

Profile of Adverse Drug Reaction Related Hospitalization in a Tertiary Care Teaching Hospital

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Abstract: Adverse drug reactions are a major problem worldwide and are one among the leading causes of morbidity and mortality. They are an important cause of hospitalization or prolongation of hospital stay. This study was conducted to find out the profile of ADR induced hospitalization in our tertiary care teaching hospital. A prospective, observational study was conducted over a period of 10 months in the department of Medicine. Cases admitted with suspected ADR in the in-patient department of Medicine were included in the study. The results showed that ADR related hospitalizations accounted for 0.24% of the total admissions to the Medicine department. Elderly male patients outnumbered females. Hypoglycemia was the commonest ADR, followed by other systems (Cutaneous, GI, CNS). Insulin and sulfonylureas were the most common suspected medications followed by antimicrobials, NSAIDs and antiplatelets. Polytherapy was the most common predisposing factor. Only 10% of ADR induced hospitalization were due to self-medication and rest 90% were due to prescribed medication.

Keywords –elderly, hypoglycemia, medicine, polytherapy

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I. Introduction

Adverse Drug Reaction (ADR) is a response to a drug which is noxious and unintended at doses normally used in humans for the prophylaxis, diagnosis or treatment of diseases, or for the modification of physiological function¹. ADRs are a major problem worldwide and are one of the leading causes of morbidity and mortality in health care facilities². In most countries, ADRs rank among the top 10 leading causes of mortality resulting in significant economic burden³.

ADRs may be of mild, moderate or serious category. An ADR is said to be serious if it is the cause of hospitalization or it leads to prolongation of hospital stay. There are very few studies related to drug induced hospitalization. Hence this study was conducted to evaluate the profile and frequency of ADR related hospitalizations in the department of Medicine of our tertiary care hospital.

II. Patients And Methods

A prospective, observational study was conducted over a period of 10 months i.e. from January 2016 to October 2016 in the Department of Medicine in collaboration with the ADR Monitoring Centre, Department of Pharmacology, S.C.B. Medical College, Cuttack. The study was approved by the Institutional Ethics Committee.

Inclusion Criteria-All adult patients (aged >14 years) presenting to the Medicine Department with suspected adverse drug reaction and considered for hospitalization and willing to participate in the study.

Exclusion Criteria-Patients with intentional or accidental poisoning and those with drug abuse.

Upon admission, a detailed history was taken regarding the drugs consumed, its class, whether prescribed or self-medicated and duration of treatment with the suspected drug. The presenting symptoms and signs were noted and routine haematological and biochemical investigations like complete blood count, blood glucose level, liver function tests, kidney function tests, coagulation profile were done. The measures taken in the hospital like whether drug was withdrawn, dose reduced or treatment continued or any other treatment given were noted. The patients were followed up during the course of hospitalization and the outcome, discharge or death was recorded.

III. Results

A total of 204 ADR induced hospitalization were observed in our tertiary care teaching hospital during the 10 month study period, out of which 91 (44.6%) were admitted to the department of Medicine while 113

(55.4%) were admitted to other departments. The burden of ADR related hospitalization in the dept. of Medicine was 0.24% in comparison to the total admitted cases in the department (37,902) in the span of 10 months.

Table 1: Age and Sex Distribution of ADR induced Hospitalized Patients

Age In Years	Male	Female	Total(%)
15-20	4	2	6(07)
21-30	6	3	9(10)
31-40	4	2	6(07)
41-50	3	6	9(10)
51-60	9	14	23(25)
61-70	16	9	25(27)
71-80	4	6	10(11)
81-90	2	1	3(03)
Total	55 (60.44%)	36 (39.56%)	91(100)

Majority of the patients belonged to the age group of 51 – 70 years, with a mean age of 54.71 years. Maximum number of male cases were in the 61-70 years age group whereas females were in 51-60 years age group. The difference of age distribution between male and female patients was statistically not significant (p=0.444).

Table 2: Profile of ADRs affecting different Organ systems and Suspected Drugs (according to WHO-ART {Adverse Reaction Terminology}, 2012)

Organ System-No (%)	ADR Profile	No. of Cases	Suspected Medications
Endocrine- 45(49)	Hypoglycemia	45	Regular Insulin, Pre-Mixed Insulin Glimiperide, Gliclazide, Glipizide
Skin And Appendage- 16(17)	FDE	3	Levofloxacin, Piroxicam, Phenytoin
	Drug Rash	7	Ceftriaxone, Paracetamol, Vancomycin, Etoricoxib, Sulfamethoxazole + Trimethoprim
	Dapsone Reaction	1	Dapsone
	SJS-TEN	5	Phenytoin, Levofloxacin, Azithromycin, Sulfadoxine + Pyrimethamine
Gastro Intestinal-6(7)	Acute Gastritis	2	Aceclofenac, Paracetamol
	Upper GI Bleed	4	Aceclofenac, Diclofenac
Liver & Biliary- 6(7)	Hepatopathy	6	Isoniazide, Rifampicin, Pyrazinamide
Blood-Platelet - 6(7)	CVA(ICH)	6	Aspirin, Clopidogrel, Sunitinib
Blood-RBC Disorder- 2(2)	Anemia	1	Methotrexate
	Haemoglobinuria	1	Primaquine
Musculoskeletal-1(1)	Myopathy	1	Prednisolone
Metabolic - 7(8)	Hyperkalemia	1	Digoxin
	Hyponatremia	6	Hydrochlorthiazide, Olanzapine, Thioridazine
Immunological - 2(2)	Anaphylaxis	2	Piroxicam, Cefaclor

The endocrine system was most commonly involved and hypoglycaemia was the leading cause of ADR related hospitalizations in 45(49%) cases. It was followed by cutaneous drug reactions (17%). Insulin and sulfonylureas were the most common suspected drugs causing ADR in our patients. Hypertension was an important co-morbid condition in antiplatelet drug associated intracerebral haemorrhage.

Table 3: Class of Suspected Drugs causing ADR induced Hospitalizations

Class Of Drugs	Percentage	Class Of Drugs	Percentage
Anti Diabetic	48.37%	Anti Hypertensive	0.83%
Anti-Microbial Agents	21.66%	Cytotoxic	0.83%
Nsaids	15.00%	Cardiac Glycoside	0.83%
Anti Platelet	7.5%	Steroid	0.83%
Anti Epileptic	2.5%	Immuno-Modulator	0.83%
Anti Psychotic	1.66%	Miscellaneous	0.83%

Anti-Diabetic Drugs Were The Most Common Class Of Drugs Causing ADR Followed By Antimicrobial Agents.

Table-4: ADR induced Hospitalization associated with Different Types of Therapies

Type Of Therapy	Mono Therapy	Poly Therapy	FDC	Total
No Of Cases	18 (19.8%)	55 (60.4%)	18 (19.8%)	91

Monotherapy(one drug) was found in 19.8% cases, poly therapy(two or more drugs) in 60.4% cases and FDC(fixed dose combinations) in 19.8% cases.

Only 10% of ADR induced hospitalization were due to self-medication and the rest 90% were due to prescribed medication.

IV. Discussion

In the Department of Medicine of our Institute, it was observed that 0.24% of patients were hospitalized due to ADR. This was lower than that observed in other studies^{2,4,5,6,7} which ranged from 0.7 % to 24.1%. This might be because some ADR cases are admitted to other departments (cutaneous ADRs to Dermatology ward, drug induced hepatitis to Hepatology ward). But under-reporting might be an important factor in our set up, either due to poor awareness about ADR reporting system or unintentional negligence in reporting the ADR.

In our study, most of the ADR were reported in the 5th and 6th decade age groups (paediatric patients were not included in our study). A total of 66% of all ADRs were reported in the age group >50 years. These findings corroborate with the results of other studies^{8,9,10} which have clearly shown that the incidence of ADRs are more common in geriatric and pediatric age group. This finding may be due to the greater vulnerability of these age group patients to drugs, presence of co-morbid conditions, multiple drug consumption and increased attendance at health care center for consultation.

ADRs were more reported in males than in females in our study. This corroborates with the result of another study¹¹, but contradicts the results of many other studies^{12,13,14}. The pharmacokinetics and pharmacodynamics of drug metabolism differ between two sexes and influenced by gender specific factors such as body fluid, hormonal transitions or medical-seeking behavior. In our region there was a limiting access of females to health care compared to males, or less reporting of ADRs by females compared to males. The cause may be various social factors that is limiting the females for health access. Disproportionately higher cases of ADR in males can also be due to increased health seeking behavior of males and self-medication practice, leading to increased chance of occurrence of reaction and increasing hospital visit for this condition.

The most common system associated with ADRs in our study was the Endocrine system (49.0%). This is in contrast to many studies who have reported a higher percentage of dermatological manifestations than other system involvement^{8,15,16,17}. This might be because our study was conducted in the Medicine department only and many cutaneous ADRs get admitted to the Dermatology department of our hospital. Hypoglycemia was the major ADR observed, in diabetic patients who were on antidiabetic medications like insulin or oral hypoglycaemic drugs. This was followed by dermatological involvement (17.0%), this could be due to increased awareness of skin reactions which are more visible and appreciable by the patients and care takers, compared to the involvement of other organ systems. Also, physicians are more careful to note skin reactions as they often present with severe and life threatening forms like Steven-Johnson's syndrome (SJS), toxic epidermal necrolysis (TEN) or erythema multiforme. Metabolic derangement was found in 8.0% of cases, followed by CNS involvement in 7.0%, GI system (7.0%) and liver & biliary system involvement (7.0%). GI system involvement was less in our study, probably because these patients might have been admitted to Gastroenterology or Hepatology wards of our hospital.

Different studies by Swami S. et al¹⁸, H. Singh et al¹⁷, Rajat et al¹⁹ and Begum et al²⁰ have shown that antimicrobial agents were the most common drugs causing ADRs in 38.31%, 28.57%, 51.0% and 42.86% respectively. But in our study it was observed that antidiabetic drugs (insulin and sulfonylureas) were the most common agents (48.37%), followed by antimicrobial agents (21.66%) and NSAIDs (15%) (Table 3). H. Singh et al¹⁷ and Leslie Jo et al⁴ found antidiabetic drugs related ADR in 14.28% and 4.8% respectively. The high incidence of antidiabetic drug related hypoglycemia seen in our study is probably because our patients were from Medicine department only, where all hypoglycemic patients are admitted on emergency basis.

Polytherapy was observed in 60.4% of our patients compared to monotherapy in 19.8% patients and fixed drug combination in 19.8% (Table 4). Carboninet al²¹ had also shown that multiple medications is one of the predisposing factor for occurrence of drug reactions. Most drug reactions due to polytherapy could be explained by drug interactions (Nikicaet al²²).

V. Conclusion

ADR related Hospitalization accounts for 0.24% of total admissions to Medicine ward in our tertiary care hospital, which may be an under reporting. Elderly patients and polytherapy are the most common predisposing factors. Hypoglycaemia is the most common cause among ADR induced hospitalization, Insulin and sulfonylureas are the most common medications associated with hypoglycaemia. Hypertension is an important co-morbid condition in antiplatelet drug associated intracerebralhaemorrhage. Hence frequent blood glucose monitoring in diabetic patients on insulin or sulfonylureas and frequent blood pressure monitoring in patients on antiplatelet may reduce the incidence of ADRs. Adequate amount of 25% Dextrose solution should be kept available in the Emergency Department and in the Medicine ward of our hospital for immediate treatment of hypoglycaemia.

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