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PATTERN OF ADVERSE DRUG REACTION IN TEACHING CARE HOSPITAL IN SOUTHERN INDIA: A RETROSPECTIVE STUDY

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ABSTRACT

Adverse drug reactions (ADRs) are the major public health problem and are considered to be a leading cause of morbidity and mortality. A Retrospective study was performed by collecting data from 2010 to 2013. The aim of this study was to assess the incidence and pattern of ADRs, assess causality, severity and preventability of ADRs, and to classify the ADRs based on WHO Adverse Reaction Terminology (WHO-ART). For Severity assessment, Modified Hartwig scale was used. Naranjo causality algorithm was used for assessing causality. Modified Schumock and Thorntons Scale were used for identifying preventability of ADR. 95 % CI interval with alpha level of 0.05 was used to identify significance of difference. A total 209 ADRs were identified out of which 53 % were male and 47 % were female patients (P=0.08). Causality assessment scale indicates 71 % ADRs were possible, 23 % ADRs were probable related to drug (P<0.001). Severity assessment reveal that 78 % were mild, 20 % moderate and 2 % ADRs were severe (P<0.001). Preventability scale indicates that 93 % of the ADR were definitely preventable. Majority of the ADR (35 %) reported were belonging to gastro-intestinal system according to WHO-ART, and most commonly reported ADR was vomiting. Although the ADRs in the present study were non serious and preventable, monitoring and management of such ADRs through therapeutic interventions would be beneficial in better patient care.

KEYWORDS: Adverse drug reactions, WHO Adverse Reaction Terminology, Causality assessment.

INTRODUCTION

In 1968, the World Health Organization (WHO) established the International Drug Monitoring Programme to collect data on adverse drug reactions and to issue public warnings when warranted.[1] But yet patient safety is one the leading topic now a days.[2] An adverse drug reaction (ADR) is one the major drug related problem and monitoring and reporting of an ADR is still at infant stage in India.[3] The WHO defines adverse drug reactions (ADRs) as "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function".[4] ADR is one of the leading cause for morbidity and mortality worldwide.[5] The overall ADRs rate is estimated to be 6.5% and 28% of these are preventable ADRs.[2]

The study of ADRs comes under the field known as pharmacovigilance.[6] Pharmacovigilance is "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems".[7] Hence it is an integral part of drug therapy and yet it is not widely practiced in Indian hospitals.[8] The main reason is lack of awareness and lack of interest of healthcare professionals in ADR reporting and documentation.[3]

Assessment of ADRs can be performed by using different scales. Few of them are as follow.

1. Severity assessment- Modified Hart wig scale
2. Causality assessment- Naranjo causality algorithm
3. Preventability assessment- Modified Schumock and Thorntons Scale.

1. **Severity assessment- Modified Hart wig scale:** This scale divides the ADRs into three categories based on severity assessment as mild, moderate and severe. Mild adverse reactions were defined as those which did not by itself require prolongation of hospitalization and could be managed by simple measures, moderate were those ADRs which needed prolongation of hospital stay of the patient for treatment of the same and severe were life threatening ADRs.[9]
2. **Causality assessment- Naranjo causality algorithm:** Causality assessment is the method by which the extent of relationship between a drug and an adverse event in a given patient, ranging from short questionnaires to comprehensive algorithms.[12] The Naranjo Algorithm is a questionnaire designed by *Naranjo et al* for determining the likelihood of whether an ADR (adverse drug reaction) is actually due to the drug rather

than the result of other factors. Probability is assigned via a score termed definite, probable, possible or doubtful. It is also called the Naranjo Scale or Naranjo Score.[10,11]

3. **Preventability assessment- Modified Schumock and Thorntons Scale:** Modified Schumock and Thornton's criteria have three sections namely definitely preventable, probably preventable and not preventable.[3]

The main objective of this study were to assess the incidence and pattern of ADRs and to perform causality, severity and preventability assessment by using Naranjo causality algorithm, Modified Hart wig scale, and Modified Schumock and Thorntons Scale respectively. Along with this the WHO-ART terminology were used in which the collected ADRs were classified based on the System Organ Classes.

Although India is a developing country, most hospitals in India do not have an ADR reporting and monitoring programme. Hence this study was designed to create awareness to the health care professionals about the importance of ADR reporting and monitoring.

MATERIALS AND METHODS

This Retrospective study was performed by collecting data from 2010 to 2013, in the department of Pharmacy Practice attached to a teaching care hospital located in south India. The data was retrieved from adverse drug reporting forms which were documented in the department.

Statistical Analysis

To identify significance of difference 95 % CI interval with alpha level of 0.05 was used. T test was performed for finding significance of difference between two groups. ANOVA was performed for finding significance of difference between more than two groups. All tests were performed by using SPSS version 19 software and Medclac version 3.2.

RESULTS

Demographic details

A total 209 ADRs were identified out of which 54.5 % were in male and 45.5 % were in female patients (P=0.08). Patients with age between 19 to 60 years (59.4%) were at higher risk of developing adverse drug reactions by prescribed medicines compare to paediatric and geriatric group.

Table No 1: Distribution of demographic details

Sl No.	Characteristics	No. of ADRs (N=209)
1.	**Age**	
	0-18	49 (23.4%)
	19-60	124 (59.4%)
	>60	36 (17.2%)
2.	Gender	
	Male	114 (54.5%)
	Female	95 (45.5%)

1. Number of ADRs reported from various departments in the hospital:

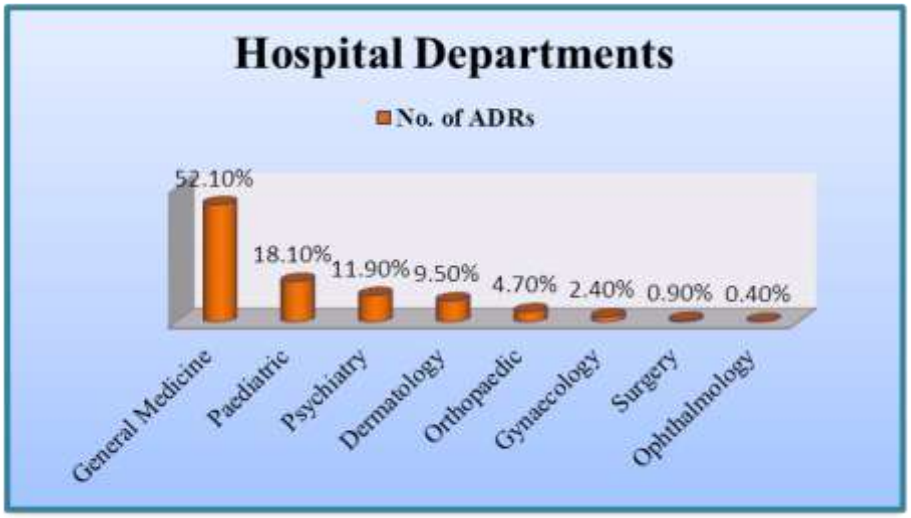

Fig 1: Distribution of number of ADRs reported from various departments in the hospital

2. Number of ADRs reported related to therapeutic class of drugs

The ADRs were categorised based on the therapeutic classes of drugs which is depicted in Table No 2.

Table No 2: Distribution of Number of ADRs reported related to therapeutic class of drugs

Sl No.	Therapeutic Classes of Dugs	No. of ADRs (N=209)
1.	Antibiotics	75 (35.9%)
2.	NSAIDs	26 (12.4%)
3.	Antihypertensives	24 (11.5%)
4.	Antidepressants	15 (7.2%)
5.	Gastrointestinal Agents	13 (6.2%)
6.	Antipsychotics	10 (4.8%)
7.	Glucocorticoids	8 (3.8%)
8.	Anticonvulsants	8 (3.8%)

9.	Antidiabetic drugs	7 (3.3%)
10.	Bronchodilators	5 (2.4%)
11.	Anxiolytics	4 (1.9%)
12.	Diuretics	4 (1.9%)
13.	Antiretroviral Agents	3 (1.4%)
14.	Antianginal drugs	1 (0.5%)
15.	Antihistamines	1 (0.5%)
16.	Antiprotozoal	1 (0.5%)
17.	Hypolipidaemic drugs	1 (0.5%)
18.	Leprostatic drugs	1 (0.5%)
19.	Sedatives	1 (0.5%)
20.	Thyroid Supplements	1 (0.5%)
	Total	**209 (100%)**

3. Antibiotics induced ADRs

Table No 3 depicted the distribution of antibiotics induced ADRs.

Table No 3: Distribution of Antibiotics induced ADRs

Sl No.	Antibiotics	No. Of Adrs (n=75)
1.	Antitubercular Antibiotics	23 (30.5%)
2.	Ceftriaxone	18 (24%)
3.	Ofloxacin	5 (6.7%)
4.	Cefixime	5 (6.7%)
5.	Cefotaxime	5 (6.7%)
6.	Linezolid	3 (4%)
7.	Ampicillin	2 (2.7%)
8.	Cefpodoxime	2 (2.7%)
9.	Doxycycline	2 (2.7%)
10.	Metronidazole	2 (2.7%)
11.	Penicillin	2 (2.7%)
12.	Piperacillin	2 (2.7%)
13.	Amikacin	1 (1.3%)
14.	Amoxycillin	1 (1.3%)
15.	Clarithromycin	1 (1.3%)
16.	Levofloxacine	1 (1.3%)
	Total	**75 (100%)**

4. Causality assessment of ADRs by Naranjo causality algorithm:

The suspected ADRs were assessed for their causality using the Naranjo Causality Algorithm which is depicted in Fig 2.

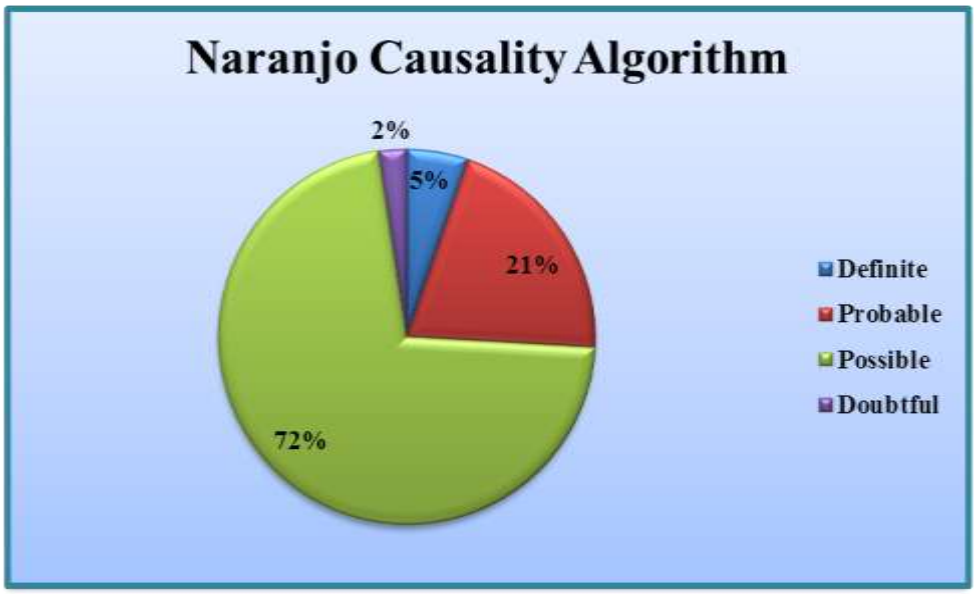

Fig 2: Causality assessment of ADRs by Naranjo causality algorithm.

5. Severity assessment of ADRs by using Modified Hart wig scale

209 ADRs were assessed for their severity using a Modified Hart wig Scale, which is a standard scale for severity assessment which is depicted in Fig 3.

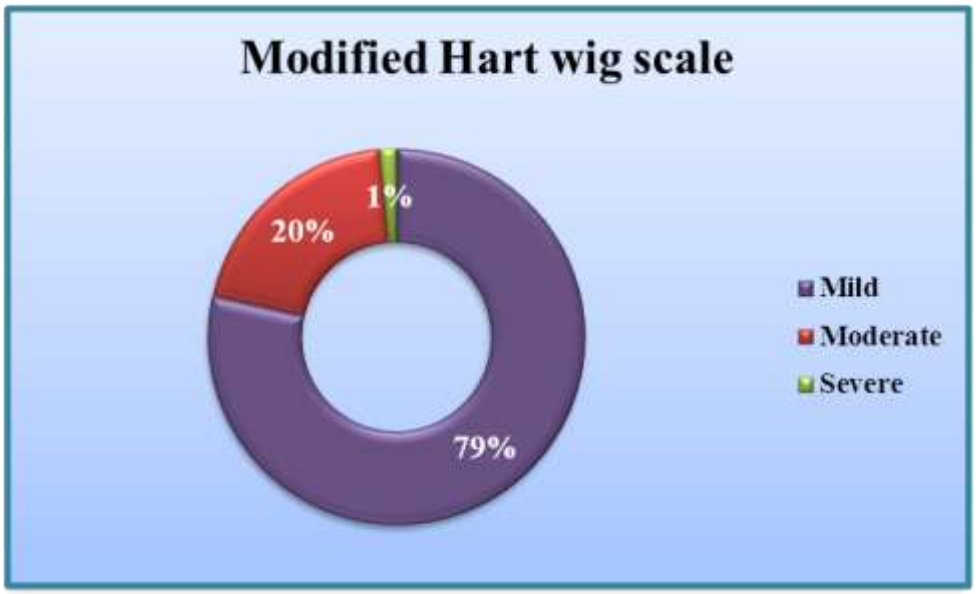

Fig 3: Distribution of Severity assessment of ADRs by using Modified Hart wig scale

6. Preventability assessment of ADRs by using Modified Schumock and Thorntons Scale: The preventability was assessed by using Modified Schumock and Thorntons Scale which is depicted in Fig 4.

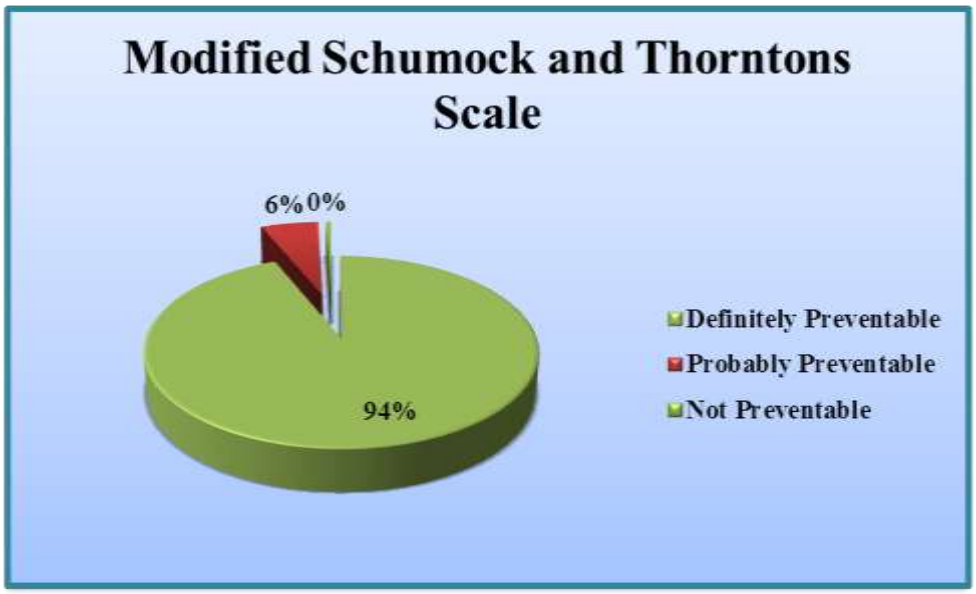

Fig 4: Distribution of preventability assessment of ADRs by using Modified Schumock and Thorntons Scale

7. Classification of ADRs according to WHO-ART System Organ Classes[12]

According to WHO-ART there are 32 System Organ Classes out of that 18 classes are found in the present study which is depicted in Table No 4.

Table No 4: Classification of ADRs according to WHO-ART System Organ Classes

Sl No.	Codes	System Organ Classes	No. of ADRs (N=209)
1	**0600**	**Gastro-intestinal system disorders**	**71 (34%)**
		Vomiting	20
		Abdominal pain	16
		Diarrhoea	11
		Constipation	9
		Mouth dry	6
		Gastritis	4
		Dyspepsia	1
		Gastritis aggravated	1
		Gastritis haemorrhagic	1
		Haemorrhage rectum	1
		Stomatitis ulcerative	1
2	**0100**	**Skin & appendages disorders**	**42 (20.1%)**
		Rash	12
		Acne	5
		Erythema multiforme	5
		Pruritus	4
		Stevens Johnson Syndrome	4
		Angioedema	3

		Psoriasis	2
		Rash erythematous	2
		Urticaria	2
		Bullous eruption	1
		Epidermal necrolysis	1
		Hypersensitivity	1
3	**0410**	**Central and peripheral nervous system disorders**	**26 (12.4%)**
		Dizziness	11
		Headache	5
		Tremor	3
		Hypertonia	2
		Extrapyramidal disorder	2
		Ataxia	1
		Convulsions	1
		Paraesthesia	1
4	**1810**	**Body as a whole-general disorders**	**16 (7.6%)**
		Oedema peripheral	7
		Hypersensitivity	3
		Chest pain	2
		Asthenia	1
		Fatigue	1
		Oedema mouth	1
		Rigors	1
5	**0800**	**Metabolic and nutritional disorders**	**10 (4.8%)**
		Alkalosis	1
		Diabetes mellitus	1
		Gout	1
		Hyperglycaemia	1
		Hyperkalaemia	1
		Hypocalcaemia	1
		Hypoglycaemia	1
		Hypokalaemia	1
		Lipodystrophy	1
		Weight increase	1
6	**1100**	**Respiratory system disorders**	**8 (3.8%)**
		Coughing	3
		Pharyngitis	2
		Dyspnoea	2
		Hypopnoea	1
7	**0700**	**Liver and biliary system disorders**	**8 (3.8%)**
		Hepatitis	7
		Hepatocellular damage	1
8	**1600**	**Neonatal & infancy disorders**	**7 (3.3%)**
		Diarrhoea neonatal	7
9	**0500**	**Psychiatric disorders**	**6 (2.9%)**
		Anxiety	3

		Anorexia	1
		Somnolence	1
		Suicide attempt	1
10	**0200**	**Musculo-skeletal system disorders**	**5 (2.4%)**
		Arthraigia	3
		Insomnia	1
		Osteoporosis	1
11	**1210**	**Red blood cell disorders**	**3 (1.4%)**
		Anaemia	1
12	**0900**	**Endocrine disorders**	**1 (0.5%)**
		Glucocorticoids increased	1
13	**1410**	**Reproductive disorders, male**	**1 (0.5%)**
		Ejaculation disorder	1
14	**1830**	**Resistance mechanism disorders**	**1 (0.5%)**
		Herpes zoster	1
15	**1030**	**Heart rate and rhythm disorders**	**1 (0.5%)**
		Bradycardia	1
16	**1010**	**Cardiovascular disorders**	**1 (0.5%)**
		Hypotension	1
17	**1300**	**Urinary system disorders**	**1 (0.5%)**
		Renal function abnormal	1
18	**0431**	**Vision disorders**	**1 (0.5%)**
		Vision abnormal	1

DISCUSSION

Adverse drug reaction is one of the major problem which leads to the non-compliance of medication. The causes for increased ADRs are self medication, polypharmacy and other drug related problems. It is the duty of the clinical pharmacist to identify and monitor the ADRs in the health care sectors.

In the present study the incidence of ADRs were more in the male patients (54.5%) than females which is similar to *Sharma Love et al.*[13] Adults are more prone for ADRs in the study when compared to paediatrics and elderly patients. The ADRs were reported more from General Medicine department 52.1% which is similar to study by *T M Vijayakumar et al.*[8]

Among all ADRs reported antibiotics were the most commonly reported class of drugs, which are similar to other studies *Camargo AL et al*[14] *and Samuel SA et al.*[15] Ceftriaxone was the drug most commonly associated with the ADRs in our study, which is similar to *Shadi Baniasadi et al.*[16]

Causality assessment of ADRs were assessed by using Naranjo causality algorithm and out of 209 cases, 150 (71.7%) were under the category of possible, which was similar to the study

by *Palanisamy et al*[6] and *Sharma Love et al.*[13] Severity assessment of ADRs by using Modified Hart wig scale, most of the ADRs belonged to mild category (78.5%), which was similar to the study by *Padmaja Uday Kumar et al.*[6] Preventability assessment of ADRs were done by using Modified Schumock and Thorntons Scale and most of the ADRs in the present study belonged to definitely preventable(93.8%), which is similar to the study conducted by *Asawari L Raut et al.*[2] According to WHO-ART the most commonly affected system organ classes was Gastro-intestinal system disorders (34%) and Skin & appendages disorders (20.1%) which were slightly similar to the study of *Shadi Baniasadi et al.*[16]

CONCLUSION

To identify and monitor ADR is one of the major duties of the clinical pharmacist. The present study mainly focused on WHO-ART system organ classification of ADRs which is one of the world wide excepted classification. A total of 209 ADRs were reported which shows male dominancy and majority in the age group of 19-60years. Most of the ADRs were reported in medicine department with ceftriaxone the commonest among Antibiotics. Gastro-intestinal system disorders with vomiting, was the commonest in the system organ classification of WHO-ART reports. Although the ADRs in the present study were non serious and preventable, monitoring and management of such ADRs through therapeutic interventions would be beneficial in better patient care. Hence pharmacists have an important responsibility in monitoring and safety of medicines.

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