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A PROSPECTIVE OBSERVATIONAL STUDY ON ADVERSE DRUG REACTIONS OF ANTIBIOTICS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

The aim of the present study was to detect and analyze adverse drug reactions of antibiotics in a tertiary care hospital. This was a prospective observational study carried out in the Department of General Medicine (Osmania General Hospital) over a period of six months. The present study was conducted to assess the prescription pattern of antibiotic usage. Standard pro-forma was used to collect the information regarding antibiotics, its dose, duration, first line of antibiotics and second line of antibiotics and adverse drug reactions. A Total of 100 ADRs was reported from 100 patients during the study period with female predominance (72%) over males. The average age of the patients in the study was found to be 55-70 years. The majority of the ADRs occurred in the age group of 40-80 years. More number of ADRs was from General Medicine Departments in which the most affected organ systems were the GIT (22%) and the skin (19%). The antibiotic classes mostly accounted were cephalosporin (16%) followed by other. The severity assessment revealed that most of them were moderate followed by mild and severe reactions. Of the reported reactions, 30 % were definitely preventable and causality assessment was done which showed that the reactions were probable, possible. Results show that cephalosporin was extensively used in the department of General medicine. The system should promote the spontaneous reporting of adverse drug reactions to antibiotics. Proper documentation and periodic reporting to regional Pharmacovigilance centre's to ensure drug.

Keywords: Adverse drug reactions, Antibiotics, Tertiary care hospital.

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INTRODUCTION

Drugs are the most common medical interventions, primarily used to relieve sufferings. But it has been recognized long ago that drug themselves can prove fatal; as the saying rightly goes ''Drugs are Double Edged Weapons''. Adverse reaction monitoring and reporting are very important in identifying the adverse reaction trends in local population.[1] The WHO defines an ADR as ''any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiologic function.'' Thus this definition excludes overdose (either accidental or intentional), drug abuse, and treatment failure and drug administration errors.[2]

Adverse Drug Reactions (ADRS) are important causes of mortality and morbidity in both hospitalized and ambulatory patients. In many countries ADRs rank among the top 10leading causes of mortality. So there is a need to study ADRs seriously to create awareness about ADRs among patients to motivate health care professionals in the hospital to report ADRs to minimize the risk. Early detection, evaluation and monitoring of ADR are essential to reduce harm to patients and thus

improve public health.[3] The safety of drug prescribing has become a highly visible topic in medicine. Patients constitute a vulnerable group with regard to rational drug prescribing since many new drugs are released into the market without the benefit of even limited experience. This deficiency causes a practitioner to often prescribe drugs in an 'off label' manner, thereby increasing the risk of drug toxicity. As more drugs are marketed and as more individuals take multiple drugs, the occurrence of Adverse Drug Reaction will probably continue to increase. Therefore, better approaches must be devised for reporting and assessment and management to find individuals who present with drug induced diseases. [3]

ADRs have a considerable negative impact on both health and healthcare costs. ADR monitoring and reporting activity is in its infancy in India. India is a developing country with a large drug consuming population. It is the fourth largest producer of pharmaceuticals in the world with more than 6000 licensed drug manufacturers and over 60,000 branded formulations. Thus it is essential that the drug treatment should be safe, efficacious and cost effective. It is also emerging as a clinical trial hub exposing larger population to newer drug treatments.

The Ministry of Health and Family Welfare had initiated the National Pharmacovigilance Program (NPP) on 1st January 2005 which was further revived in July 2010. This program is overseen by the Central Drugs Standard Control Organization (CDSCO), New Delhi .4 Antibiotics belong to different classes such as penicillin's, cephalosporins, sulfonamides, and amino glycosides, and they vary in respect of their mechanism of actions and adverse effects. Antibiotics are used commonly in routine practice for treatment and prophylaxis of various disease conditions4 .Over half of all hospitalized patients are treated with antimicrobial agents and their use account for 20–50% of drug expenditures in hospitals. The total costs associated with antibiotics are not only related to antibiotic use itself, but also to co-medication and adverse drug events. The main aim of this study was to detect and analyze Adverse Drug Reactions (ADR) to antimicrobial drugs in hospitalized patients of a tertiary care hospital.

METHODOLOGY

A prospective observational study on adverse drug reaction is carried out in Department of General Medicine of Osmania General Hospital Hyderabad, India a tertiary care hospital for a period of 6 months on 100 cases. The present study was approved by Institutional Ethics Committee (MCP/PD/PR/10). The present study was conducted to assess the prescription pattern of antibiotic usage. Standard pro-forma was used to collect the information regarding antibiotics, its dose, duration, first line of antibiotics and second line of antibiotics and adverse drug reactions. Patient of all age groups of either gender more than 18 years who developed adverse drug reactions of antibiotics in hospital or admitted due to ADRs were included for the study. Patients with intentional and accidental poisoning, patient doesn't want to give consent and patients suffering from severe hepatic, renal and cardiac impairment were excluded from the study. The data for the study were taken from Case sheets, investigation reports of patients who had experienced an ADR, personal interviews with reporting persons or clinicians, patient's attendant, past history of medication use. The socio demographic clinical characteristics and medication prescribed was documented in special design form. Analysis was carried out to assess the prevalence, severity and significance identified using Microsoft excels.

RESULTS

During the study period, a total of 100 antibiotic Adverse Drug Reactions were reported among 100 patients admitted for antibiotic use. The incidence rate of antibiotic Adverse Drug Reactions was found to be 100%. Six month study revealed that Figure 1 shows female patients 72 (72%) predominated over males 28 (28%) in ADR occurrence. Figure 2 shows the age wise distribution of the total population and revealed that the average age of the patients in the study was found to be 55-80 years. The majority of the ADRs occurred in the age group of 51-60 years. The antibiotic classes affected with ADRs are shown in (Table 1) which revealed that cephalosporin's were the most accounted antibiotic class 16 (34.69%) followed by fluoro-quinolones 13, aminoglycosides 13, penicillins 11, miscellaneous antibiotics 7, Sulphonamide 7, Tetracycline 5, Azoles 4. Of the reported ADRs, Type A 13 (16.25%) was the most common compared to Type B 45(56.25%) reactions according to the ADR classification by Rawlin and Thomson (Figure 3). In 20% cases the suspected drug was withdrawn while no change was made with the suspected drug in 1% and the dose was altered in (5%) cases. From this study, it was found out that there was a recovery from ADRs in total of 100 patients 100 % although 20% had fatal ADRs.

Figure 4 shows the probability assessment of reported ADRs as per the Naranjo scale and revealed that 1 (1%) were High probable, 89 (89%) were possible, 6 (6%) were doubt full 4 (4%). Figure 5 shows the distribution of patients outcomes of ADRs in which life threatening 15, hospitalized 22 and discharged 63 patients. Figure 6 shows the distribution of ADRs based on common, uncommon, rare and very rare.

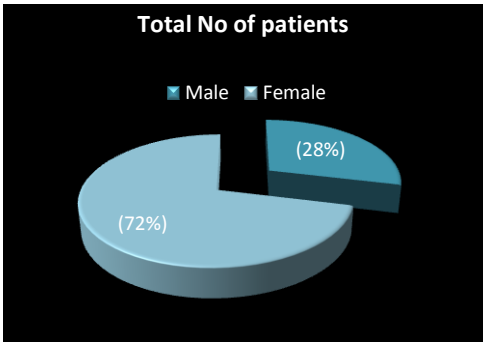

Figure 1: Distribution of Subjects Based Upon the Gender.

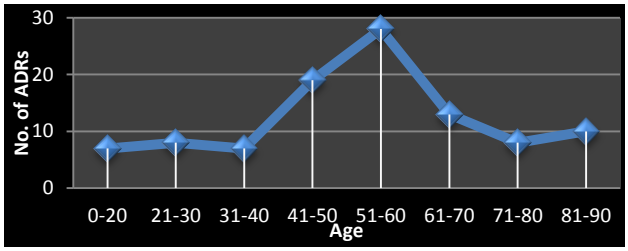

Figure 2: ADR based on age distribution of patients.

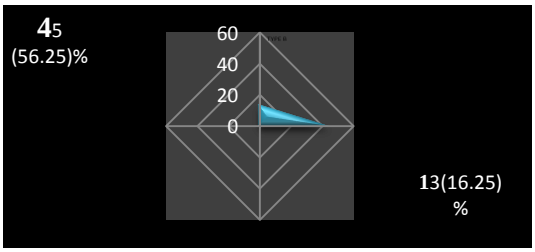

Figure 3: Classifications of ADRS based on Rawlin and Thomson

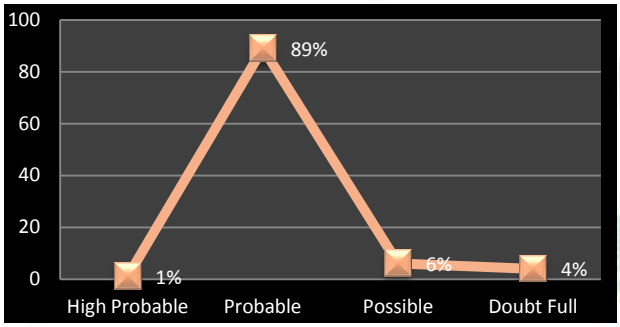

Figure 4: Probability assessment (using the Naranjo scale)

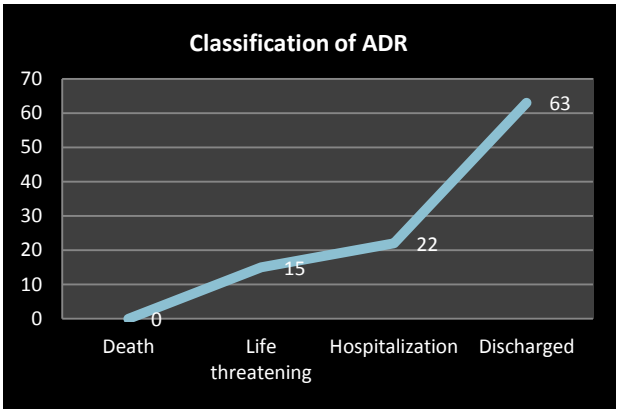

Figure 5: Distribution of patients based on outcomes of ADR

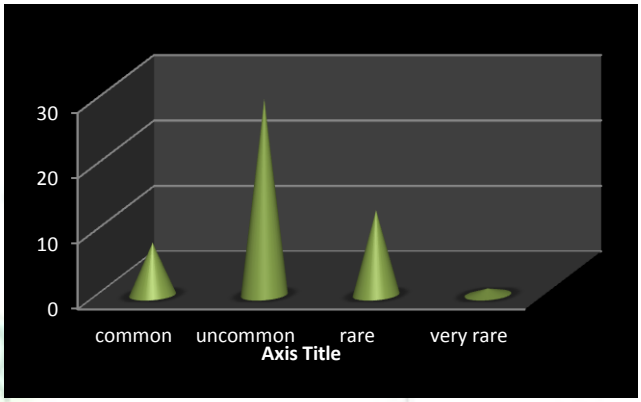

Figure 6: Classification of ADR common, uncommon, rare, very rare

Table 1: Adverse drug reactions observed during the studyClass of Antibiotics and shows Therapeutic class of antibiotics implicated to cause ADR (n=100)

S. No.	Class of Drug	Name of Drug	Adverse drug reaction	No. of ADRs (100)	% of ADR
1	**Sulphonamide**	Sulfadoxine	Serious allergic skin reaction	1	1%
		Mafenide	Metabolic acidosis	2	2%
		Sulfasalazine	Headache	2	2%
		Sulfadiazine	Allergic skin reactions	1	1%
		Sulfimoxole	Crystalluria	1	1%
2	**Sulphonamides and cotrimaxazole**	Cotrimoxazole	Megaloblasticanemia	1	1%
		Trimethoprim	Ulcers on tongue	1	1%
3	**Penicillin's**	Penicillamine	Good pastures syndrome	1	1%
		Penicillin g	JarischHerxheimer reaction, Hyperkalaemia	4	4%
		Ampicillin	Black hairy tongue	4	4%
		Ticarcillin	Bleeding	1	1%
		Carbenicillin	Bleeding	1	1%
4	**Cephalosporins**	Ciprofloxacin	Swelling of lips, Severe headache, Pulmonary edema	3	3%
		Cefaclor	Drug fever skin rashes	2	2%
		Cefotaxime	Asthma	1	1%
		Cefixime	Diarrhoea	1	1%
		Ceftriaxone	Angioedema	1	1%
		Cephalexin	Hallucinations	3	3%
		Cefazolin	Hallucinations	2	2%
		Cefpodoxime	Asthma	1	1%
		Cefipime	Disulfuram like reaction	1	1%

		Cefadroxil	General moniliaris	1	1%
5	**Beta lactam inhibitors**	Amoxcillin and clavunic acid	Moderate rise in(ALT)	1	1%
6	**Tetracycline**	Demeclocycline	Diabetes insipidus	1	1%
		Minocycline	Ataxia vertigo nystagmus	1	1%
		Tetracycline	Skin rashes, Maculopupular and Erythromatous rashes	2	2%
		Oxytetracycline	Renal damage	1	1%
7	**Aminoglycosides**	Neomycin	Ototoxicity	5	5%
		Amikacin	Hypotension	3	3%
		Framycetin	Skin rashes	1	1%
		Gentamicin	Incresaed Blood urea nitrogen	3	3%
		Tobramycin	Ototoxicity	1	1%
8	**Microlide antibiotics**	Azithromycin	Abdominal pain	2	2%
		Erythromycin	Seizures	3	3%
9	**Quinolones**	Ofloxacin	Dry mouth* Insomnia	1	1%
		Naliddixic acid	Seizures	1	1%
10	**Chloramphenicol**	Chloramphenicol	Gray baby syndrome	4	4%
11	**Nitroimidazole**	Metronidazole	Insomnia	3	3%
		Tinidazole	Metallic taste	1	1%
12	**Antitubercular drugs**	Pyrazinamide	Hepatotoxicity	2	2%
		Streptomycin	Pain at the site of injection	2	2%
		Cycloserine	Convulsions	1	1%
		Ethambutol	Optic neuritis	1	1%
		Isoniazid	Hepatitis	2	2%
		Para amino salicylic acid	Abdominal pain	2	2%
		Ethionamide	Hair loss	1	1%
		Rifabutin	Neutropenia	1	1%
		Kanamycin	Nephrotoxicity	1	1%
13	**Antileprotic drugs**	Clofazimine	Brownish discolouration of skin	1	1%
		Dapsone	Steven Johnson syndrome	1	1%
14	**Anti viral drugs**	Ganciclovir	Bone marrow toxicity	1	1%
		Foscarnet	Kidney damage	1	1%
		Zidovudine	Anemia	1	1%
		Acyclovir	Headache	1	1%
15	**Anti fungal drugs**	Voriconazole	Impaired vision	1	1%
		Griseofulvin	Skin rashes	1	1%
		Fluconazole	Thrombocytopenia	1	1%
16	**Miscellneous antibiotics**	Clindamycin	Damage of nerves	3	3%
		Vancomycin	Nephrotoxicity	2	2%
		Bacitracin	Abdominal pain	1	1%
		Linezolid	Vaginal candiasis	1	1%

Table 2: Types of reactions observed (n=100):

S. No.	Types of Reactions	No. of ADR	% of ADR
1.	Serious allergic skin reaction	3	3%
2.	Metabolic acidosis	2	2%
3.	Headache	2	2%
4.	Diptheria	1	1%
5.	Crystalluria	2	2%
6.	Haemolytic anemia	1	1%
7.	Hallucination	3	3%
8.	Megaloblasticanemia	1	1%
9.	Ulcers on tongue	1	1%
10.	Ototoxicity	1	1%
11.	Hypotension	1	1%
12.	Angioedema	1	1%
13.	Incresaed Blood urea nitrogen (BUN)	1	1%
14.	Skin rashes	5	5%
15.	Drug fever skin rashes	1	1%

16.	Swelling of lips	1	1%
17.	Dizziness	3	3%
18.	Anemia	3	3%
19.	Nephrotoxicity	2	2%
20.	Vestibular damage	1	1%
21.	Rashes	1	1%
22.	Hepatitis with cholestatic jaundice	1	1%
23.	Damage of nerves	1	1%
24.	General moniliaris	1	1%
25.	Abdominal pain	5	5%
26.	Diptheria	1	1%
27.	Vaginal candiasis	1	1%
28.	Rashes all over the body	1	1%
29.	Erythema peeling and burning of skin	1	1%
30.	Impaired vision	1	1%
31.	Cardiac arrhythmias	1	1%
32.	Thrombocytopenia	1	1%
33.	Black hairy tongue	1	1%
34.	Bleeding	2	2%
35.	Diarrhoea	3	3%
36.	Hyperkalaemia	2	2%
37.	Good pastures syndrome	1	1%
38.	Asthma	1	1%
39.	Migrane	1	1%
40.	Diabetes insipidus	1	1%
41.	JarischHerxheimer reaction	1	1%
42.	Moderate rise in(ALT)	1	1%
43.	Thrombophilibitis	1	1%
44.	Muscle twitching	1	1%
45.	Bone marrow toxicity	1	1%
46.	Kidney damage	2	2%
47.	Disulfuram like reaction	1	1%
48.	Pulmonary edema	1	1%
49.	Brownish black discolouration of skin	1	1%
50.	Steven Johnson syndrome	1	1%
51.	Inflamation of tongue	1	1%
52.	Gray baby syndrome	1	1%
53.	Insomnia	1	1%
54.	Metallic taste	1	1%
55.	Seizures	3	3%
56.	Constipation	1	1%
57.	Hepatotoxicity	1	1%
58.	Pain at the site of injection	1	1%
	Convulsions	1	1%
60.	Optic neuritis	1	1%
61.	Hepatitis	1	1%
62.	Hair loss	1	1%
63.	Neutropenia	1	1%
64.	Ataxia vertigo nystagmus	1	1%
65.	Dry mouth* insomnia	1	1%
66.	Skin rashes	7	7%
67.	Severe rashes	1	1%

DISCUSSION

Antimicrobials are the most frequently prescribed drugs among hospitalized patients especially in Department of General Medicine and DVL. Total of 100 ADRs were reported from 100 patients during the study period with female predominance (72%) over males. The average age of the patients in the study was found to be 55-80 years. The majority of the ADRs occurred in the age group of 51-60 years. The cephalosporins were the most used antibiotic class in the inpatient settings, so that the reported ADRs were also more in these drug classes. A study revealed the predominance of cephalosporins where as Aminoglycosides were most accounted in a other study.[4,5] while vancomycin and penicillins were most frequent in the other studies.[6-8] Analysis of the type

of reported ADRs according to Rawlin and Thomson scale revealed Type B predominance.[7] This result is in line with the all the reported reactions were Type B reactions.[8-10] Type A reactions are dose related and thus were preventable from their known pharmacology and therefore all of them were potentially avoidable.[11] Eva states that Type B reactions comprise approximately 10–15% of all ADRs and include hypersensitivity drug reactions.[12] The present study hints that pharmacists' involvement may not only greatly increase the reporting rate but also quality of reporting. It is suggested that the most appropriate approach of medication control to minimize the incidence of ADR is screening the total medication of the individual patient by a hospital/clinical pharmacist and by taking history of allergy as well as past medication and medical history. Hospital/clinical pharmacists have also a greater role to play in the area of Pharmacovigilance to strengthen the national Pharmacovigilance program. Developing and maintaining electronic documentation of patients' medical records may serve as a valuable tool to detect early signals of potential ADRs. In addition, creating intranet facilities within a hospital may help in easy access for healthcare professionals to updated patients' medical records resulting in possible detection and prevention of ADRs. Also, the implementation of a computerized reporting system in hospital setup may hasten reporting of ADRs and is suggested.

CONCLUSION

A relatively high incidence of adverse drug events have been recorded which shows that not only Geriatric patients, but also adults are more susceptible to adverse drug effects. A number of drugs in combination were used, and ADEs often get multiplied. Careful therapeutic monitoring and dose individualization is necessary. This study strongly suggests that there is greater need for streamlining of hospital based ADR reporting and monitoring system to create awareness; and to promote the reporting of ADR among healthcare professionals of the country. Measures to improve detection and reporting of ADR by all health care professionals should be undertaken, to ensure patient's safety.

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