PATTERN OF ADVERSE DRUG REACTIONS IN NEPHROLOGY WARD: A SOUTH INDIAN TERTIARY CARE HOSPITAL BASED STUDY

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Summary

Adverse drug reactions constitute a potentially avoidable component that contributes to patient's morbidity and mortality. The objective of this study is to find out the incidence rates and assess the severity of adverse drug reactions among inpatients of nephrology ward. A prospective observational study was conducted for a period of six months from Dec 2009 to May 2010. Data of all the reported adverse drug reactions observed in the patient population is collected and evaluated to understand the pattern of adverse drug reactions. Out of the 205 patients, admitted during the study period, 24 patients were found to have ADR's, which makes an incidence rate of 11.7%. Among these 24 patients who developed adverse drug reactions, it is seen that 75% were males and almost 37.5% of

them belonged to the age group of 40-60 years. The major co-morbid conditions noticed in the study were Hypertension 19 (79.16%) and Diabetes Mellitus 17 (70.83%). The most common class of drugs involved in causing adverse reactions were Steroids 10 (35.71%), Antibiotics 4 (14.28%) and Diuretics 2 (7.14%). Upon causality assessment 18 (64.3%) were found to be of possible association with the drug and on assessment it was found that definite improvement was seen, but only in 6 (21.4%) adverse reactions reported. On severity assessment, it was observed that 17 (60.71%) of the adverse reactions were of mild severity. In majority, 21 (75%) of the adverse reactions, there was a complete recovery at the time of discharge. In conclusion, adverse drug reactions represent an important clinical issue and it is necessary to monitor them for ensuring better healthcare.

Key words: Adverse drug reactions (ADRs), Adverse drug events (ADEs), Kasturba Hospital (KH)

Adverse drug reactions (ADRs) and adverse drug events (ADEs) pose a clinical problem in hospitals since all medical products entail inherent risk [1]. ADRs are considered as one among the leading causes of morbidity and mortality. These have a considerable impact on global health and also on health care costs; they account for 5% of all hospital admissions, and even increase the costs of patient care [1, 2]. ADRs are one of the most common causes of withdrawal of a certain drug from the market, with consequent enormous financial implications for the pharmaceutical industry [3].

According to World Health Organization (WHO) definition, ADR is defined as "A response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function" [4]. ADRs include adverse effects, extension effects, drug interactions, idiosyncratic reactions, and hypersensitivity reactions [5]. Drug event monitoring is a method of active pharmacovigiliance surveillance which helps to prevent ADRs and ADEs. Active surveillance can be achieved by reviewing medical records or interviewing patients and/or physicians to ensure complete and accurate data on adverse events. Reporting of ADRs has become an important component of monitoring and evaluation activities performed in hospitals. Such ADR reporting programs encourage surveillance for ADRs, promote the reporting of ADRs and stimulate the education of health professionals regarding potential ADRs. [6] Knowledge on ADRs helps in assessing the epidemiology of adverse events of hospital, and is a valuable parameter to reduce disease morbidity, drug related problems and optimize the patient care.

Kidney is the primary route of elimination for most of the drugs and their metabolites. Many drugs that are either eliminated by the kidney or have metabolites eliminated by the kidney can accumulate in the blood of patients with impaired renal function. This accumulation can cause severe and even life threatening adverse events, which can be aggravated by co-morbid conditions. It is important to determine the role of renal dysfunction in the occurrence of ADRs. As studies in India with regard to ADRs among hospitalized patients with renal dysfunction are limited, this study provides a valuable data on pattern of adverse events seen among renal failure patients of this hospital [7].

Kasturba Hospital (KH) is a 1400-bedded tertiary care teaching hospital in South India. An ADR reporting program exists in the hospital since July 2001 and the same is coordinated by the department of pharmacy practice of the hospital. The ADR reporting unit of KH was one among the peripheral centres of the national Pharmacovigilance program. The present study is undertaken to characterize the ADRs reported in our hospital with regard to the demographics of patients affected, drugs and reaction characteristics, outcomes, causality, severity, preventability and predisposing factors of the ADRs.

Material and Methods

The prospective study was conducted in the Nephrology department of the Kasturba hospital, Manipal for a period of six months i.e. from December 2009 to May 2010. A spontaneous reporting technique was followed which was co-ordinated by clinical pharmacists. The ethical approval was obtained from the University ethics committee before conducting the study. Patients admitted for a minimum of 48 hours and have developed ADR during the stay has been evaluated based on WHO definitions.

Clinical Pharmacists attended daily ward rounds with the Nephrologist in the hospital as part of the clinical services. During the ward rounds, clinical pharmacists encouraged doctors and other healthcare professionals to report the suspected Adverse Drug Events (ADE's) and have actively monitored those ADR's. On intimation of suspected ADR, the details of it are collected by patient medication history interview, reviewing the case file and based on the reporters comment. The collected data was recorded in the ADR reporting and documentation form for further assessment.

Data on the reported ADR's were evaluated to understand the pattern of ADR's with respect to patient demographics, nature of the reaction, characteristics of the drug involved, and outcome of the reactions. Causality assessment was done using Naranjo Scale to establish the association between the suspected drug and the clinical event. Severity and Predictability of the reported ADR's were assessed using Hartwig et.al. Scale. Preventability and the Presence of Predisposing factors for the reported adverse drug reactions were also analysed.

Results and Discussion

Demography status of study population

A total of 205 patients are included in the study. Mean age of the population is 48.58±16.23 years and majority of individuals are men (74.15%). The average number of medications used per day was seen to be 12.08±6.30

(minimum of 3 and maximum of 27 medicines/ day). Majority of the study population were of stage 5 renal failure and the median duration of hospital stay was found to be 14 days. Among the 205, only 24 patients were found to have Adverse Drug Reactions, which makes incidence rates of 11.7% which is comparable to the study of Lazarou et al which was 10.9% (8). Total number of drugs administered was 374, out of which 17 drugs were involved in 28 adverse drug events. Among 24 patients who developed ADR's, it was found that 75% were males and around 37.5% of them belonged to the age group of 40-60 years. The demographic status is summarised in the Table 1.

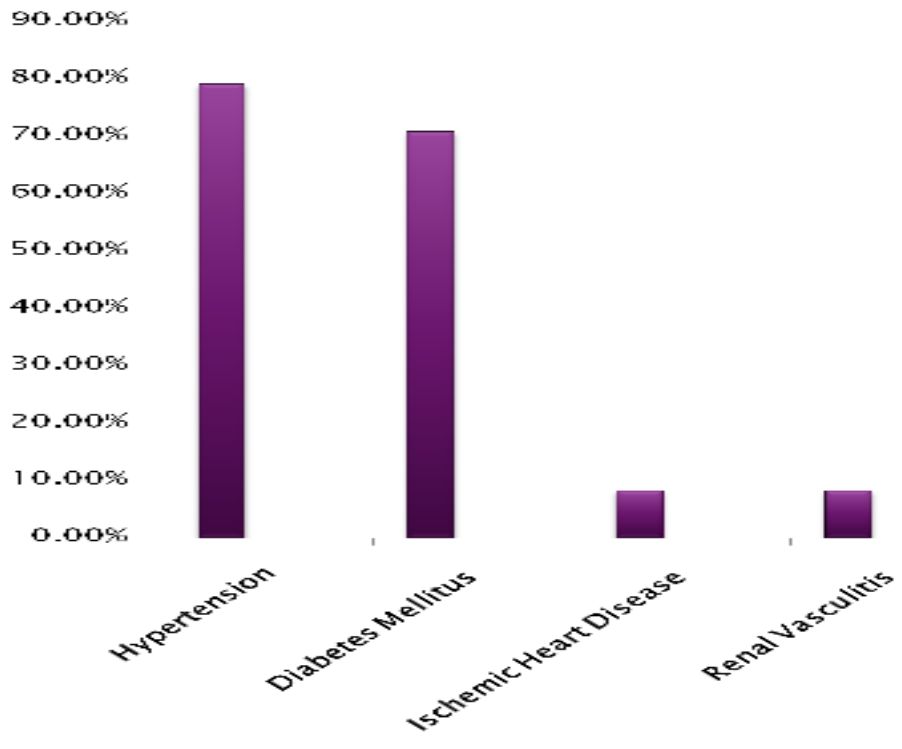
Table 1: Demographic features

	n = 24	%
Men/ Women	17/6	75/25
Age, Years		
Mean ± SD	49±15.94	
Range	10-80	

Clinical Characteristics of the Study Population

The analyses of clinical characteristics revealed that 6 (29%) patients had more than 2 co-morbid factors in the diagnosis. The major co-morbid conditions noticed in the study were Hypertension 19 (79.16%), Diabetes Mellitus 17 (70.83%), Ischemic Heart Disease 2 (8.33%), Renal Vasculitis 2 (8.33%), and COPD 1 (4.1%). It is summarized in the Figure: 1.

Figure1: Comorbidities



Endocrine system was the most common organ system affected by the ADR's in our study. The result has been summarized in the Table 2. This finding is inconsistent with many studies which have reported a higher percentage of dermatological manifestations than others as in the study done by Jha et al on prevalence of adverse drug reactions in the different hospitals of Kathmandu Valley (9). The most common class of drugs involved in causing ADR's were Steroids 10 (35.71%), Antibiotics 4 (14.28%) and Diuretics 2 (7.14%) . This finding is similar to that of "Adverse drug reactions in nephrology ward inpatients which was done by Joshua et al (7).

Table 2: Drug classes and major organ systems involved in Adverse drug Reactions

Drug Class	Renal/ Electrolyte	GIT	Endocrine	Blood	CNS	Cutaneous	Others
Steroids			5		1	2	2
Antibiotics		3		1			
Diuretics	2						

Causality Assessment of ADRs

According to the causality assessment done by Karch and Lasagna scale, 10 (35.7%) of ADR's were found to be of possible association while other 18 (64.3%) were found be of probable associations with the drug. This is in consistent to the study conducted in a South Indian secondary care hospital done by Rajendran et al (10). Assessment done by Naranjo algorithm shows that definite improvement was seen only in 6 (21.4%) ADR's. Among majority of them, 24 (85.71%) rechallenge was not done. On severity assessment, it was observed that 17 (60.71%) of the ADR's were of mild severity and 11 (39.28%) ADR's were of moderate type, with most of them 11 (39.28%) referring to level 2 severity, where the suspected drug needs to be withheld, discontinued or otherwise changed. This is similar to the study done by Jha et al and Kumar et al. (9, 11).

All the ADR's were assessed for their predictability and preventability. On evaluation, it was observed that 22 (78.57%) of the ADR's were predictable and 23 (82.14%) were found to be definitely preventable.

Assessment of outcomes has shown that, majority 21 (75%) of the ADR's, there was a complete recovery of the reactions at the time of discharge and for 6 (21.43%) of ADR's, the outcome was unknown. No fatal reactions were reported. While assessing the management of ADR's, it was revealed that in 11 (39.28%) of ADR's the drug was withdrawn, 3 (10.71%) ADR's drug doses was altered and among 14 (50%) of ADR's no changes was made in the therapy. The two important predisposing factors for the occurrence of ADR's, observed in this study, were extensive polypharmacy; (91.66%) and comorbidities; 8 (57.14%). The causality assessment data has been presented in the Table 3.

Table 3: Causality Assessment: Naranjo Scale	
Probable Association	35.7%
Possible Association	64.3%
On Dechallenge	
Definite Improvement	21.4%
No Dechallenge	64.28%
On Rechallenge	
No Rechallenge	85.71%
On Assessment of Predictability & Preventability	
Predictable	78.57%
Definitely Preventable	82.14%
Probably Preventable	17.86%
On Assessing the Management	
Drug Withdrawn	39.28%
Dose Altered	10.71%
No Change	50%
Treatment Given	
Symptomatic	57.14%
Specific	42.86%
Outcome	
Recovery	75%
On Severity Assessment	

Mild	60.71%
Level 1	21.43%
Level 2	39.28%
Moderate	39.29%
Level 3	21.43%
Level 4 (a)	17.86%
Predisposing Factors	
Polypharmacy	71.43%
Comorbidities	57.14%

Conclusions

Drugs which get cleared renally should be adjusted to prevent adverse reactions in renal dysfunction patients. The present study shows that higher incidence of ADRs was observed due to the extensive polypharmacy and comorbidities. Therefore, nephrologists should be very vigilant in prescribing drugs to renally impaired patients as it can lead to unwanted reactions. Reporting and monitoring of ADRs among renal failure patients of Nephrology unit of this hospital is essential to ensure safe pharmacotherapy.

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