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MONITORING AND REPORTED THE ADVERSE DRUG REACTIONS OF DIFFERENT DRUGS IN RURAL GOVERNMENT HOSPITAL IN NALGONDA SPONTANEOUS REPORTING METHOD

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ABSTRACT

Adverse drug reactions (ADRs) are one of the major problems associated with medicines. The effectiveness and success of any pharmacovigilance system depends highly on the participation of all health care professionals. An observational, prospective study was conducted based on ADRs reported between Feb 2nd to 18th march to the ADR reporting unit of the hospital. The ADRs reported by spontaneous reporting system were from patients attending in-patient department (IPD) and casualty of IGGMC&H Nalgonda Evaluation of the data was done for various parameters which included patient demographics, drug and reaction characteristics, and outcome of the reactions. Assessment was also done for causality and severity Total 75 ADRs were reported with in the period from 2nd Feb. to 18th March. Cefrioxome were the drug class most commonly involved and next Cefixime a well-established agent was the individual drug most frequently reported in this study. Upon causality assessment, majority of the reports were rated as probable (13.043%). The pattern of ADRs reported in our hospital is comparable with the results of studies conducted in hospital set up elsewhere. Cefrioxome were causing maximum ADRs. This study provides a database of ADRs due to common drugs used in our hospital, which will help clinicians for optimum and safe use of these drugs. Hence strict vigilance is required for the use of these likely drugs and their safety assessment.

KEYWORDS

Adverse drug reaction, Hospital based monitoring and Pharmacovigilance.

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INTRODUCTION

Adverse drug reactions (ADRs) are one of the major problems with medicines. The World Health Organization (WHO) defined as any response to a drug that is noxious and unintended, and that occurs at doses used in humans for prophylaxis, diagnosis, or therapy excluding failure to accomplish the intended purpose. ADRs can cause short and long-

term hospitalization and mortality (WHO). It is imperative to monitor ADRs in order to minimize or prevent harm to patients arising from their drugs, to detect ADRs before they are clinically manifested, and to obtain much more knowledge to ensure safe use of drugs.

ADR reporting covers all pharmaceutical products, biological, herbal drugs, cosmetics and medical devices circulating in the India market. For those conducting clinical trials phase 1-4 it is mandatory to report all adverse event encountered to the Authority.

Reported the pharmacists have a reasonable knowledge and are supportive of the yellow card spontaneous ADR reporting scheme. However, education and training are important in maintaining and increasing ADR reporting by pharmacists. Under reporting of ADR is a global issue of major concern. As in most of the pharmacovigilance system around the world. The major weaknesses of Pharmacovigilance program are the lack of awareness among health care professionals regarding pharmacovigilance; under-reporting is another limitation. Other reasons for under-reporting include uncertainly regarding the types of reaction to report, and a lack of awareness about the existence, function and purpose of the national ADR reporting scheme.

India, ADRs have recently emerged as leading killers. The management of drug-induced illnesses requires more than 100 billion US dollars annually. These astronomical figures are currently unmatched by money involved in any single disease management presently. Fortunately, several studies have shown that most ADRs are preventable, provided that the drugs are used rationally. But unfortunately, the most common system failure has been to disseminate the knowledge of pharmacovigilance to the individuals actually involved in prescribing, i.e., the physicians. Principles and practice of pharmacovigilance seem to be more often discussed in an academic manner, rather than in a pragmatic or applied sense. Several times, such discussion is held amongst pharmacologists and pharmacists who are not directly involved in patient care; and physicians who treat cases and use drugs generally keep themselves uninvolved. Drug safety has been included in curriculum guidelines of Indian medical undergraduates, but little is done in this regard. Prevention is considered to be better than cure, as elsewhere in medicine; application of the same principle has given a new dimension to the study of pharmacovigilance.

Subjects and Methods

This study was a concurrent, spontaneous reporting, involving both active and passive methods. Active methods include physicians, pharmacists and nurses actively looking for suspected ADRs and passive methods include stimulating prescribers to report suspected ADRs. The study was conducted in a 35-bed internal medicine ward of the Rural Government Hospital, Nalgonda. Over a period of 3 consecutive months, is starting from Feb 2016 to March 2016.

All the physicians in the ward were informed about the study, outlining the ADRs' negative impact and were asked to report all observed adverse events. In order to ensure that the rate of notifications remains constant during the whole study period, the physicians were regularly reminded about the study taking place.

An Adverse Drug Reaction Reporting Form was designed and made available at all nursing stations of the ward of the hospital for easy access to all healthcare professionals. The Adverse Drug Reaction Reporting Form was prepared with reference to the ADR reporting form of the Indian Pharmacopeia Commission (IPC). This includes information about the patient, like name, age, sex, medication history, diagnosis history, name of the suspected drug along with batch number, lot number manufacturing date and expiry date. The route of drug administration, frequency and dose is also mentioned in the form. Basic information of adverse reaction caused by the suspected drug was also included. We defined adverse drug reactions according to the World Health Organization definition, as being all "noxious and unintended drug response, which occur at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiological

function (WHO, 1972). By this definition, ADRs primarily include allergic reactions and adverse effects. Therefore, we excluded all the intentional overdoses, poisonings and therapeutic failures.

In addition, the patient's medication history was also taken and any co-morbidity identified to assess the causality relationship between the suspected drug and reaction. Patients who developed an ADR were interviewed daily from the day the ADR was reported with regard to consumption of any other medication. The relationship between ADR and the suspected drug was assessed. The severity of the ADRs was also assessed in different categories as mild, moderate and severe for each ADR. All the reported ADRs were assessed for their preventability criteria. Personalized letters and circulars signed by the director of the hospital were circulated to all residents and practitioners, visiting practitioners and nursing stations. These letters contained information on the number of suspected ADRs that had been reported till date, need for continuing reporting of ADRs and a request to maintain a high degree of suspicion for the ADRs. The data observed were analyzed in order to study the characteristics of the ADRs and to determine the nature and pattern of ADRs related to hospital admission and difference in the severity of ADRs and management and outcome of management of the reported ADRs. Causality assessment is the method by which the extent of relationship between a drug and a suspected reaction is established. The assessment of causality relationship is often subjective, based upon an individual clinician's assessment. One clinician's judgement may appear unlikely to another clinician. If an ADR is suspected, the assessment starts with collection of all the relevant data pertaining to patient demographics, medications, including non-prescription (OTC) drugs, comprehensive ADR details including a description of the reaction, time of onset and duration of the reaction, complications and/or sequelae treatment of the reaction and outcome of the treatment and further relevant investigation reports. The collected data were used to correlate and categorize the relationship between the suspected drug and the adverse drug reaction. The data were also analyzed as per severity (Mild, Moderate and Severe) of the suspected adverse drug reaction and categories as death, life threatening, hospitalization (initial or prolonged), disability, congenital anomaly, required intervention to prevent permanent impairment or damage, not serious, and others.

Total 60 ADRs were reported in the span of period from Feb 8. 2016 to March 18. 2016. The year wise distribution of ADR indicates that almost similar number of ADRs were reported in each year but in year June 06 to May 07 there was slight rise in the number of ADRs might be due to the epidemic of chickenguinea.

Out of total ADRs 60 male suffered from ADRs while only 36 Males. Females 24 affected more due to ADRs as compared to males. All were mostly in age group of 13- 80 years

It was seen that most of the ADRs were reported from the other departments like Skin (10%), Chest and TB (08%) etc.

In this study, RS is the most commonly affected organ system (21%). CVS (03%) Gastrointestinal tract system (GIT) is involved in 26% of ADRs. Other organ systems involved are central nervous system (CNS) 13%, autonomic nervous system (ANS).

Wide varieties of side effects are observed. The most important were gastrointestinal such asdyspepsia, nausea, vomiting gastritis and cutaneous reactions such as fixed drug eruption, itching, urticaria, maculopapular rashes, vasculitis phototoxic reactions, erythema multiforme, toxic epidermal necrosis and diclopian, paractamal Steven Johnson syndrome.

The top tine drugs causing ADRs in our study are shown in. Cefpodoxime proxetil (60%) ranitidine (23%), ampicilline (20%), cefotixme (28%), rifampicin (03%), diazepam (05%), stropotomysin (03%), dicylopin (08%), choulroqinine (1%), Paractamal (01%) has found to be most commonly offending drug. Thirty four ADRs were reported serious, as per WHO definition, out of these were CVS (03%), anaphylaxis nephrotoxicity and angioedema paractamal,

Upon causality assessment, majority of the reports were rated as probable (53.7%). 60 possible and only 34 ADRs were classified as certain. Mild and moderate reactions accounted for 50.5 and 43.9%, respectively.

The routes of administration of drugs are depicted. Majority of ADRs were noted with oral route of administration (49%). Drugs administered by parenteral route (26%), accounted. While of the drugs given topically (16) caused ADRs.

DISCUSSION

In our study 2% of ADRs were associated with hospital admissions. Our findings are similar to other reports generated elsewhere which estimated that 1-3% of all hospital admissions are caused by ADRs However, ADRs experienced by hospitalized patients gave an incidence of 2%, which is lower than other studies in Western populations but more than the reports generated in India and other developing countries. Although our study used a spontaneous reporting system for ADR monitoring, the presence of clinical pharmacists in the wards and their constant encouragement might have helped clinicians and nurses to notify ADRs that resulted in better reporting than comparable studies in India.

The demographic details of our study showed female gender predominance over males, which was similar to that of other studies reported in the literature. Previous studies have shown that a larger percentage of ADRs was reported from geriatric and paediatric populations which were similar to our results. Under-reporting by doctors is well known, and in India also, the spontaneous reporting system has produced lower rates of reporting. Clinical pharmacy was introduced to the hospital in 1998 but the ADR monitoring and reporting programme was not introduced until 2004 because pharmacovigilance was poorly developed in our country. At the same time, as part of the routine clinical pharmacy services, ADR monitoring was done by the clinical pharmacists in the hospital without further documentation and reporting. In the present study, pharmacists were involved in ADR monitoring by way of creating awareness, documentation and assessment of the reports but did not report the suspected ADEs themselves. In addition, pharmacists also assessed the patients for ADR related issues during drug therapy monitoring and when such issues were identified, they were brought to the notice of the treating clinician for further evaluation, thus effectively addressing the problem of under-reporting. Pharmacists, of late, have been encouraged to participate in the ADR monitoring programme globally and our efforts show that it will be beneficial to involve pharmacists in such programmes in India also.

We did not formally assess the preventability of ADRs. At the same time, we have observed a significant number of ADRs falling into the type H category which may potentially not be preventable. This may indicate that drug therapy is fairly well managed. This view is also supported by the fact that only 3.7% of the hospitalized patients had ADRs. The hospital follows the essential drugs concept and has a list of essential drugs (n = 126) based on the WHO list of essential drugs. This restricted list may also have contributed to the better understanding and therapeutic management of the patients. Also, since most of the patients are repeat patients to the hospital, their therapeutic issues are fairly well known to the clinicians.

The most common systems associated with ADRs in our study were skin and the central nervous system. This finding is consistent with many studies which have reported a higher percentage of dermatological manifestations than others. The gastrointestinal system has also been reported to be involved in the majority of ADRs. In our study, this formed the third largest report on ADRs. In our study, antibiotics (6) and NASIDS (4) were the most commonly involved drug classes in ADRs. This finding is consistent with the studies reported by Saikumar *et al and* Shankar *et al* reported the highest percentage for NASIDS drugs, which was second in our study. The most common drugs involved in ADRs were old drugs such as ampicillin, ciprofloxacin, Rantac etc. Since the hospital uses drugs that are included in the essential drug list which does not include many recently

introduced drugs, ADRs of such drugs could not be generated here.

The costs incurred in managing ADRs in our patients seem to be lower than those reported by various authors in India and elsewhere. This may be because the room rent, medical care and nursing care were not included in the total cost incurred in managing ADRs. Also, drugs are purchased for the entire state by the government resulting in huge cost savings. It may be inferred that the patients would have incurred an expenditure of about three times the expenditure incurred at this hospital if they were treated in private hospitals.

ADR monitoring was introduced in the hospital in the year 2004. However, the programme has so far been implemented only in the in-patient medical wards of the hospital. With the encouraging support of the hospital authorities and clinicians of the hospital, we believe that it will be possible to expand the programme to other departments of the hospital in future.

RESULTS

Table No.1: Age wise distribution of No. of adrs

S.No	Years	No of adrs	Percentage (%)
1	13-24	15	24%
2	25-37	10	16%
3	38-49	15	25%
4	50-62	8	13%
5	63-75	6	10%
6	75-80	6	10%
7	Total	60	100%

Table No.2: Sex wise Distribution of ADRs

S.No	Sex	No of adrs	Percentage (%)
1	Male	36	60%
2	Female	24	40%
3	Total	60	100%

Table No.3: Department wise distribution of adrs

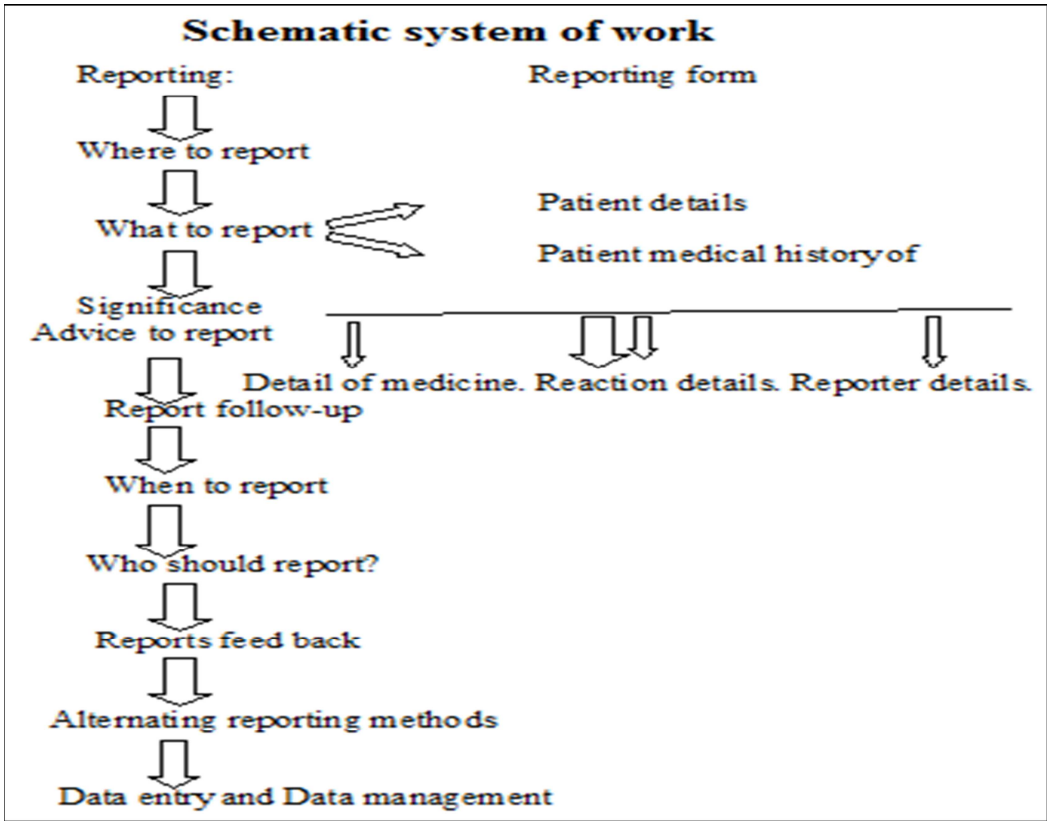
S.No	Department	No of adrs	Percentage (%)
1	Skin	06	10%
2	Chest pain	05	08%
3	CVS	02	03%
4	RS	13	21%
5	CNS	08	13%
6	GIT	08	26%
7	Others	18	30%
8	Total	60	100%

Table No.4: Organ system affected by adrs

S.No	Organ	No of adrs	Percentage (%)
1	Skin	06	10%
2	GIT	08	13%
3	CNS	08	13%
4	RS	18	30%
5	CVS	02	03%
6	Other	18	30%
7	Total	60	100%

Table No.5: Top 10 drug causing adrs

S.No	Drugs	No of adrs	Percentage (%)
1	Cefpodoxineproxetil	36	60%
2	Ranitidine	14	23%
3	Cefotixme	17	28%
4	Ampicillin	12	20%
5	Rifampicin	2	3%
6	Diazepam	3	5%
7	Streptomycin	2	3%
8	Dicylopin	5	8%
9	Cholroquinine	1	1%
10	Paracetamol	1	1%



Material

Version-1.2

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by Healthcare Professionals

INDIAN PHARMACOPOEIA COMMISSION
(National Coordination Centre-Pharmacovigilance Programme of India)
Ministry of Health & Family Welfare, Government of India
Sector-23, Raj Nagar, Ghaziabad-201002

FOR AMC/NCC USE ONLY

AMC Report No. :

Report Type ☐ Initial ☐ Follow up

Worldwide Unique No. :

A. PATIENT INFORMATION

1. Patient Initials _____

2. Age at time of Event or Date of Birth _____

3. M ☐ F ☐ Other ☐

4. Weight_____Kgs

12. Relevant tests/ laboratory data with dates

B. SUSPECTED ADVERSE REACTION

5. Date of reaction started (dd/mm/yyyy)

6. Date of recovery (dd/mm/yyyy)

7. Describe reaction or problem

13. Relevant medical/ medication history (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction etc.)

14. Seriousness of the reaction: No ☐ if Yes ☐ (please tick anyone)

☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly
☐ Life threatening ☐ Required intervention to Prevent permanent
☐ Hospitalization/Prolonged impairment/damage
☐ Disability ☐ Other (specify)

15. Outcomes

☐ Recovered ☐ Recovering ☐ Not recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S)

S.No	8. Name (Brand/Generic)	Manufacturer (if known)	Batch No. / Lot No.	Exp. Date (if known)	Dose used	Route used	Frequency (OD, BD etc.)	Therapy dates		Indication	Causality Assessment
								Date started	Date stopped		
i											
ii											
iii											
Iv											

S.No as per C	9. Action Taken (please tick)						10. Reaction reappeared after reintroduction (please tick)			
	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	Yes	No	Effect unknown	Dose (if reintroduced)
i										
ii										
iii										
iv										

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S.No	Name (Brand/Generic)	Dose used	Route used	Frequency (OD, BD, etc.)	Therapy dates		Indication
					Date started	Date stopped	
i							
ii							
iii							

Additional Information:

D. REPORTER DETAILS

16. Name and Professional Address:_____
_____
Pin:_____E-mail_____
Tel. No. (with STD code)_____
Occupation:_____ Signature:_____

17. Date of this report (dd/mm/yyyy):

Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Programme staff is not expected to and will not disclose the reporter's identity in response to a request from the public. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction.

Figure No.1: Schematic system of work

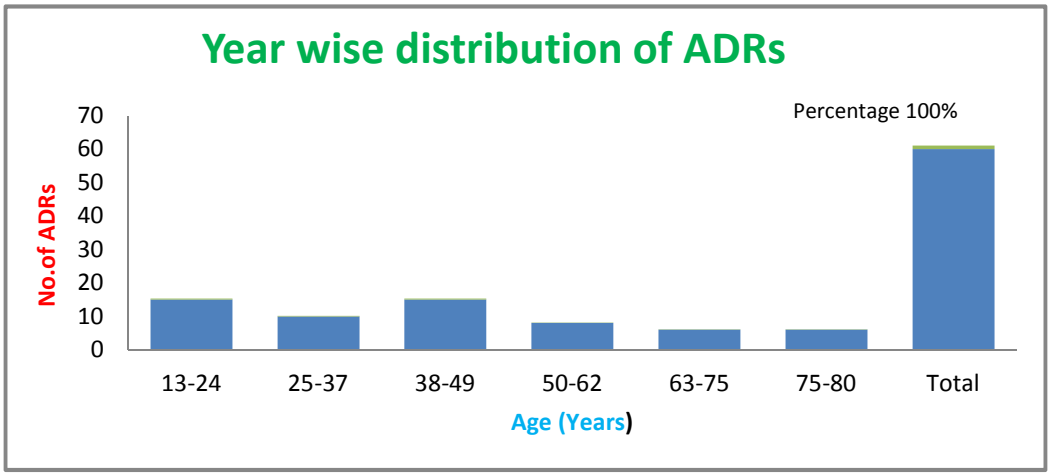


Figure No.2: Year wise distribution of ADRs
NOTE: From the above data 13-80 age of persons are more affected ADRS

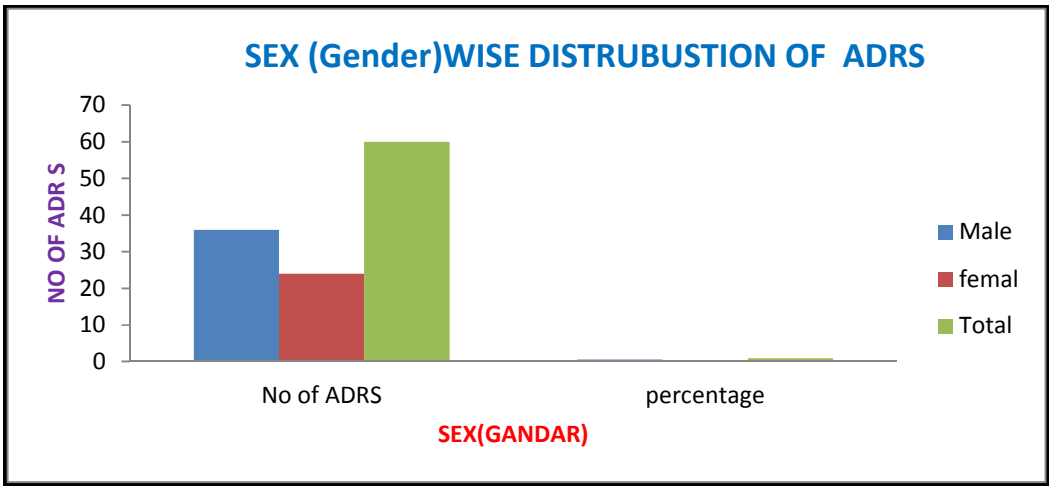


Figure No.3
NOTE: Sex wise distrubustion of ADRS

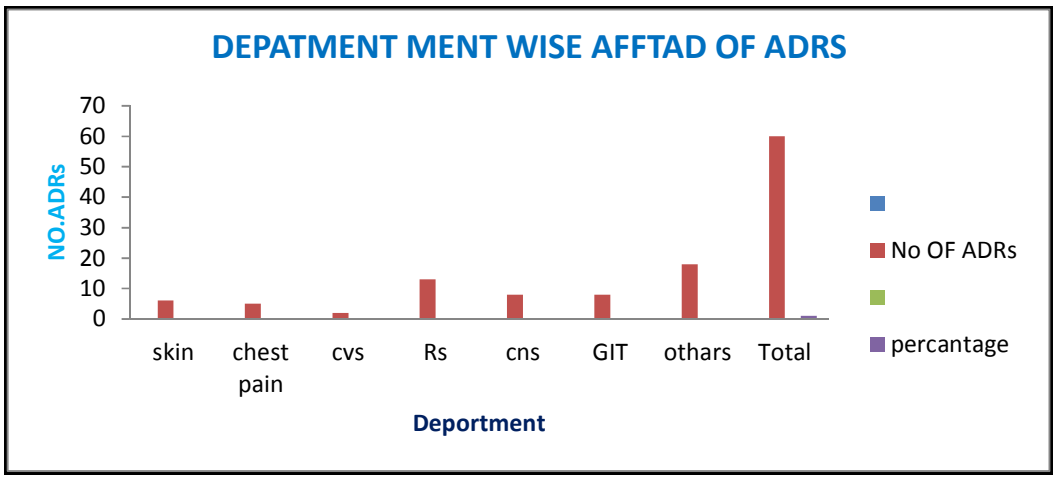


Figure No.4
NOTE: Department wise organ affected of adrs

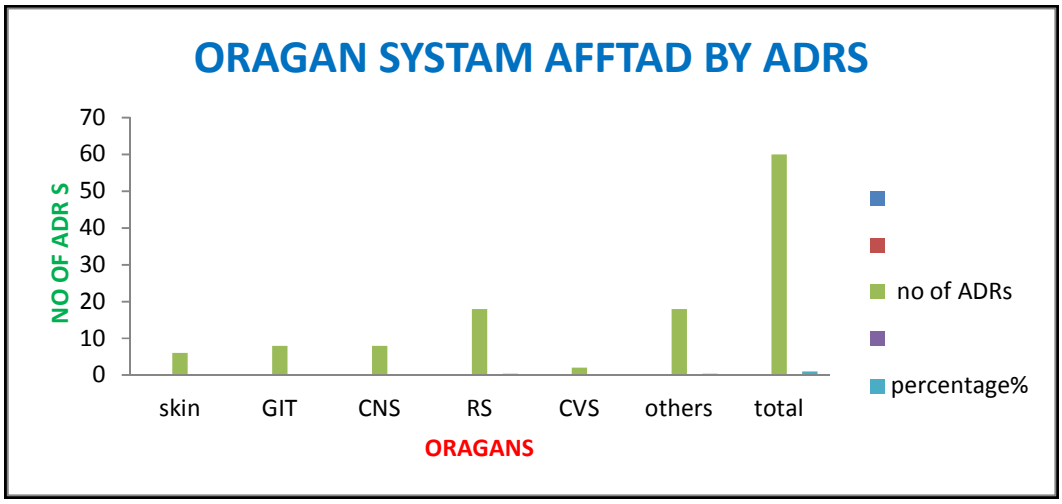


Figure No.5
NOTE: Oragan systam afftad by adrs

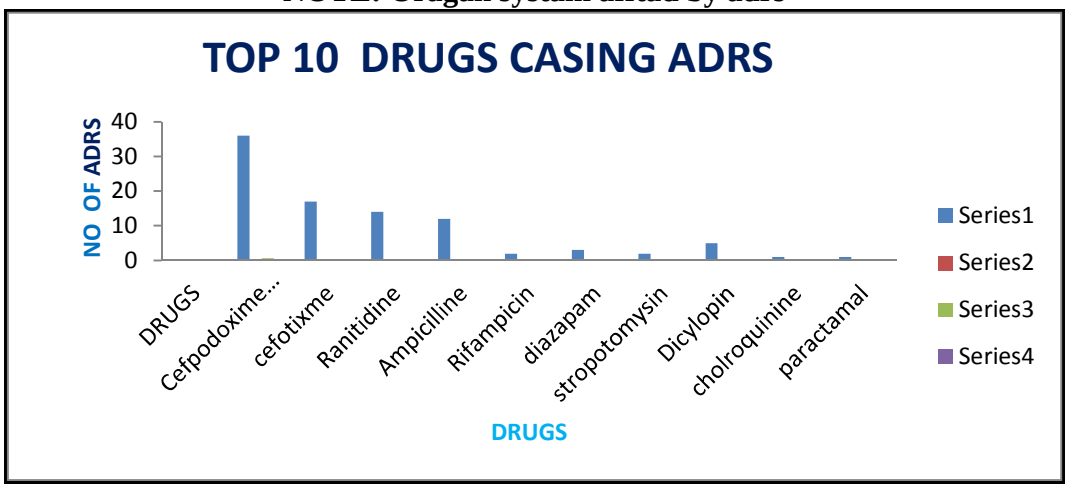


Figure No.6
NOTE: Top 10 drugs casing adrs such git toxicity

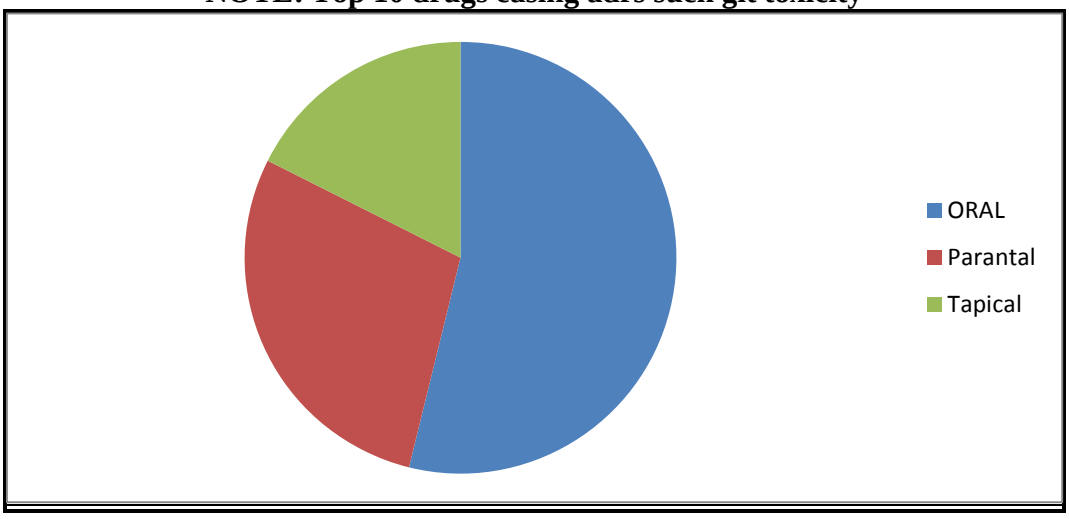


Figure No.7: Routes of administration of drugs

CONCLUSION

The stimulated spontaneous reporting used in the present study turned out to be a pragmatic method which allowed the detection and characterization of ADRs. However, monitoring of adverse drug reactions is an ongoing ceaseless and continuing process. Since newer and newer drugs hit the market, the need for pharmacovigilance grows more than ever before. Monitoring of the adverse effects of newer drugs, particularly of serious nature, is mandatory. Imparting knowledge and awareness of ADRs reporting among health care professionals would introduce the reporting culture among medical practitioners and increase the reporting rates of ADRs. Careful consideration involved in planning and monitoring of drug therapy will lead to prevention of ADRs. On balance, this study suggests that hospital-based monitoring is a good method to detect known and unknown links between drug exposure and ADRs.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. The role of national centres, World Health Organization - international drug monitoring 1972, Technical report series 498 Geneva, Available from: http://www.who-umc.org/graphics/9277, pdf, Lloyd J, Raven A. EEC note for guidance, Good clinical practice for trials on medicinal products in the European community, *Handbook of clinical research, London: Churchill Livingstone*, 1994, 436.
2. Pirmohamed M, Breckenridge A M, Kitteringham N R, Park B K. Adverse drug reactions, *BMJ*, 316(4), 1998, 1295-98.
3. Einarson T R. Drug-related hospital admissions, *Ann Pharmacother*, 27(7-8), 1993, 832-40.
4. Bates D W, Cullen D J, Laird N, Petersen L A, Small S D, Servi D *et al*. Incidence of adverse drug events and potential adverse drug events Implications for prevention. ADE Prevention Study Group, *JAMA.*, 274(1), 29-34.
5. Bates D W, Spell N, Cullen D J, Burdick E, Laird N, Petersen L A *et al*. The costs of adverse drug events in hospitalized patients, adverse drug events prevention study group, *JAMA*, 277(4), 1997, 307-11.
6. Lazarou J, Pomeranz B H, Corey P N. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies, *JAMA*, 279(15), 1998, 1200-1205.
7. Parker C W. Allergic reactions in man, *Pharmacol Rev*, 34(1), 1983, 85-194.
8. Rawlins M D, Thompson J W, Davies D M. Pathogenesis of adverse drug reactions, Textbook of adverse drug reactions, *Oxford University Press*, 1977, 10.
9. Naranjo C A, Busto U, Sellers E M, Sandor P, Ruiz I, Roberts E A *et al*. A method for estimating the probability of adverse drug reactions, *Clin Pharmacol Ther*, 30(2), 1981, 239-45.
10. Wenchen K W, Nicholas P. Evaluation of outpatient adverse drug reactions leading to hospitalization, *Am J Health Syst Pharma*, 60(3), 2003, 251-254.
11. Protocol for National Pharmacovigilance Program, CDSCO, Ministry of Health and Family Welfare Government of India, November 2004, Available form: http://www.pharmainfo.net/pharma-student-magazine/pharmacovigilance-indian scenario.
12. Edward R, Aronson J K. Adverse drug reactions: Definitions, diagnosis, and management, *Lancet*, 356(9237), 2000, 1255-1259.
13. Murphy B M, Frigo L C. Development, implementation and results of a successful

multidisciplinary adverse drug reaction reporting program in a university teaching hospital, *Hosp Pharm*, 28(12), 1993, 1199-1204.

14. Arulmani R, Rajendran S D, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in India, *Br J Clin Pharmacol*, 65(2), 2008, 210-216.
15. Vander Linden P D, van der Lei J, Vlug A E, Stricker B H. Skin reactions to antibacterial agents in general practice, *J Clin Epidemiol*, 51(9), 1998, 703-708.
16. Giovanni P, Francesco S, Paola C, Ilaria M, Achille P C. Adverse reactions induced by NSAIDs and antibacterials, *Drug Safety*, 29(3), 2006, 449-459.
17. Elena Lopez-Gonzalez, Maria T. Determinants of under-reporting of adverse drug reactions, *Drug safety*, 32(1), 2009, 19-31.

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