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EVALUATION OF EVIDENCE BASED ADVERSE DRUG REACTIONS AND PHARMACOVIGILANCE USING ASSESSMENT SCALES IN TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

OBJECTIVE: Evaluation of evidence based adverse drug reactions and Pharmacovigilance assessment scales in tertiary care teaching hospital. **MATERIALS & METHODS:** The study is an observational Prospective was designed from January 2014 to June 2016 (30 months) in which incidence of adverse drug reactions was calculated. A total of 450 adverse drug reactions were observed from 5640 patients. Pharmacovigilance assessment on adverse drug reactions were assessed by five international scales based on causality, probability, severity, preventability and type of class. These scales as follows Causality by WHO-UMC Scale, Probability by Naranjo's scale, and Severity by Hartwig & Siegel scale, Preventability by Modified Schumock & Thornton and type of classification by modified by Wills and Brown. **RESULTS:** Prevalence of ADR's was found to be 8.02% and male to female ratio was 0.81. ADR's mostly occurred in the age group 41-50 (57.4%). Ski and gastrointestinal was found to be the most commonly affected organ system (24.29%) among which rashes and urticaria were the most common type of ADR'S reported, majority of the adverse drug reactions were due to Antimicrobials (22.42%). For Casuality of ADR's according to Naranjo Scale 26.16% of adverse drug reactions were assessed to be probable, using WHO-UMC scale 33.64% were considered as probable. Similarly Severity assessment shows majority of the reactions as moderate (53.27%). **CONCLUSION:** Adverse drug reactions are commonly observed in wards because of wrong administrations and dose, other factors genetically drugs produce reactions. one should need to observe the patient prescription and compliance towards medications. so that we can minimize the adverse drug reactions.

KEYWORDS: ADR's mostly occurred in the age group 41-50 (57.4%).

INTRODUCTION

World Health Organization defines adverse drug reactions (ADRs) as 'a reaction which is noxious and unintended and which occurs at doses normally used in humans for prevention, diagnosis or therapy of disease, or for the modification of physiological functions'.[1,2,3] Using this definition, therapeutic failures, drug abuse and intentional or accidental poisoning (overdose) are not considered ADRs, nor are adverse events that occur as a result of intentional non-compliance or errors in drug administration.[4] ADRs have a major impact on public health by imposing a considerable economic burden on patients, society and already stretched health care system.[5] Adverse drug reaction (ADR) is a dominant ubiquitous and preventable public health issue with its incidence in Indian population ranging between 1.8% and 25.1%, with 8% resulting in hospitalization.[6,7] Doctors should be aware and oriented to identify the condition earliest and manage appropriately as early diagnosis & treatment has a substantial effect on the management and final outcome. Indiscriminate use of drugs, polypharmacy and multi organ involvement often poses problem in identifying the responsible drug.[8,9] There is a need to study ADRs and ADRs reporting to minimize the risk of medicines. Pharmacovigilance is the study of the safety of drugs marketed drugs examined under the practical conditions of clinical use in large populations.4 Early detection, evaluation and monitoring of ADR are essential to reduce harm to patients and thus improve public health.[10] Pharmacovigilance or ADR monitoring, launched by WHO in the 1960s in the wake of 'thalidomide' disaster, is currently an integrated global effort of more than 70 countries worldwide.[11,12] After decades of hibernation, the need for an efficient pharmacovigilance programme was felt, the result of which was the institution of National Pharmacovigilance Programme in November 2004.Under this programme, the Central Drugs Standards Control Organization, New

Delhi officiates as the central co-ordinating body under which two zonal, five regional and 24 peripheral centres have been established. The objective of this programme is to create awareness among the health professionals on ADR monitoring and to encourage a reporting culture.[13,14] To achieve the long term objective 'Centre of Excellence' for Pharmacovigilance in India, the PvPI National Coordinating Centre collaborating with the WHO Collaborating Centre - Uppsala Monitoring Centre(UMC) based in Sweden.[15,16,17] We performed a prospective analysis of ADRs caused by medicines prescribed in the department of medicine, pediatrics, dermatology in the Guntur General Hospital. to define prevalence and to assess risk factors, causality, severity, preventability, outcome, management of these reactions.

METHODOLOGY

Study Design: An Observational Prospective Study.
Study Period: January 2014 to June 2016 (30 months).
Study Site: Government General Hospital (GGH), a 1300 bedded tertiary care teaching hospital, Guntur.
Study Materials: Pharmacovigilance Programe of India(PvPI) issued adverse drug reactions form, Informed consent form, Assessment These scales as follows Causality by WHO-UMC Scale, Probability by Naranjo's scale, and Severity by Hartwig & Siegel scale, Preventability by Modified Schumock & Thornton and type of classification by modified by Wills and Brown.

Inclusion Criteria

- All the patients who have suspected adverse drug reactions after drug treatment in the in-patient departments at tertiary care hospital(s) only.
- All the patients who are hospitalized due to suspected ADR(s) in the in-patient department(s) and patients with drug therapy with various diseases with co-morbidities were selected.
- Patients only on allopathic treatment, irrespective of age and gender.
- Collections of data from permitted departments

Exclusion Criteria

- Patients who are on alternative system(s) of medicines.
- Hospital rules are not allowed some departments.

STUDY PROCEDURE

One of the Costal big hospital for treating patients , providing good patient compliance on treatment and good hygienic condition to stay in-patients depatmetns, free medication distributions most diseases. Who have come from various districts of andhrapradesh to take treatment or any physician referral primary health care centers cases come to out-patients department to check up their health with particular departments. So that some patients referred by physician to stay in in-patients ward to give treatment on the basis of clinical condition of the patients in respective departments. There I used observe the adverse drug reactions and patient specific information was collected in IPC- suspected adverse drug reactions forms. An informed consent was taken from the patients for participating in the study. The study was initiated after approval from the Institutional Human Ethical Committee (IHEC). The suspected or identified ADR'S were recorded in IPC- suspected adverse drug reactions forms Assessment These scales as follows Causality by WHO-UMC Scale, Probability by Naranjo's scale, and Severity by Hartwig & Siegel scale, Preventability by Modified Schumock & Thornton and type of classification by modified by Wills and Brown. to understand the type of reaction.

RESULTS

A total of 446 adverse drug reactions were identified in a study period of 30 months i.e. from January 2014 to June 2016. **Fig-1** states that out of 446 ADR's majority of ADR's were reported from General medicine (33.85%) followed by Dermatology (14.4%) and Pediatrics (9.1%), oncology (7.8) followed by other departments. Overall prevalence rate of ADR's was found to be 10.02%.

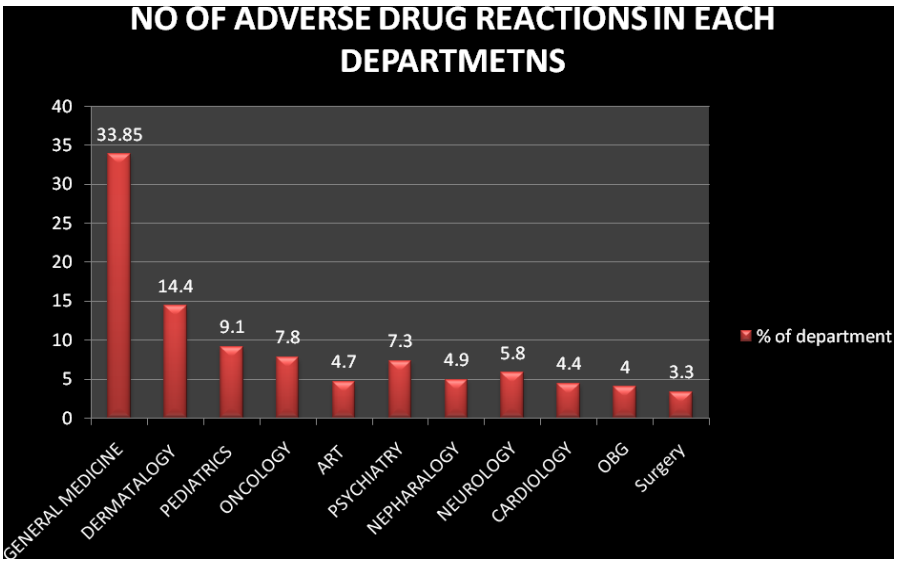

FIGURE 1: % OF ADVERSE DRUG REACTIONS OBSERVED IN IN-PATIENTS WARD OF HOSPITAL

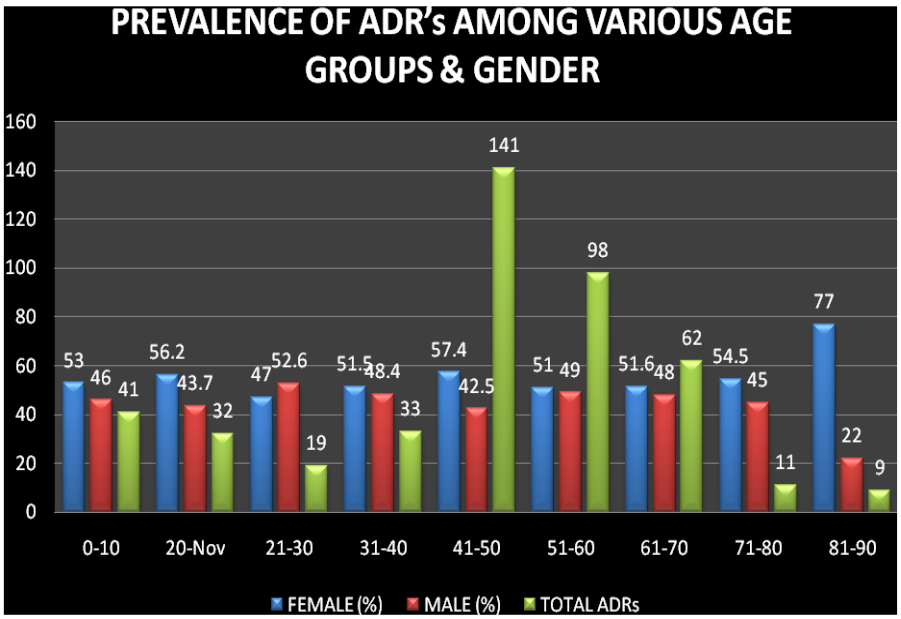

FIGURE: 2. % of PREVALENCE OF ADR's AMONG VARIOUS AGE GROUPS & GENDER

PREVALENCE OF ADR's AMONG VARIOUS AGE GROUPS AND GENDER.

Figure-2 describes about the ADR's mostly occurred in the age group between 41-50 (31.61.%) followed by the age group of 51-60 (21.9.%) and least susceptible age group was 71-80 & 81-90 (0.93%). The female patients (57.4%) experienced more number of ADR'S compared to male patients (42.5%). The male to female ratio was 1:.8.

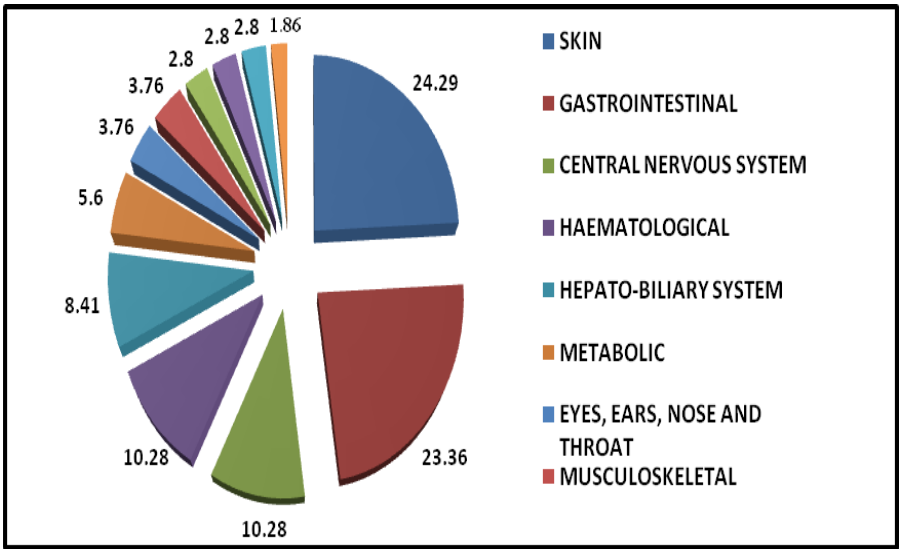

FIGURE-3 ORGAN SYSTEMS AFFECTED BY ADVERSE DRUG REACTION

FIGURE-3 describes that skin was found to be most commonly affected organ system (24.29%) among which rashes and urticaria were the most common type of ADR'S reported, followed by Gastro-intestinal System (23.36%), Central nervous system (10.28), Hematological (10.28) least affected was renal system (1.86%) and others included edematous reactions.

TABLE: 1 RISK FACTORS

S.NO	VARIABLE	NO. OF ADR'S	PERCENTAGE OF ADR'S (%)
1.	**AGE**		
	0-10	41	9.1
	11-20	32	7.1
	21-30	19	4.2
	31-40	33	7.3

	41-50	141	31.6
	51-60	98	21.9
	61-70	62	13.9
	71-80	11	2.4
	81-90	9	2.0
2.	**NO. OF MEDICATIONS**		
	<6	223	50.0
	6-10	180	40.3
	>11	43	9.9
3.	**DURATION OF TREATMENT**		
	< one week	71	15.9
	< 15 days	260	61.1
	>1 month	115	25.7
4.	**NO. OF DIAGNOSIS**		
	Single	126	28.03
	Double	257	57.00
	Multiple	63	14.95
5.	**GENDER**		
	Female	242	56.22
	Male	204	45.73
6.	**SOCIAL HABITS**		
	Smoker	29	6.54
	Alcoholic	46	10.28
	Both	59	13.08

ASSOCIATED WITH ADVERSE DRUG REACTIONS.

Table-1. Adverse drug reactions produced by various risk factors it may be genetically some drugs produce reactions immediately.commenly observed factor is drug – drug reactions and drug –food interactions and poly-pharmacy. About 66.35% of ADR observed were due to polypharmacy i.e. 6-10 medications/ prescription & 52.33% of ADR were due to prolonged treatments (> 1month). It was also found that 57% of the patients suffered from more than one disease. 13.08% of patients reporting ADR were both smoker and alcoholic.

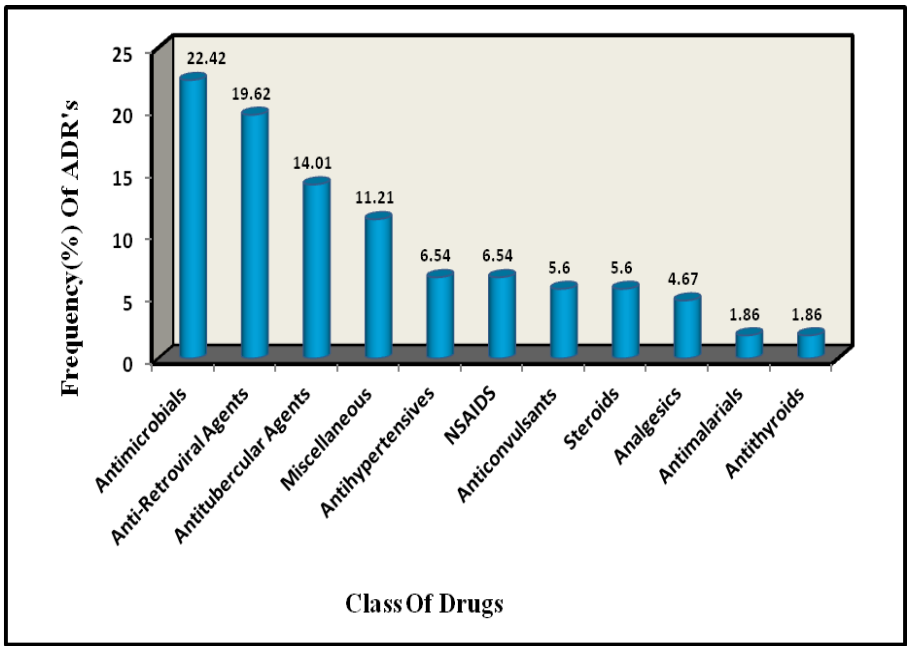

FIGURE-4 PRESCRIBED CLASS OF DRUGS AND ADVERSE DRUG REACTIONS

FIGURE-4 describes that majority of the adverse drug reactions were due to Antimicrobials (22.42%). Among which Amoxicillin & Potassium clavulanate caused the highest percentage of ADR's followed by Antiretroviral agents(19.62%) among which anemia was the most common adverse reaction caused. The drug classes which caused least ADR's were Antithyroid agents and Anti-malarials (1.86%).

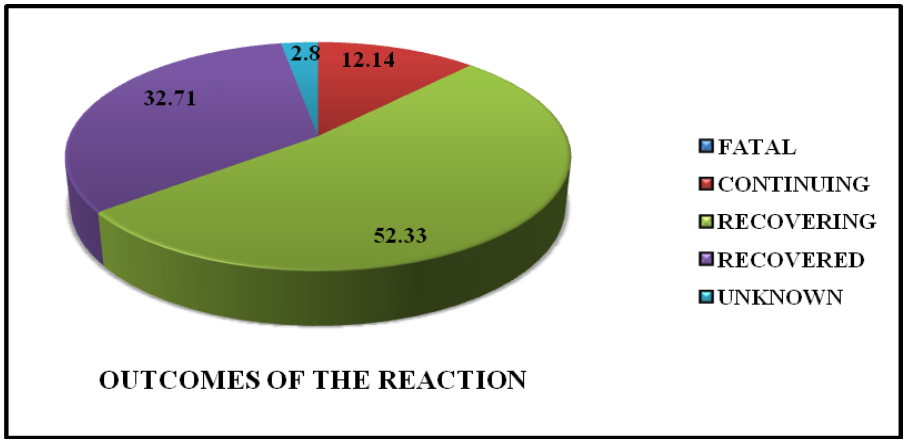

FIGURE-5 OUT COMES OF THE REACTIONS

FIGURE-05 describes the outcomes of suspected ADR'S which were evaluated to understand the condition of patient the majority of ADR's (52.33%) were Recovering, 32.71% were found to be recovered, and 2.80% of the ADR's were of unknown outcome. There were no Fatal Adverse drug reactions reported.

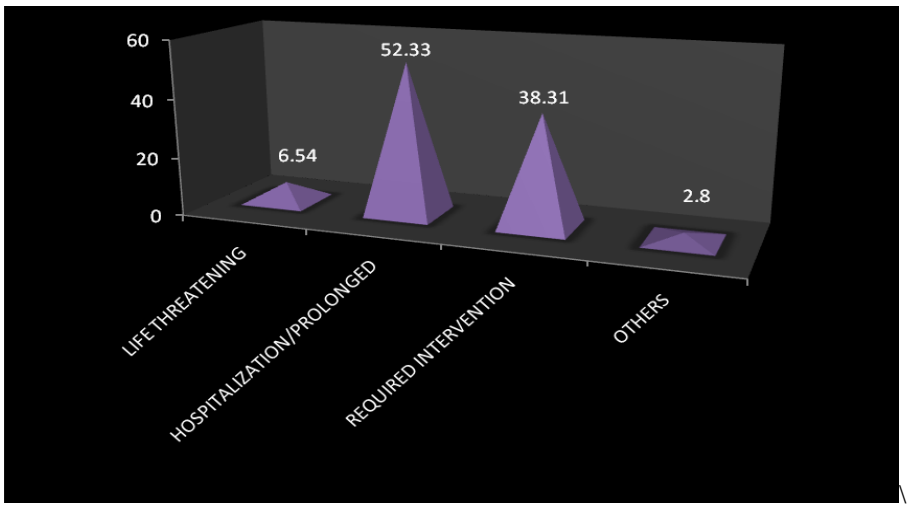

FIGURE-06-SERIOUSNESS OF ADVERSE DRUG REACTIONS

FIGURE-6 is regarding seriousness of the reaction majority of the Adverse drug reactions (ADR's) led to Hospitalization/Prolonged (52.33%) followed by which required intervention were 38.31% and life threatening ADR's were 6.54%.

ASSESSMENT OF PHARMACOVIGILANCE ON ADVERSE DRUG REACTIONS

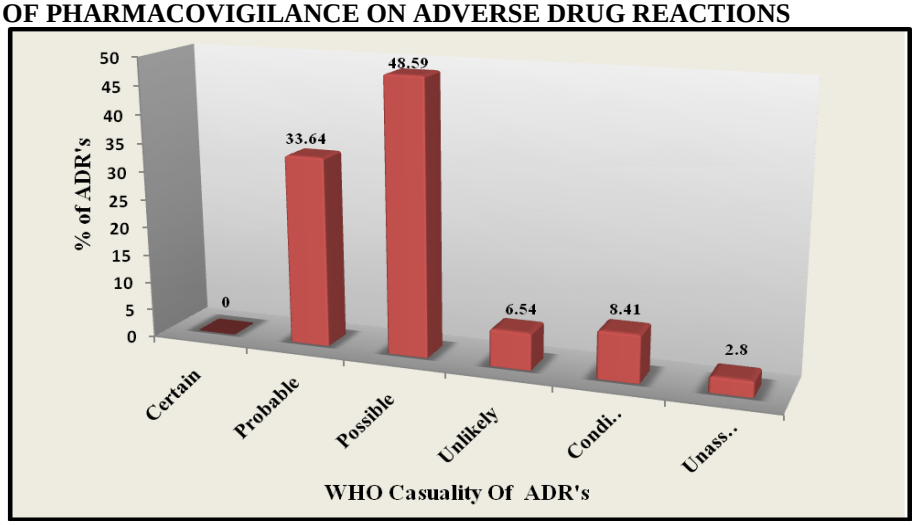

FIGURE: 7 CAUSALITY ASSESSMENT by WHO CASUALITY SCALES

FIGURE-7 reveals that out of the total number of 446 adverse drug reactions 151(33.64%) were considered as probable, 219(48.59%) were considered as possible & 13(2.80%) could not be categorized and were placed under unassessable.

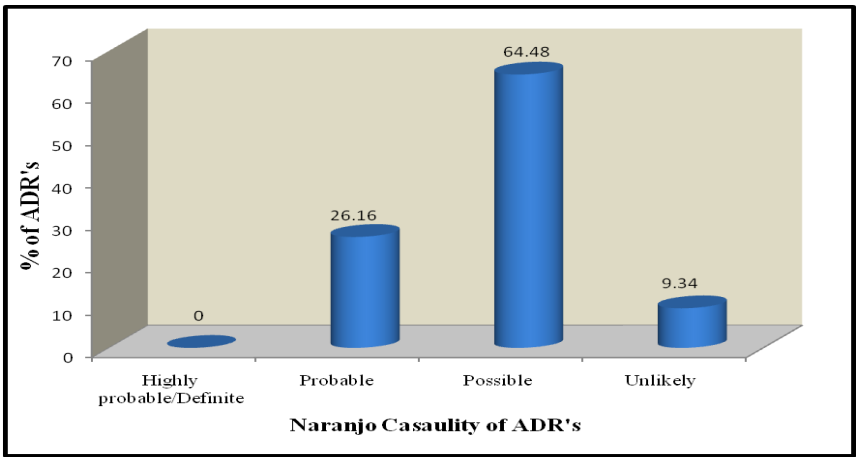

FIGURE-8 NARANJO PROBABILITY SCALE

FIGURE-8 describes that 115(26.16%) of adverse drug reactions were assessed to be probable, 288(64.48%) as possible and 43(9.34%) as unlikely by using Naranjo probability scale.

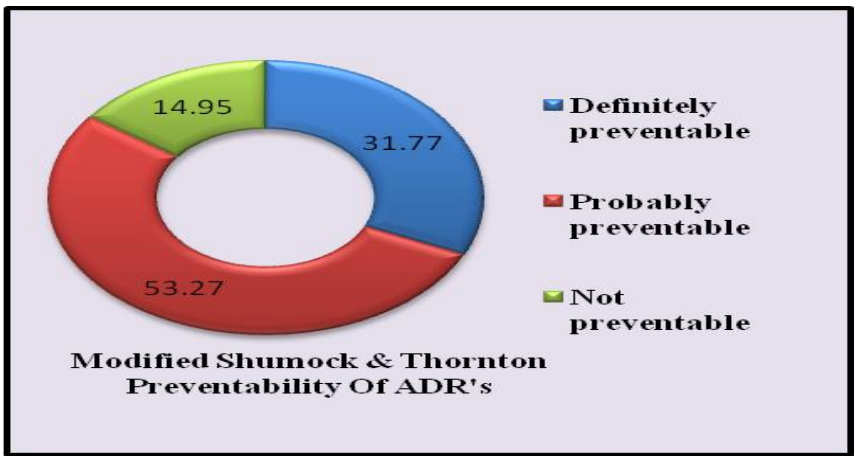

FIGURE: 9 MODIFIED **SHUMOCK &THORNTON PREVENTABILITY OF ADVERSE DRUG REACTIONS**

FIGURE-9 states that 143 (31.77%) were definitely preventable where as 240 (53.27%) were probably preventable and 67 (14.95%) were not preventable by using modified Shumock and Thornton preventability scale.

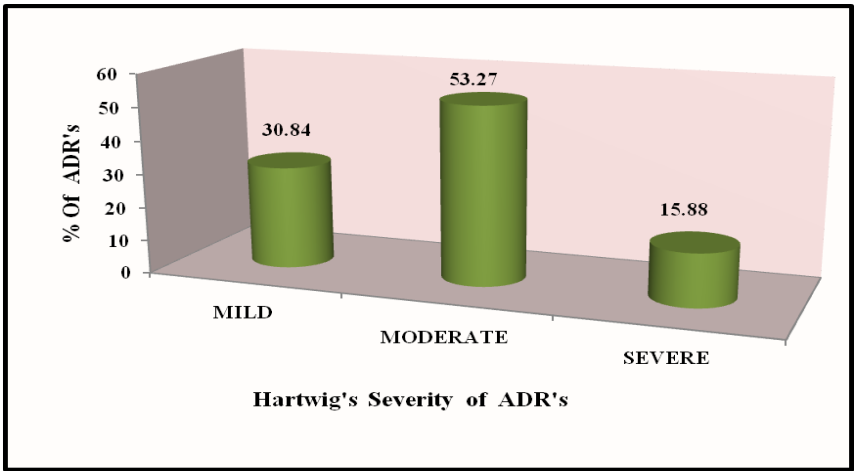

FIGURE-10 HARTWIG'S SEVERITY SCALE

It explains that the majority of the reactions are Moderate (53.27%) followed by Mild (30.84%) and Severe (15.88%) by using Hartwig's severity scale.

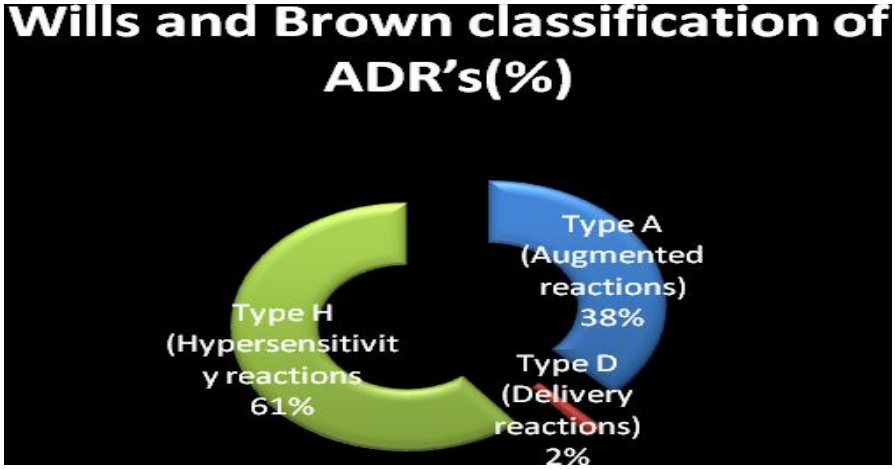

FIGURE: 11 WILLS AND BROWN CLASSIFICATIONS

Describes that out of 446 adverse drug reactions are identified 61% were Type-H (Hypersensitivity reactions) TYPE- A (Augmented reactions) are 38 %, other reactions TYPE-D (Delivery reactions) is 2 % respectively.

TABLE-2 MANAGEMENT OF ADVERSE DRUG REACTIONS

TREATMENT	NO. OF ADR's	PERCENTAGE OF ADR's (%)
Stopped the medication	149	33.40
Continue the same	41	9.19
Added another drug to treat the ADR	154	34.52
Reduce the dose	46	10.31
Substituted another drug	56	12.55
TOTAL	446	

Table-2 states that majority of the ADR's were managed by adding another drug to treat the adverse drug reaction (34.52%) followed by 33.40% of the suspected drug stopped. The least was continuing the same therapy (9.19%) & reducing the dose of the suspected drug (10.31%).

DISCUSSION

The main study was conducted in a period of 30 months i.e. from january-2014 to june-2016 on prevalence of adverse drug reactions and importance of reporting adverse drug reactions and assessment using scales. Submitting to the Pharmacovigilance center.

The study an observational bases adverse drug reactions has identified in General Medicine, oncology, Pediatrics, and dermatology, ART and neurology and psychiatry and other departments **[Figure-1].** The causality, severity, preventability and risk factors of ADR's reported by patient and diagnosed by health care professionals were assessed.

Out of 446 adverse drug reactions reported and assessed, 57.4% of ADR's were in the age groups of 41-50yrs similar results were observed in other studies. [16] The reasons that could be responsible are patients at this age group suffer with many co-morbidities such as diabetes, hypertension so this age group used more number of medications and complained for drug related adverse events. Females (54.14%) were more prone to ADR's than males (45.85%) **[Figure-2].** This might be because of Women in comparison to men have lower bodyweight and organ size, more body fat, different gastric motility and lower glomerular filtration rate. These differences can affect the way the body deals with drugs by altering the pharmacokinetics and pharmacodynamics, of the drugs including drug absorption, distribution, metabolism and elimination.

The most common organ systems associated with ADR'S in our study were skin, followed by gastrointestinal and CNS **[Figure-3]** This finding was consistent with many studies.[3],[5],[7] Antimicrobials were the drug class that led to major reactions as they were mostly prescribed drugs which was similar to other studies **[Fig-4].**[3],[15] Taking more medications (polypharmacy), co-morbidities and increased duration of therapy were the contributing risk factors for ADR'S **[Table-1]** in our study which was comparable with other studies. [10] Patients who were on Antiretroviral and

hypertension and diabetes used the medicines for more than 1month. Majority of the ADR'S were associated with oral therapy (71.02%) followed by parenteral (25.23%) and topical (3.73%). In our study most of the ADR'S were possible (48.59%) in WHO-UMC causality assessment **[Figure-7]** which is quite consistent with the studies**.**[11] None of the reactions was categorized into certain as rechallenging of the drugs was not made as it may worsen the patient condition. According to the Naranjo probability scale maximum ADR'S were possible (64.48%) **[Figure-8].** Comparison of causality scales showed poor agreement in previous studies [11] and the reason described was due to different definitions of causality criteria for assessing ADR'S. Severity assessment of ADR'S showed that the majority of reactions were moderate **[Figure-9]** and similar findings were reported in other study. [11]Most of the reactions would have been preventable if proper precautions were taken like treating the patient with supportive measures **[Figure-6].** Majority of the reactions lead to hospitalization (52.33%) **[Figure-5]** this was due to use of antiretroviral and comarbidities. Regarding the outcomes of the reaction recovering reactions were more (52.33%) when compared to results of other studies**.** [3] This was due to patients with mild reactions were still recovering at the time of discharge and there outcomes were unknown. In our study 34.57% of the reactions were managed by adding another drug which in turn lead to increased cost of therapy and prolonged hospitalization **[Table-2].** Withdrawal of the suspected drug and use of antidote such as systemic and topical steroids, and oral antihistamines were given most commonly for ADR management.[11]

These adverse drug reactions are should be monitored and assessed by international scales, on the basis whether drug has to continued or stopped, alternative methods. Dose adjustment s has to made accordingly conditions of the patients. Health care professionals should need have knowledge and practice and reporting of adverse drug reactions to Pharmacovigilance program of India (PvPI) peripheral centers. So that we can minimize the adverse drug reactions or withdrawal of the drug market if drug has proper signal.

CONCLUSION

As our study results says one should which indicated the baseline information on prevalence of Adverse drug reactions and their distribution among the various Age groups, Gender, Organ system affected & Therapeutic class of drugs we conclude that measures should be implemented for the Systemic review of patients past & present medical/medication history for the early detection of adverse drug reactions targeting specific drugs of major systems i.e. Skin, Gastrointestinal, Central nervous system, Cardiovascular system, Hepatic & renal systems and also regular monitoring of adverse drug reactions is an important tool to prevent organ damage, reducing the morbidity and mortality.

Future prospective

Our Future scope will include extension of Pharmacovigilance (PV) services to Primary health care centers and register medical practiceners (RMP) and awareness to Pharmacovigilance programe in India & use of trigger tool methodology for ADR detection & reporting. We believe that our study may be useful in extensive ADR monitoring, and framing polices towards ADR reporting to promote rational use of drugs ensuring patient compliance & safety associated with public health. We recommend further studies of similar kind involving several other departments for longer study periods to be conducted in order to strengthen the effectiveness of Pharmacovigilance (PV) activities in India.

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