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Original Research Article

A retrospective study of adverse drug reactions in a tertiary care center

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ABSTRACT

Background: Adverse drug reactions (ADRs) are a major concern in clinical practice. Reporting of ADRs either through health care professionals or the patients themselves is of utmost importance to give an accurate estimate of the prevalence, severity and preventability of ADRs. Present study was conducted to evaluate the prevalence of adverse drug reactions in a tertiary care hospital in Hubballi, Karnataka, India.
Methods: This was a retrospective observational study, extending over 6 months (May 2019 to October 2019). A total of 124 cases comprising patients of either sex and age group ranging from 1month to 72 years were studied. The data was collected using CDSCO ADR reporting form. "Naranjo's Assessment Scale" was used for causality assessment and severity assessment was done in accordance with "Hartwig and Siegel scale".
Results: The study showed majority of ADRs were from General Medicine department and affected skin and appendages (59%). Skin rashes 44 (31.7%) were found to be the most commonly reported ADRs most of them were with antimicrobials 67 (54%). After causality assessment 83 (66.9%) of the cases were classified as probable and 41 (33.1%) were classified as possible. Majority of serious ADRs were not preventable in our study.
Conclusions: ADRs are a major cause of morbidity worldwide. Frequency of ADRs can be reduced by careful follow up and a robust hospital-based pharmacovigilance setup. Measures to improve detection and reporting of adverse drug reactions by all health care professionals is recommended.

Keywords: Adverse drug reactions, Causality, Pharmacovigilance, Preventability, Retrospective

INTRODUCTION

Drug is the single active chemical entity present in a medicine that is used for diagnosis, prevention, treatment/ cure of a disease. The World Health Organization (WHO) defines drug as "any substance or product that is used or intended to be used to modify or explore the physiological system, or pathological state for the benefit of the recipient".[1] Despite all the benefits of the drugs, the adverse drug reactions associated with them are also very common. Adverse drug reaction has been described by the WHO as a "noxious, unintended and undesired effect of a drug, which occur at doses used in humans for prophylaxis, diagnosis or cure of a disease."[2] Every time the patient is exposed to a new medication, the risk of Adverse drug reactions (ADRs) is present, as we cannot predict the incidence. Thus, no drug is absolutely safe, even when prescribed in therapeutic doses.[3]

ADRs are an important public health problem in terms of mortality, morbidity and costs.[4] Studies reveal that ADRs are leading to hospitalization and constitute a significant economic burden on patients in India. A study showed that hospital admissions due to ADRs accounted for 0.7% of total admissions and deaths due to ADRs accounted for 1.8% of total admissions in a territory referral center in South India.[5]

Pharmacovigilance is a science related to the detection, assessment, understanding and prevention of adverse

effects, particularly long-term and short-term adverse effects of medicines.[6] Spontaneous reporting of suspected ADRs by health professionals, followed by evaluation and incorporation into databases, allows for ongoing ascertainment of the benefit-risk ratio of a given medication, and constitutes one of the best methods for generating signals about unexpected and uncommon ADRs.[4] However, under-reporting of ADRs is widespread and a daunting challenge in pharmacovigilance (PV). It is estimated that only 6% of all adverse reactions are reported.[7] A study done on reasons for under reporting in India showed lethargy, indifference, insecurity, complacency, workload, lack of training as the common factors responsible.[8]

Present study was conducted to evaluate the nature, incidence, severity, causality and preventability of adverse drug reactions among patients visiting the hospital and to recognize the commonest adverse drug reactions amongst them and the drugs associated with them.

METHODS

This study was conducted at Karnataka Institute of Medical Sciences, Hubballi, Karnataka, India. This was a retrospective observational study. The data was obtained from CDSCO ADR reporting form used in the hospital for reporting ADRs to the ADR monitoring center as a part of the Pharmacovigilance Program of India. All the ADRs occurred from May 2019 to October 2019 were assessed.

Causality assessment was done based on Naranjo's probability scale. The total score was calculated based on the score and it was categorized as definite (score >9), probable (score 5-8), possible (score1-4) and doubtful (if the score is 0).[9] Modified Hartwig's criteria was used to assess the severity of ADRs into three categories: Levels 1 and 2 was classified as mild category; levels 3 and 4 as moderate category; levels 5, 6, and 7 were grouped as the severe category.[10] Preventability of the ADRs were classified into definitely preventable, probably preventable and not preventable based on the modified Shumock et al, criteria.[11]

The data was analyzed using Statistical Package for the Social Sciences (SPSS), IBM Corporation, version 21 and summarized using frequencies and percentages.

RESULTS

In this study period extending over a period of 6 months (May 2019 to October 2019) a total of 124 ADRs were studied.

Out of 124 patients, 72 (58%) patients were male while 52 (41.9%) patients were female (Figure 1).

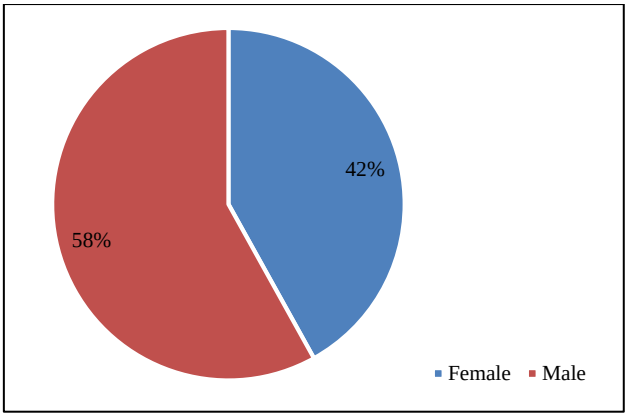

Figure 1: Gender distribution.

The mean age of the patients was 34.5±14.7. The youngest patient was of 1 year and the oldest was of 72 years. Maximum patients belonged to the age group of 41-50 year.

Out of 124 ADRs, 76 (61.3%) ADRs were reported from the General Medicine department followed by OBG 15 (12.1%), Dermatology, Venerology and Leprosy 15 (12.1%), Surgery 10 (8.1%), Pediatrics 3 (2.4%), Orthopedics 3 (2.4%), and ENT 1 (0.8%) departments (Figure 2).

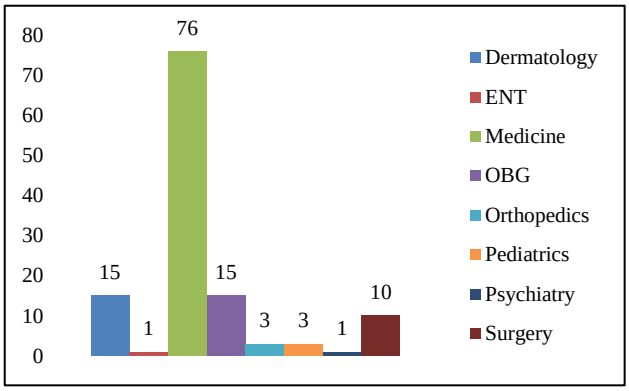

Figure 2: Department wise distribution of ADRs.

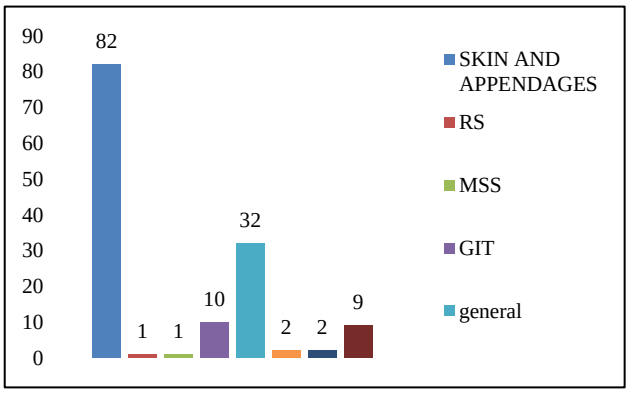

Figure 3: Distribution of adverse drug reactions in various organ systems.

Of the systems studied, majority ADRs were from skin and appendages (59%), followed by General (23%), GIT (7.2%), CNS (6.5%), CVS (1.4%), ENT (1.4%), RS (0.7%) and musculo-skeletal system (0.7%) (Figure 3).

The most common type of ADR was skin rashes in 44 (31.7%) of the cases. anaphylaxis was seen in 15 (10.8%) and 14 (10.1%) presented with SJS. 12 (8.6%) of the patients had hypersensitivity reaction and 10 (7.2%) complained of urticaria.

Table 1: Analysis of ADRs based on causality, severity and preventability.

Parameter	No. of ADRs	Percentage
Causality		
Definite	0	0
Possible	41	33.1
Probable	83	66.9
Uncertain	0	0
Severity		
Mild	20	16.1
Moderate	75	60.5
Severe	29	23.4
Preventability		
Not preventable	87	70.2
Definitely preventable	34	27.4
Probably preventable	3	2.4

The causality assessment was done according to Naranjo's probability scale and was found that 83 (66.9%) were probable and 41 (33.1%) were possible. None of the ADRs were definite or doubtful, in this study (Table 1).

Most of the ADRs which were observed in the study were moderate 75 (60.5%). 29 (23.4%) were mild while 20 (16.1%) were severe (Figure 4).

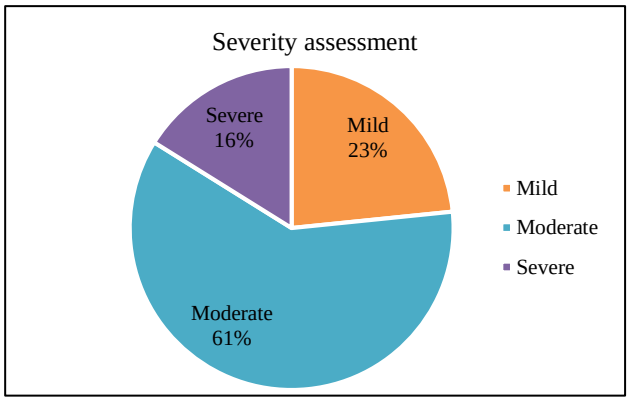

Figure 4: Severity assessment of the ADRs by 'Hartwig and Siegel scale'.

The preventability assessment was based on the modified Shumock and Thornton criteria. Out of 124 ADRs, majority 87 (70.2%) were not preventable, 34 (27.4%) ADRs were definitely preventable and 3 (2.4%) were probably preventable (Table 1).

Out of 110 serious ADRs, majority required intervention to prevent permanent impairment/damage 40 (36.4%) followed by 29 (26.4%) life-threatening ADRs. 41 (37.3%) required initial or prolongation of hospitalization (Figure 5).

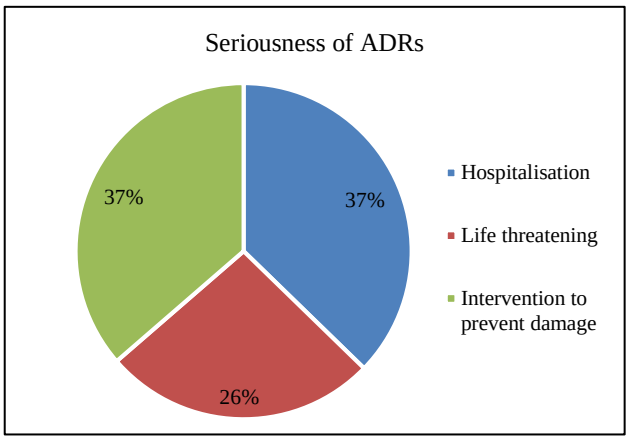

Figure 5: Seriousness assessment among ADRs recognised as serious (n=110).

The drug class most commonly associated with ADR's was Antimicrobials 67 (54%), followed by antiepileptic drugs 24 (19.4%), NSAIDs 10 (8.1%), hematinics 9 (7.3%), H2 antihistamines and PPIs 4 (3.2%), immunosuppressant and antineoplastic 4 (3.2) and 0.8% ADRs were from drug classes antihypertensive, oral hypo glycemic agents and antidepressants each 3 (2.4%) were from other classes (Table 2).

Table 2: Analysis of ADRs based on drug group.

Drurs	Frequency	Percentage
Antiepileptic	24	19.4
Antihypertensive	1	0.8
Antimicrobials	67	54.0
H_2 antihistamines and PPIs	4	3.2
Hematinics	9	7.3
Immunosuppressants and antineoplastic	4	3.2
NSAID	10	8.1
Oral hypoglycemics agents	1	0.8
Others	3	2.4
Anti-depressants	1	0.8

DISCUSSION

In the present study, the mean age of the study subjects is 34.5±14.7 years; this is quite similar to study conducted by Prajapati et al.[12] There were 72 men and 52 women with a male: female ratio of 1.38:1. These results do not

support previous findings that female gender is a risk factor for the development of adverse drug reactions.[13]

The incidence of ADRs was more in general medicine department this can be related to more inflow of patients in that department. This was also observed in study done by Raja and Venkatasubbaiah et al.[13,14]

In this study, skin and appendages constituted the most common system affected, accounting for (59.2%) of total ADRs reported with the predominant symptom being skin rashes seen in 44 (31.7%) of the patients, urticaria in 10 (7.2%). This is in congruence with studies conducted earlier by Kumar et al and Bhabhor et al.[2,15] However, Abhishake et al, and Sajin et al, reported different results, documenting gastrointestinal problems to be 39% and 33%, respectively, being most prevalent manifestation among patients with reported ADR.[3,16] General was the next most common system affected in this study, total reported ADRs were (19.4%) with 15 (10.8%) having anaphylaxis, 12 (8.6%) had hypersensitivity reaction and 3 (2.2%) had fever with chills.

The causality assessment of ADRs was done using the Naranjo scale. According to causality relationship 83 (66.9%) of the cases were classified as probable and 41 (33.1%) were classified as possible. None of the ADRs were definite and doubtful according to the causality assessment. The causality assessment in a study by Raja et al showed the most common one was probable ADR in 62.5% cases, possible in 32.3%, and 2.5% cases were uncertain which were in accordance with the present study though the authors had no cases of uncertain ADRs.[13]

Assessment of severity is also essential to take necessary action. In this study most of the reactions were moderate 75 (60.5%) followed by mild 29 (23.4%) and 20 (16.1%) showed severe reaction; this is similar to the study by Rani et al.[17]

Preventability assessment helps in improving rational drug use. In this study, according to the preventability assessment, 2.4% of the cases were evaluated as probably preventable, 27.4% as definitely preventable and 70.2% as not preventable. Similar results were found in the study done by Sriram et al.[18] Majority of serious ADRs were not preventable in our study. This can be explained by the fact that most of the reactions involving skin and its appendages are idiosyncratic. The non-preventability of these ADRs also indicates that drug treatment in the hospital is reasonably rational.

The seriousness of the reaction gives information on the risk involved, which is an important parameter to be considered in the marketing of drugs. Among the 110 ADRs which were found to be serious, 40 (36.4%) required intervention to prevent permanent damage and 41 (37.3%) increased hospitalization or prolonged hospital stay. In a study conducted by Prajapati et al also majority of the ADRs led to the hospitalization/ prolonged hospitalization (42.1%) and required intervention (43.7%) and a considerable number of serious ADRs were identified.[12]

Of all the drugs, antimicrobials were the most common cause of ADRs as they were the most commonly prescribed drugs. This was in concurrence with other similar studies by Adhikari A et al, Raja S et al, Venkatasubbaiah M, and Rani J.[13,14,17,19,20] However, Prashanthi B et al, observed anti-inflammatory agents and immunosuppressive drugs to be the most common cause of ADRs.[21]

CONCLUSION

ADRs are a rising concern in present day medical practice. With the number of drugs being marketed increasing every year, it is of paramount importance to have an in-depth knowledge of their possible adverse reactions. The study conducted showed the pattern of ADRs; most of ADRs were related to skin and appendages; antimicrobials most commonly caused ADRs. Anticipating, preventing, recognizing and responding to ADRs should be the prime concern of the clinicians so as to minimize the incidence of ADRs. A robust mechanism for reporting of ADRs is required and the clinician is to be always on the lookout for ADRs. Moreover, the patients also need to be counselled regarding to the side effects and reactions that the drug can cause so that they can seek help before it worsens. Detection, prevention and treatment of ADRs will not only improve the quality of life of the patient but will also reduce the cost.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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