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A PROSPECTIVE STUDY ON ADVERSE DRUG REACTIONS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

The aim of the present study was to detect and analyze the adverse drug reactions (ADRs) of antibiotics and other drugs in a tertiary care hospital. A total of 61 ADRs were reported during the study period with male predominance (51.85%) and geriatric age group. Number of ADRs was reported more from General Medicine (45.90%) and ICU (21.31%) departments in which the most affected organ systems were the GIT (34.42%), skin (18.03%) and Central Nervous System **7**(11.47%). The class of drugs most commonly associated with the reported ADRs was antimicrobials 20(32.75%). The severity assessment revealed that most of them were mild level 1 (32.78%) followed by moderate and severe reactions. Of the reported reactions 57.37% of ADRs were definitely preventable, 29.50% of ADRs were probably preventable and 13.11% were not preventable. The study concluded that ADRs to antibiotics are common and less compared to other studies. Proper monitoring and reporting can ensure drug safety profile of drug.

Keywords: Adverse Drug Reactions; Antibiotics; Prospective study; Drug safety

INTRODUCTION

Adverse drug reaction (ADR) monitoring and reporting are very important for any drugs and is an integral element in drug safety surveillance and Pharmacovigilance.[1] ADR is any undesirable effect of a drug beyond its anticipated therapeutics occurring during clinical practice. The World Health Organization (WHO) defines an Adverse Drug Reaction (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 psychological functions. [2]

ADRs can occur in all settings where healthcare is provided. Most of the current evidence comes from hospitals because the risks associated with hospital treatment are higher, or where most of the antibiotics used. The majority of ADRs occur as a result of the extension of the desired pharmacologic effects of a drug, often due to the substantial variability in the pharmacokinetics and pharmacodynamics. Pharmacological, immunological, and genetic factors are involved in the pathogenesis of ADRs. Immunological and genetic factors may play a role in the reaction of the body toward the drugs given. [3]

Drug toxicity is a major problem in providing health care to patients at a global level. Various newer drugs are being introduced every year to combat the diseases. Hence, there is a need for an active surveillance system to monitoring the harmful effects of drugs. Adverse reactions can occur with any class of drugs and several studies revealed that the incidence is more in case of antibiotics. Pharmacovigilance is therefore one of the most important post marketing tools in ensuring the safety of pharmaceuticals and related health products.

The safety of drug profile has become a highly considerable issue in healthcare and various research suggesting that there is important Adverse Drug

Reaction caused by commonly used medications. Therefore, better approaches must be devised for monitoring and assessment of patients who present with drug induced diseases.

A Pharmacovigilance Study of Antihypertensive Medicines in a South Delhi Hospital for a period of 4 months has been carried out by Hussain et al. Total 250 patients, 106 male and 144 female were enrolled in the study and 34 ADRs were observed. Of the 34 ADRs, 18 were mild, 14 moderate and 2 were classified as severe [bronchospasm with metoprolol (100 mg) and severe hypotension with atenolol (50 mg)]. [4]

A prospective, spontaneous reporting of adverse drug reactions in a South Indian hospital has been carried out over a period of 7 months. A total of 270 suspected ADRs were reported and evaluated from 164 patients. Among them, 3.7% of the hospitalized patients experienced an ADR, 0.7% of the admissions were due to ADRs and 1.8% had a fatal ADR. The gastrointestinal system (36.3%) was most commonly involved with an ADR. The drug class most commonly implicated with ADRs was cardiovascular (18.3%). Majority (47%) of the reactions were 'moderate' in severity. The total cost incurred in managing all the reported ADRs was Rs 76 564 (US$ 1595) with an average cost of Rs 690 (US$ 15) per ADR. [5]

Various types of prospective studies have been carried out to monitoring ADRs in different hospitals. [6-12]

Most of the hospitalized patients were treated with antimicrobial agents including 70% of ICU patients. The total costs associated with antibiotics were more and related to antibiotic use itself, but also to co-medication and adverse drug events. [13,14]

Beyond doubt the pharmacist's involvement in the ADR reporting system has had a positive impact. They are useful assets to the clinicians as they can assist busy physicians in better management of suspected reactions. It has been shown that adverse reaction reports from pharmacists may identify other problems than those reported by physicians. All professionals being active in the health care system must be alert to the occurrence of unwanted effects in patients and must be prepared and know how to report them.

The aim of the present study was to detect and analyze the suspected adverse drug reactions of antibiotics and other drugs in a tertiary care hospital.

MATERIALS AND METHODS

A prospective study was carried out in Narayana Hrudayalaya Malla Reddy hospital- Suraram, a tertiary referral center during August 2014 to February 2015 for 6 months period and hospitalized patients were recruited from various wards based on inclusion and exclusion criteria. The data for the study taken from case sheets, investigation reports of patients who had experienced an ADR, personal interviews with reporting persons or clinicians, and patients were monitored daily and medical records were examined. Suspected ADRs detected were identified from objective finding i.e. from biochemical investigation results and subjective markers of ADRs were identified through review of clinicians and nurse's notes.

Each Adverse Drug Reaction evaluated for its causality and severity based on "Naranjo's causality assessment scale" and "Modified Hartwig and Siegel scale". "Schumock and Thronton scale" was applied to assess preventability of Adverse Drug Reactions. Reported ADRs were classified according to Wills and Brown classification. Descriptive statistical analysis was performed for data analysis.

RESULTS AND DISCUSSION

During the study period, a total of 61 Adverse Drug Reactions (ADRs) were documented from 954 patients recruited. Among 954 patients, 595 patients were adults, 189 patients were geriatrics and 168 were paediatrics. During the study period there was 1 ADR reported related hospital admission. Twenty-eight ADRs were documented from Male and 26 ADRs were documented from Female. More Adverse Drug Reactions (12) were observed in geriatrics patients (above 59 years), 11 ADRs from age group of 30-39 years and 40-49, respectively, 10 ADRs from age group of 50-59 years groups.

Fig. 1 showed that maximum number of ADRs were reported from the general medicine 28 (45.90%) followed by Intensive Care Unit 13 (21.31%), Surgical 7 (11.47%), Cardiology 4 (6.55%), Paediatrics 3 (4.91%), Post- operative 3 (4.91%), Orthopedics 2 (3.27%).

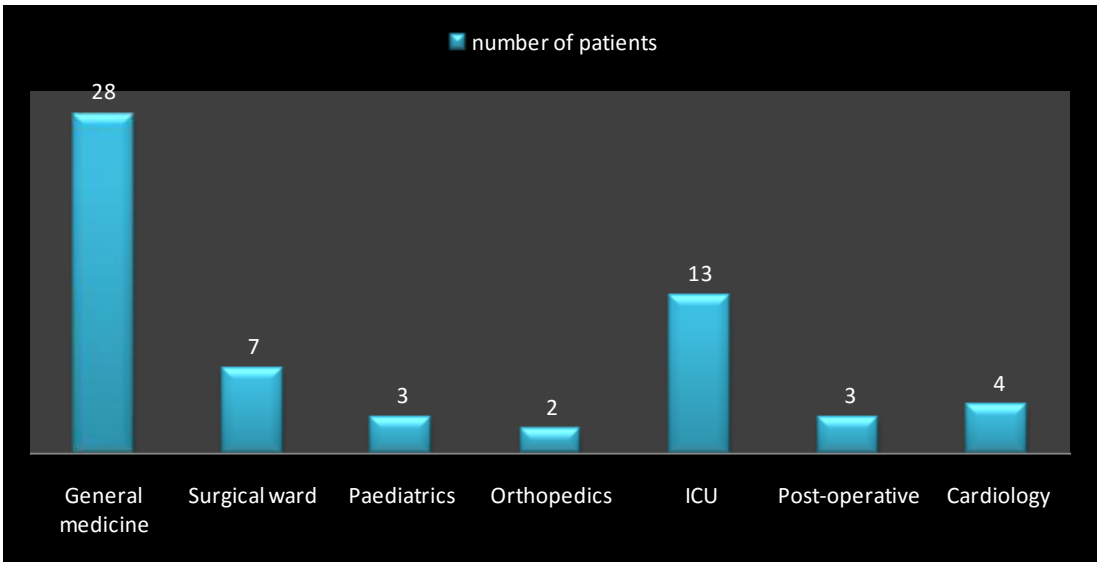

Figure 1: Distribution of reported ADRs in various departments (n=61)

The results revealed that GIT 21 (34.42%) commonly involved organ system associated with ADRs was organ system, ADRs associated due to antibiotics followed by the skin 11 (18.03%), Central Nervous system 7 (11.47%). The class of drugs most commonly associated with the reported Adverse Drug Reactions was antimicrobials 20 (32.75 %) which include beta lactam antibiotics, macrolides, tetracyclines, cephalosporins, aminoglycoside antibiotics. All documented ADRs after confirmation from duty doctor in charge, were classified according to Wills and Brown classification. In this study, Type A Augmented reactions were found to be 62.295%, followed by Type U 22.950% and remaining were classified as Type H 9.836% and Type C 4.918%.

According to Naranjo's scale causality assessment, 47.54% of ADRs were probable, 34.42% were possible and 18.03% of them categorized as definite (Fig. 2). Severity of the suspected ADRs assessed in Fig. 3 using Hartwig and Siegel scale revealed that 18.03% of ADRs were moderate (level 3), 32.78% of ADRs were mild (level 1), 18.03% of ADRs were moderate (level 4a), 21.31% were mild (level 2) and 8.19% were severe (level 5), 1.63% of ADRs were moderate (level 4b).

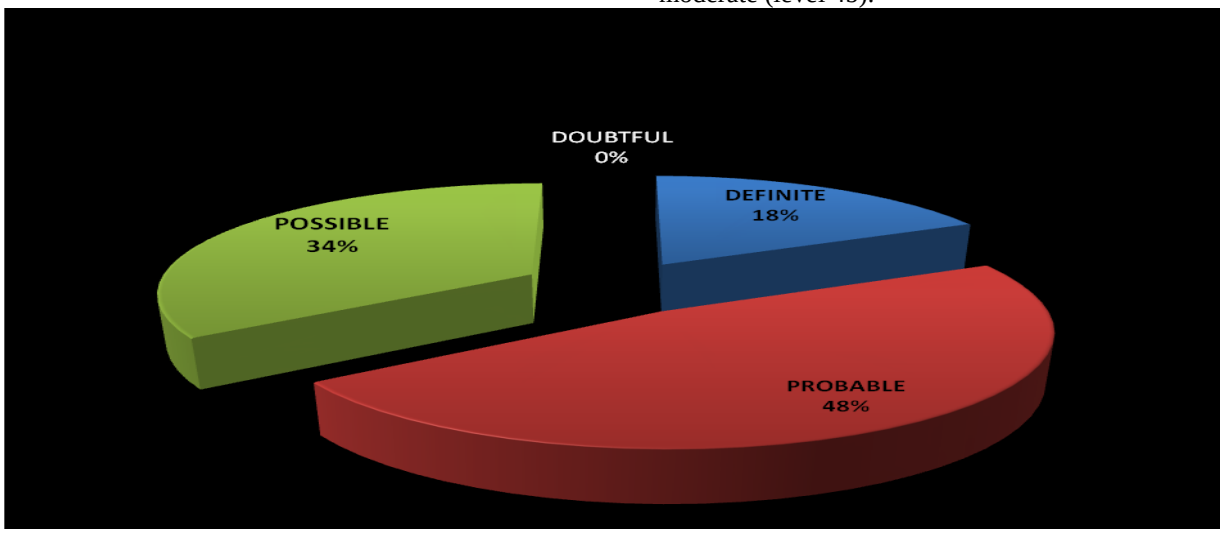

Figure 2: Causality assessment of individual ADRs by Naranjo algorithm

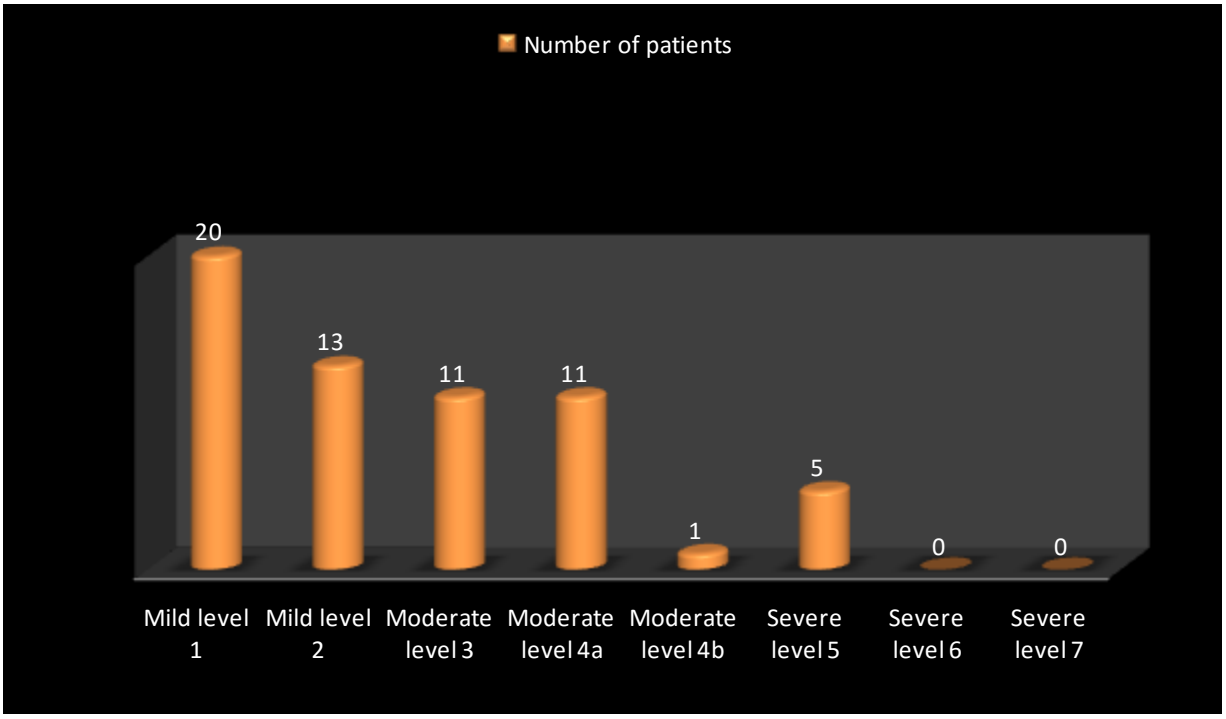

Figure 3: Analysis of ADRs based on the severity by modified Hartwig and Siegel scale

Preventability of suspected ADRs were assessed by using Schumock and Thronton scale, preventability analysis revealed that 57.37% of ADRs were Definitely preventable, 29.50% of ADRs were probably preventable and 13.11% were not preventable (Fig.4).

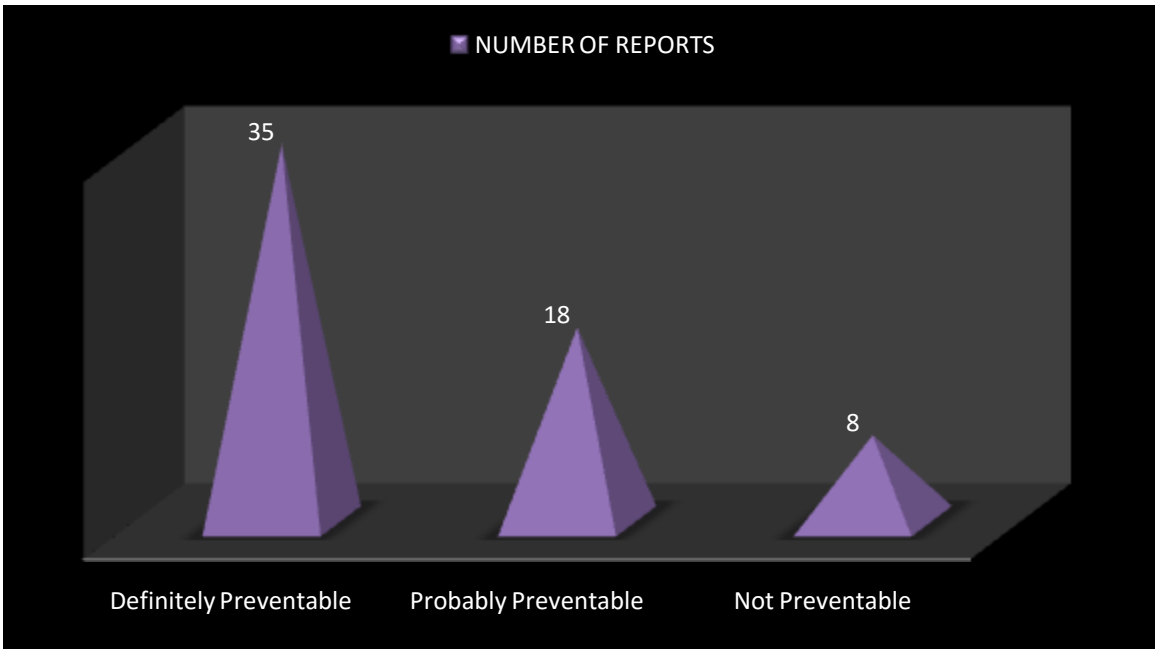

Figure 4: Preventability assessment of reported ADRs by Schumock & Thronton scale

In this study, it was found out that patients with ADRs, 31.1% of patients were recovered and 40.98% were recovering during treatment, although no fatal cases were reported and 18% cases were unknown (Fig. 5).

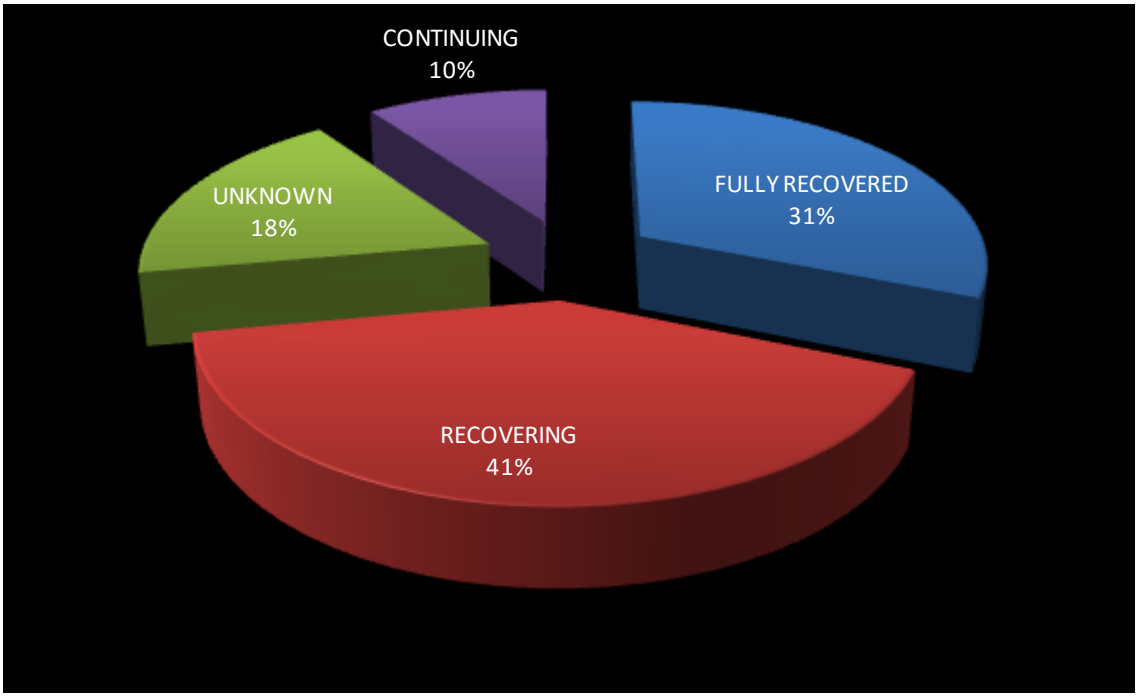

Figure 5: Outcome of reported ADRs

In 21.31% patients, the offending drug was withdrawn, another drug was added to relieve the symptoms in 9.83% patients and the dose was reduced to ameliorate the symptoms in 29.50% patients (Fig.6).

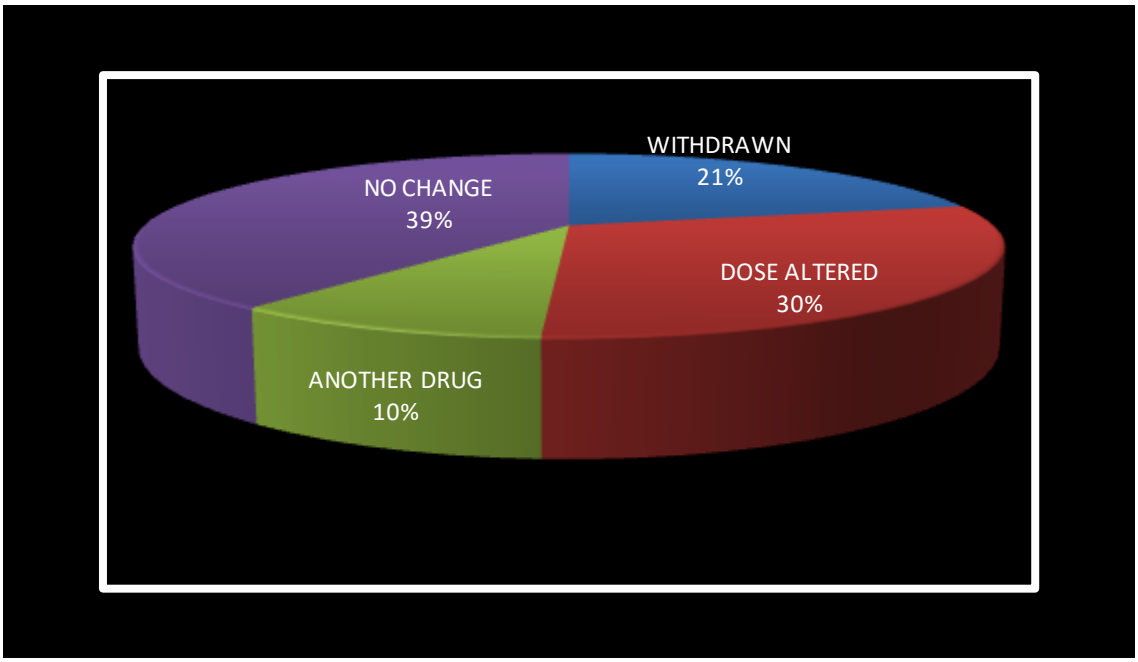

Figure 6: Management of ADRs

The most commonly reported ADRs in patients were 6 cases of vomiting, 4 cases of diarrhoea, 4 cases of rashes, 3 cases of hypokalemia, various Adverse Drug Reactions were detected with suspected drugs and depicted in Table 1.

Table 1: Adverse drug reactions detected with suspected drugs

S.N.	Type of ADR	Number	Male/Female Ratio	Suspected Drug
1.	Hypokalemia	3(4.91%)	2/1	Amphotericin B(2), Furosemide(1)
2.	Rashes	4(6.55%)	1/3	Ceftriaxone(4)
3.	Upper GI Bleeding	1(1.63%)	1/0	Aspirin(1)
4.	Phlebitis	2(3.27%)	1/1	Diazepam(1), cefepime(1)
5.	Acute liver injury	1(1.63%)	0/1	Simvastatin(1)
6.	Vomiting	6(9.83%)	3/3	Doxycycline(1), metronidazole(2), acetaminophen(1), digoxin(1), nifedipine(1),
7.	Diarrhea	4(6.55%)	1/3	Metronidazole(1), pantoprazole(1), clavulanic acid(1), piperacillin+tazobactum(1)
8.	Ankle edema	2(3.27%)	0/2	Nifedipine(2)
9.	Dizziness	2(3.27%)	1/1	Amlodipine(2)
10.	Cough	2(3.27%)	1/1	Ramipril(1), Enalapril(1)
11.	Weakness in lower limbs, unable to walk	1(1.63%)	1/0	Amlodipine(1)
12.	Hypoglycemia	2(3.27%)	2/0	Insulin(1), Glynase+ofloxacin(1)
13.	Mouth infection	1(1.63%)	0/1	Idoxyuridine(1)
14.	Headache with giddiness	1(1.63%)	0/1	Phenytoin(1)
15.	Vertigo	1(1.63%)	0/1	Azithromycin(1)
16.	Heart burns	1(1.63%)	1/0	Diclofenac(1)
17.	Constipation	3(4.91%)	0/3	Pantoprazole(2), furosemide(1)
18.	Abdominal cramps	1(1.63%)	1/0	Lactulose(1)
19.	Fatigue	1(1.63%)	1/0	Metformin+glimiperide(1)
20.	Decreased sleep	1(1.63%)	0/1	Pregabalin(1)
21.	Gastritis	1(1.63%)	0/1	Prednisolone(1)
22.	Inflammation at injection site	1(1.63%)	1/0	Amikacin(1)
23.	Headache	2(3.27%)	1/1	Ceftriaxone(1), Montelukast(1)
24.	Hiccups	1(1.63%)	1/0	Ondansetron(1)
25.	Pruritis	1(1.63%)	1/0	Ceftriaxone(1)
26.	Stiffness of body muscles	1(1.63%)	1/0	Haloperidol(1)
27.	Seizures	1(1.63%)	1/0	Haloperidol(1)
28.	Anxiety(mood changes)	1(1.63%)	1/0	Valproic acid(1)
29.	Back pain	1(1.63%)	1/0	Valproic acid(1)
30.	Tachycardia	3(4.91%)	2/1	Clopidogrel(1), Salbutamol(2)
31.	Acidity	1(1.63%)	1/0	Telmisartan(1)
32.	Burning micturition	1(1.63%)	1/0	Ofloxacin(1)
33.	Gastric irritation	1(1.63%)	1/0	Clopidogrel(1)
34.	Hypotension	1(1.63%)	1/0	IsosorbideMononitrate+ Carvedilol
35.	Local irritation	1(1.63%)	1/0	Clindamycin(1)
36.	Abdominal pain	1(1.63%)	1/0	Piperacillin+Tazobactum(1)
37.	Blurred vision with giddiness	1(1.63%)	1/0	Spironolactone(1)
38.	Chest pain	1(1.63%)	1/0	Dopamine(1)

DISCUSSION

The incidence rate of antibiotic adverse reactions in this study was found to be comparatively low compared to other studies. Adverse Drug Reactions (ADRs) reported from male patients were 51.85% which was found to be higher than female patients of 48.14%. These results were similar to the study observed in Shalini Chawla et al. [15]

Analysis of the age wise distribution showed the predominance of geriatric patients followed by adults. Maximum number of ADRs were reported with the age above 60 years (22.22%) followed by age group of 30-39 years (20.37%), which was similar to the results of other study by Dilip et al.[16]

Majority (45.90%) of ADRs were documented from General Medicine ward. The most commonly observed ADRs were vomiting (9.83%). The GI system (34.42%) followed by Cutaneous system (18.03%) and Central nervous system (11.47%) were considered to be more frequently affected organ system with ADRs. These data correlate with the reported study of ImanKarimzadeh et al. [17]

Analysis of causality assessment of suspected ADRs using Naranjo's scale showed that 47.54% of them were probable, 34.42% were possible and 18.03% categorized as definite, which was similar to the results of other study by Arulmani et al. [18]

In this study, Severity of the suspected ADRs were assessed using Hartwig and Siegel Adverse Drug Reaction Severity Assessment Scale, and it was revealed that 32.78% of the ADRs were mild (level 1). This is in line with study of G. Parthasarathi et al. [19] Preventability assessment shows that 57.37% of the ADRs were definitely preventable, 29.50% of the ADRs were probably preventable which was similar to the study by Shamna et al.[20] The present study reported predominance of Type A Augmented reactions (62.295%), these reactions were predicted by known pharmacology of the drug and Type U reactions were found to be 22.950%. This result is in line with the reports generated by Arulmani et al. [18]

The study results showed that antibiotics were the class of drugs causing the highest number of ADRs. This was similar to the previous study reported by ImanKarimzadeh et al. [17]

CONCLUSIONS

Adverse drug events are common problem in hospitalized patients and results mainly from system failure such as lack of sufficient patient information and/or drug information.

The objective of study was to detect and analyze the ADRs of the drugs in a tertiary hospital. The study concluded that ADRs to antibiotics are common and less compared to other studies. Detection and Prevention of ADRs at the earliest is very important, as they can cause not only morbidity and mortality but also increase the health care cost in their management.

The acceptance of the clinical pharmacist's interventions by a physician implies a successful measure of the pharmacist's activities while a reduction in the number of ADRs reflects a measure of clinical outcome success. The active involvement of well trained pharmacist in the area of ADRs detection, reporting and monitoring could improve the scenario.

The effort of this study revealed the occurrence of comparatively less number of antibiotic adverse reactions and their impact on patients of a developing country like India. The results provided an insight to the healthcare providers on the importance of monitoring and reporting of Adverse Drug Reactions. Proper documentation and periodic reporting to regional pharmacovigilance centers can ensure drug safety to antibiotics and other drugs.

REFERENCES

1. Databases of ADRs, Guidance Notes for Adverse Drug Reaction Reporting, http://www.drugoffice.gov.hk/eps/do/en/doc/adr_guidance_notes.pdf
2. Parthasarathi G, Nyfort-Hansen K, Nahata MC. A textbook of Clinical Pharmacy Practice: Essential Concepts and Skills. 1st ed., Hyderabad: Orient Longman: 2004.
3. Alomar MJ. Saudi Pharm J, 2014; 22(2): 83–94.
4. Hussain A, Aqil M, Alam MS, Khan MR, Kapur P, Pillai KK. Indian J Pharm Sci, 2009;71(3): 338-41.
5. Ramesh M, Pandit J, Parthasarathi G. Pharmacoepidemiology and Drug Safety, 12(8):687-692.
6. Bhabhor PH, Patel TK, Vahora R, Patel PB, Desai N. Intern J. of Basic Clin Pharmacol, 2014; 3(6): 1078.
7. Shrivastava M, Uchit G, Chakravarti A, Joshi G, Mahatme M, Chaudhari H. J Assoc Physicians India, 2011;59:296-9.
8. Mary E, Robinson, FR, Miller JC, Hayes JR, Nahat MC. Drug Safety, 2012; 27(11): 819-829.
9. Pirmohamed P, James S, Meakin S, Green C, Scott AC, Walley TJ, Farrar K, Park BK, Breckenridge AM. BMJ, 2004;329:15
10. Dager WE, Gulseth MP. Am J Health Syst Pharm, 2007;64:1071-1079;

11. Alam K, Shakya R, Ojha P. Nepal J of Epidemiol, 2014; 4(1): 330-36.
12. Miguel A, Azevedo LP, Araujo M, Pereira AC. Pharmacoepidemiology and Drug Safety, 2012; 21(11): 1139–1154.
13. Granowitz, Eric V, Brown, RB. Crit Care Clin, 2008; 24:421–442.
14. Stavreva G, Pendicheva D, Pandurska A, Marev R. Trakia J Sci, 2008; 6 (1): 7-9.
15. Chawla S, Kalra BS, Poojasahni PD. J Pharmacol Pharmacother, 2011; 2(3):196-198.
16. Dilip C, Lisa M, Saraswathi R, Divya R. Indian J of Pharmacy Practice. 2012; 5; (2): 28-32.
17. Karimzadeh I, Namazi S, Shalviri G, Gholami K, African Jo of Pharmacy and Pharmacology. 2011; 5(4): 493-499.
18. Arulmani R, Rajendran SD, Suresh B. Br J Clin Pharmacol, 2008; 65(2): 210–216.
19. Parthasarathi G, Pandit J, Ramesh M. Pharmacoepidemiol Drug Saf, 2003;12(8):687-692.
20. Shamna M, Dilip C, Ajmal M, Mohan PL, Shinu C, Jafer CP, Mohammed Y. Saudi Pharm J, 2014; 22(4): 303-308.