identified as certain, 121(36.7%) as probable and 207(62.7%) as possible.

Using modified Hartwig's classification for severity it was found out that 129(39.1%) ADRs were mild, 201(60.9%) moderate and 0 in severe grade.

Assessment of outcome showed 256(77.6%) patients recovered from the reaction and 69 (21%) were recovering at the time of reporting ADR. 2(0.6%) patients had not recovered from ADR. In 3(0.9%) reports outcome was unknown due to loss of follow up as shown in the table 4.

**Table 4: Outcome of ADRs.**

| Category | Number of ADRs (%) |
|---|---|
| Recovered | 256 (77.6) |
| Recovering | 69 (21) |
| Not recovered | 2 (0.6) |
| Recovered with sequelae | 0 |
| Fatal | 0 |
| Unknown | 3 (0.9) |

## DISCUSSION

Out of 330 ADRs reported in our study the frequency was more common in the females 217(65.8%). Similar finding is seen in other studies.[10,11] Also one of the studies reported that women were more susceptible to ADRs than men due to an association of factors like greater concentration of adipose tissue and hormonal determinants that can affect metabolism may lead to the development of ADR.[6]

Highest percentage of ADRs was observed in the middle age group patients. Similar finding was seen in study by Jha N et al.[12]

Evaluation for seriousness showed 29(8.78%) ADRs. The most common reason for considering as serious reaction was prolongation of hospitalization in 23(6.96%) cases. Similar findings were seen in other studies.[13,14] 4(1.2%) ADRs were life threatening in the current study and similar pattern was reported in another study.[13] 2(0.6%) cases needed an intervention to prevent permanent disability like ototoxicity and hearing loss in both the ears caused by kanamycin and decreased vision which was due to ethambutol. These patients were advised to use hearing aid and consult ophthalmologist respectively.

In our study cutaneous ADRs like maculopapular rash, itching, urticaria, hypersensitivity reactions, Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN) were the most frequent 134(40.6%). This observation was consistent with other studies who also reported cutaneous reactions as the most frequent ones.[15,16] Antiretroviral agents were the most prevalent drugs responsible for cutaneous ADRs.

In our study cardiovascular ADRs were the second most frequently reported 58(17.6%). Amlodipine was the drug responsible for ADR like edema and postural hypotension. Gastrointestinal ADRs were the third most frequent 55(16.7%) which included diarrhea, vomiting and pain abdomen. Metformin was the drug mainly responsible for diarrhea. In contrast to the findings of our study Haile DB et al. reported that metabolic ADRs were most frequent followed by gastrointestinal ADRs.[4]

Antimicrobials 39(11.8%), antitubercular drugs 25(7.6%), NSAIDs and corticosteroids 18 each (5.5%) were the next most common drugs responsible for ADRs in our study. Study by Jha et al.[12] showed that antimicrobials were the most common causative drugs, whereas Pudukadan et al.[17] found NSAIDs to be the most common offending drug in their study. This variation is because of different patterns of drug usage in different populations.

Many studies have shown that patients taking more medications suffer from ADRs.[18,19] Similarly, our study also showed that polypharmacy is a risk factor for ADRs as most of the patients 69.6% were on two or more medications. Majority of the patients had co-morbidities which resulted in polypharmacy that lead to the occurrence of ADRs. 92(27.8%) patients on rational FDCs prescribed from dermatology department and ART center were also one of the reasons for additional ADRs.

Causality assessment in our study identified 121(36.7%) as probable, 207(62.7%) as possible and 2(0.6%) as certain due to re-challenge test or due to patient's ADR history to the same drug.

Severity assessment showed that, 129(39.1%) ADRs were identified as mild, 201 (60.9%) as moderate and none are severe. In this study most of the reactions were of moderate severity grade that might be due to the major contribution of cutaneous ADRs like rashes. Similarly, in the study by Geer MI et al. a smaller number of reactions belonged to severe grade.[20]

Assessment of outcome showed 256(77.6%) patients recovered from the reaction and 69(21%) were recovering at the time of reporting ADR. Shajahan J et al. showed in their study that 64.3% patients recovered from the reaction and 30% were recovering.[21]

## CONCLUSION

Based on these findings the major risk factor associated with ADR was polypharmacy. It is important to identify and avoid risk factors of ADRs to target the intervention. This can be avoided by rational drug usage, knowing the history of previous drug reactions to any specific drug and also by ruling out possible drug interactions and cautiously using drugs in special groups. Thus, there is

need for the prevention of ADR related health problems to protect patients from prolonged hospitalization and increase hospital expense occurring due to these reactions.

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