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A STUDY ON SCREENING OF ADVERSE DRUG REACTIONS IN THE DEPARTMENT OF DERMATOLOGY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: Adverse drug reaction is a response to a drug which is noxious and unintended and which occurs at doses normally used for prophylaxis, diagnosis or therapy of disease, or for modification of physiological function. **Objectives:** To screen and evaluate the incidence of adverse drug reactions in the dermatology department and to identify common class of drugs responsible for ADRs and categorize the adverse drug reactions by using WHO causality assessment scale. **Methods:** A prospective observational study was conducted in Inpatient and outpatient department of dermatology in RIMS Government general hospital, Kadapa. The present study was conducted for a period of 6 months from November-2016 to April 2017. All the recruited subjects (N=500) in the both in-patient and out-patient Department of Dermatology were screened. **Results:** During the study period a total of 500 patients were screened in the department of dermatology for adverse drug reactions (ADR). Out of which 17 patients encountered for ADR. Out of 17 ADRs, 6 ADRs encountered during treatment in the department of dermatology, 5 ADRs were ADR related admitted admission into department of dermatology, 6 ADRs were identified during refer from other department. The incidence of the study was 3.5%. Causality assessment of ADRs by NARANJO scale was found to be Definite-0%, Probable-35.30%, Possible-64.70% and Doubtful-0%. In our study out of 17 patients, in 8 patients suspected drug was discontinued, in 7 patients the drug has been not changed, dose reduction was done in the 2 patients. **Conclusion:** From the results it was concluded that steroids and anti-retrovirals are most common implicated drugs responsible for adverse drug reactions and most effected organ system is skin and a wide clinical spectrum of ADRs ranging from mild maculopapular rash to serious stevens johnson syndrome was observed. Educating the patients and health care professionals on adverse drug reactions prevention can reduce the chances of occurrence of ADRs in hospitals.

KEYWORDS: Adverse drug reaction, anti-retrovirals, stevens johnson syndrome, rashes.

INTRODUCTION

Skin plays an important role in most people's self-esteem. Dermatological diseases are commonly encountered in community. They vary widely as result of geographical location, climate, socio-economic status, personal habits and internal factors such as age, gender and heredity. Some common skin diseases in the dermatology are tineapedis, tineacruris, acne, drug induced lesions, psoriasis,dermatitis, urticaria, acneform rashes, miliaria, Pityriasisversicolar, Melasma, Pyoderma, wart, vitiligo, male pattern baldness, polymorphic light eruptions, Furuncle, Herpes zoster, Lichen planus, Folliculitis, Hyperpigmentation, Eczema, Lichen simplex, Candidiasi, Hansen's disease, Impetigo, Keloid, Xerosis, Alopecia areata, Striae. Category of some commonly prescribed drugs in dermatology are Antifungal, Antibiotics, anti-histamins, Corticosteroids, Antiacne, Adsorbants and protectives, Keratolytics, Proton pump inhibitors, Antipsoriasis, Antihelminthics, Antiemetics, NSAIDs, Astringents, Ecto-parasiticides, Moisturisers, Vasodilators, H2 blockers, Anticancer drugs, Phenol, Chelating agents and glycosides[1-5]. According to World Health Organization (WHO) "Adverse drug reaction is a response to a drug which is noxious and unintended and which occurs at doses normally used for prophylaxis, diagnosis or therapy of disease, or for modification of physiological function.

Classification of Adverse Drug Reactions

Type A (Augmented)

- Dose dependent
- Preventable in most part by slow introduction of dosages
- Predictable by pharmacological mechanism

Example: NSAIDS induced gastric ulcers.

Type B (Bizarre)
- Rare
- Unpredictable, mechanisms are unknown,

Example: Allergic reactions.

Type C (Continuous)
- Dose related and time related
- Related to cumulative dose of drug
- Chronic effects

Example: Hypothalamic pituitary adrenal axis suppression by corticosteroids.

Type D (Delayed effect)
- Time related
- Delayed
- Becomes apparent after use of drug

Example: Teratogens or carcinogens

Type E (Rebound effect)
- Withdrawl
- Occurs when the medication is stopped

Example: Beta blocker withdrawl

Type F (Failure of therapy)
- Unexpected failure of therapy.
- May be caused by a drug interaction.

Example: CYP450 enzyme interactions

Report of ADR's

The Report should be on a standardized ADR reporting form. This form can be downloaded from http://www.ipc.gov.in/ and http://www.cdsco.nic.in/. Dully filled the ADRs in the reporting from when an ADR is encountered. Use a separate from for each patient and filled with the complete information. The completed ADR form is then returned to the nearestadverse drug reaction Monitoring Centre (AMC) or to National Coordinating Centre. The causality assessment is carried out at Adverse Drug Reaction Monitoring Centres (AMCs) by using WHO-UMC scale[6-8]. The analyzed forms are forwarded to the National Coordinating Centre through the ADR database. Finally the data is analyzed and forwarded to the Global Pharmacovigilance Database managed by WHO Uppsala Monitoring Center in Sweden. The reports are periodically reviewed by the National Coordinating Centre. The information generated on the basis of these reports helps in continuous assessment of the benefit risk ratio of medicines.

Aim

The aim of our study is to screen adverse drug reactions in the department of dermatology.

Objectives
- To screen and evaluate the incidence of adverse drug reactions in the dermatology department.
- To identify common class of drugs responsible for ADRs and categorize the adverse drug reactions by using WHO causality assessment scale.
- To report any suspected adverse drug reactions.

METHODOLOGY

Study design and study period
- A prospective observational study was conducted in Inpatient and outpatient Department of Dermatology in RIMS Government general hospital Kadapa.
- The present study was conducted for a period of 6 months from November-2016 to April 2017.

Source of data

Data was collected from treatment charts and through medication history interview of the subjects included in the study at O.P and I.P departments.

Sample size

All the recruited subjects (N=500) in the both in-patient and out-patient Department of Dermatology were screened.

Inclusion criteria

The study includes if the subject satisfies any of the following criteria
- Patients of both genders presenting to department of dermatology.
- Patients with any suspected ADRs referred to department of dermatology.
- ADR related admission into the hospital

Exclusion criteria

The study excludes
- Pediatrics
- Geriatrics
- Pregnant & lactating women were excluded.

Method of collection of data

It is a prospective observational study to be conducted in RIMS hospital in the departments of dermatology. Informed consent was obtained from the study participants after explaining the study.

Statistical analysis: All data of recruited subjects were recorded in a Microsoft excel spread sheet. Descriptive statistics were used to calculate patient demographic variables.

RESULTS

Demographic details of Patients: During the study period a total of 500 patients were screened in the

department of dermatology for adverse drug reactions (ADR). Out of which 17 patients encountered ADR.

Out of 17 ADRs, 6 ADRs encountered during treatment in the department of dermatology, 5 ADRs were ADR related admitted admission into department of dermatology, 6 ADRs were identified during refer from other department.

Table 1: Detection of overall ADRs

Total No of Patients Screened In Dermatology	ADRS Identified During Treatment	ADRS Related Admission	ADRS Referred From Other Departments
500	6	5	6

Age

The study results showed 7 who had encountered ADRs during the study period were in the age group 51-60 years. The incidence of the study was 3.5%.

Table 2: Patients Demographics.

AGE	MALES	FEMALES	NO. OF ADRS	INCIDENCE
18-20	52	28	1	3.5%
21-30	34	56	2	
31-40	36	66	3	
41-50	28	40	3	
51-60	49	51	7	
61-65	28	32	1	

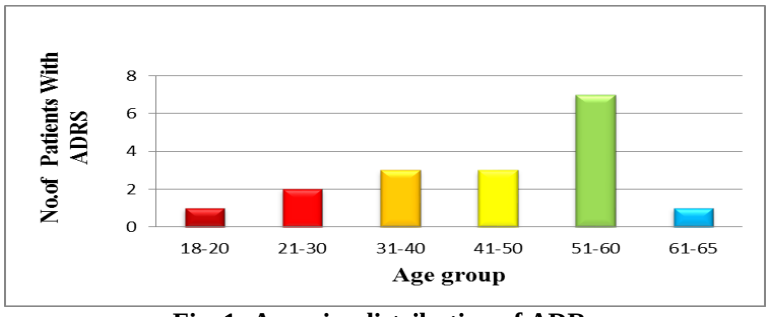

Fig. 1: Age wise distribution of ADRs

The study results showed male patients were 6(35.29%), and female patients were 11(64.71%).

Table 3: Gender wise distribution of ADRs

Gender	No of patients with ADRs	Percentage
MALE	6	35.29%
FEMALE	11	64.71%
TOTAL	17	100%

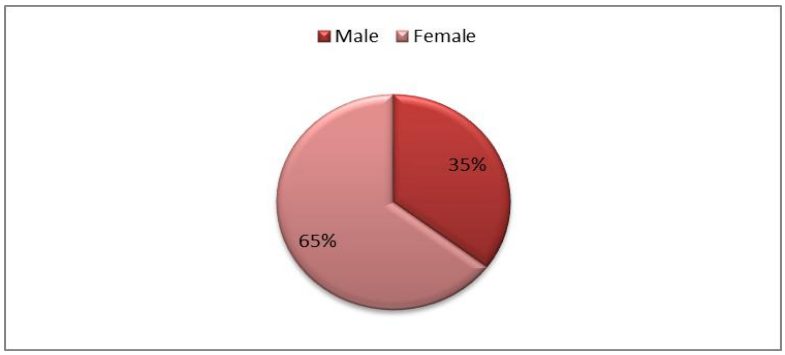

Figure 2: Gender wise distribution of ADRs.

The study results showed the classification of ADR"s encountered into Type A and Type B based Thompson"s and Rawlins classification. The type A ADR's were 6(35.30%) and type B reactions were 11 (64.70%).

Table 4: Classification of ADR's.

Types	No.of ADRs	Percentage %
TYPE A	6	35.30 %
TYPE B	11	64.70 %
TOTAL	17	100%

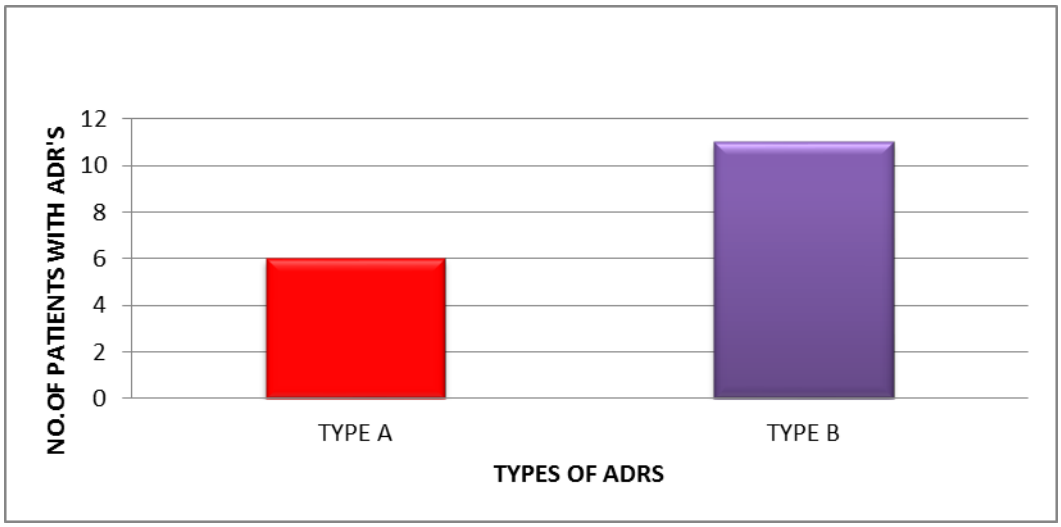

Figure 3: Classification of ADR's.

From our study we found that therapeutic class of most commonly implicated ADRs was corticosteroids (23.52%), antiretrovirals (23.52%), antibiotics (11.76%) and antiepileptics (11.76%).

Table 5: Therapeutic Drug Classes implicated in ADR.

Therapeutic Category Of Drug	ADR'S	No of Adrs	Percentage (%)
Corticosteroids: Dexamethsone	Blurred vision, hypertension, pedal edema, vertigo.	4	23.52 %
Antiepileptic: Phenytoin	Erythroderma	1	11.76%
Carbamazepine	Stevens Johnson syndrome	1	
Antibiotics: Amoxicillin and Clavulonic acid	Stevens Johnson syndrome,	1	11.76%
Ceftriaxone	Skin rash	1	
SSRI: escitalopram	Skin rash	1	5.88 %
Antipsoritic: Acetretin	Breathlessness	1	5.88%
Antiretroviral: Telenovir+Lamivudine+efavirenz	skin rash, maculopapular rash, prolific papular eruptions,	3	23.52%
Zudovidine+lamivudine+neviripine	pruritic papular eruptions	1	
Antimalarial chloroquine	Bleeding	1	5.88%
DMARDs sulfasalazine	Stevens Johnson syndrome toxic epidermal necrosis overlap	1	5.88%
Other ($KMNO_4$)	Skin eruptions	1	5.88%
TOTAL		17	100%

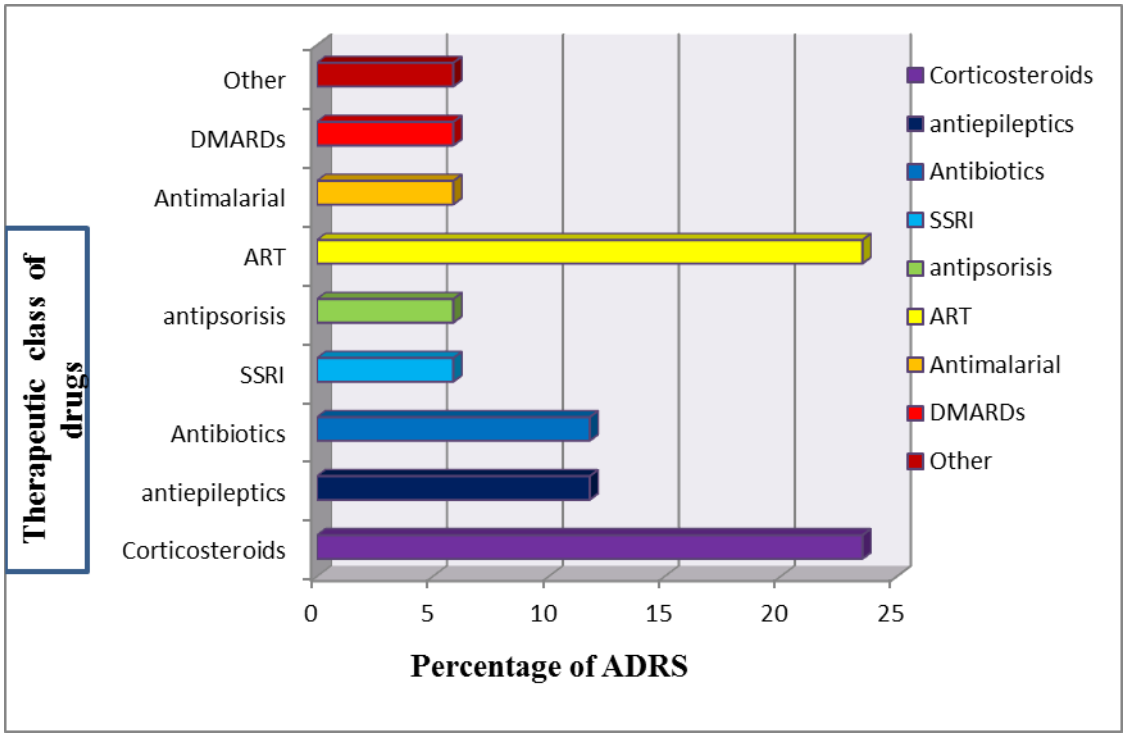

Figure 4: Therapeutic Drug Classes implicated in ADR.

Various organ systems affected by ADRs encountered during the study period. The most organ systems affected by ADR‟s were Dermatological (64.70%) followed by CNS (11.78%), hematology (5.88%), respiratory system (5.88%), cardiology (5.88%) and nephrology (5.88%).

Table 6: Organ systems affected by ADR's.

S.NO	Organ system	No. of ADR's	Percentage (%)
1	Dermatological	11	64.70%
2	Gastrointestinal Tract	0	0%
3	Hematological	1	5.88%
4	Central Nervous System	2	11.78%
5	Respiratory System	1	5.88%
6	Cardiology	1	5.88%
7	ENT	0	0%
8	Immunology	0	0%
9	Nephrology	1	5.88%
	TOTAL	**17**	**100%**

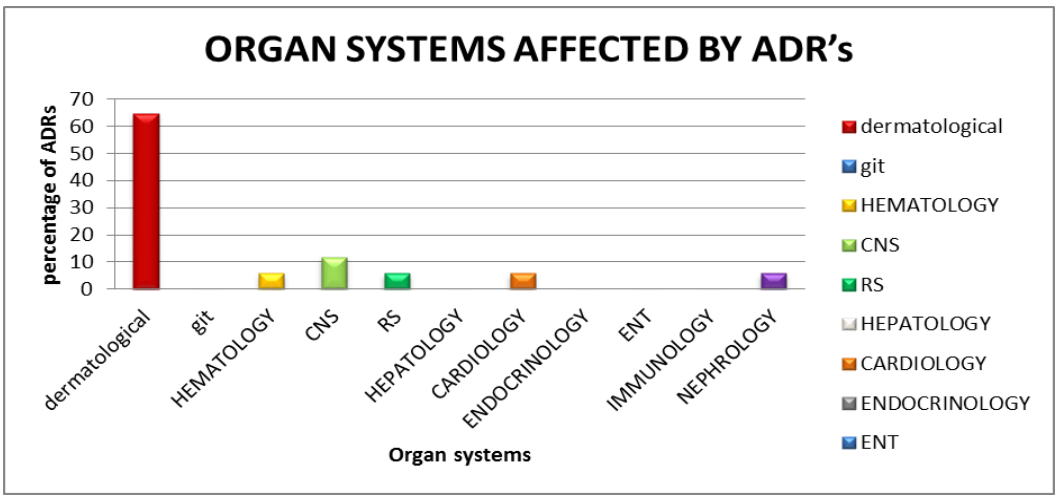

Figure 5: Therapeutic Drug Class implicated in ADR.

Causality assessment of ADRs by WHO scale was found to be Certain-29.45%, Probable-47.03%, Possible-23.52%, unlikely-0%, Conditional-0%, Unaccessable-0.

Table 7: Causality assessment of ADRs by WHO Scale.

S.NO	PROBABILITY	WHO N=17(%)
1	CERTAIN	5(29.45%)
2	PROBABLE/LIKELY	8(47.03%)
3	POSSIBLE	4(23.52%)
4	UNLIKELY	0
5	CONDITIONAL	0
6	UNACCESSABLE	0
TOTAL		17(100%)

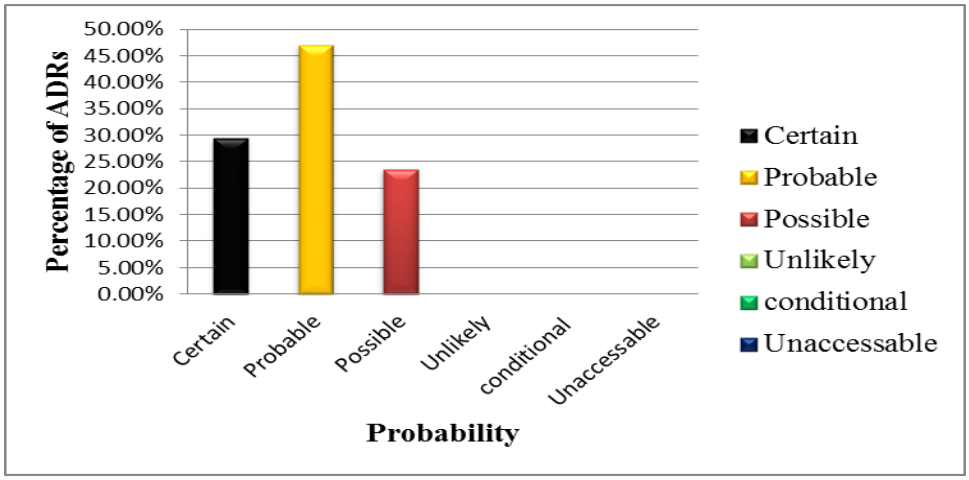

Figure 6: Causality assessment of ADRs by WHO SCALE.

Causality assessment of ADRs by NARANJO scale was found to be Definite-0%, Probable-35.30%, Possible-64.70% and Doubtful-0%.

Table 8: Casuality assessment of ADRs by Naranjo Scale.,

S.NO	Probability	No. of ADRS	Percentage of ADRs
1	Definite	0	0%
2	Probable	6	35.30%
3	Possible	11	64.70%
4	Doubtful	0	0%
Total		17	100%

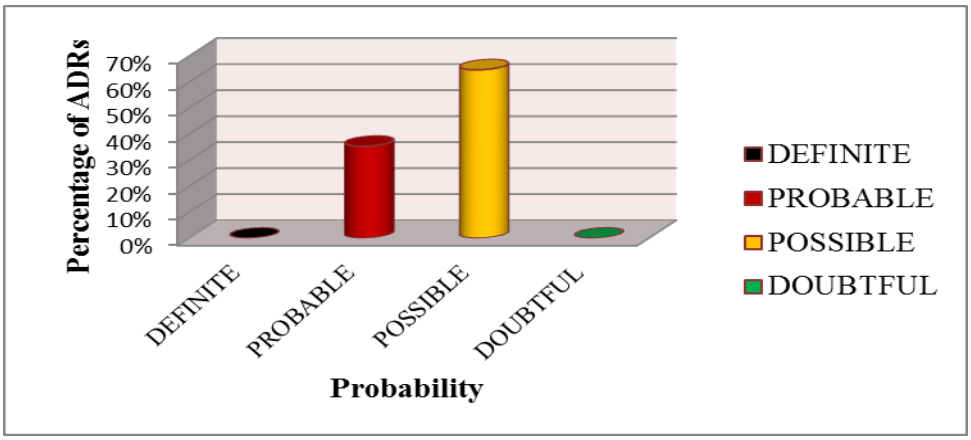

Figure 7: Causality assessment of ADRs by WHO Scale.

Severity of ADRs encountered during the study period was determined by using the Hartwig‟s Severity Assessment Scale. The results of the assessment of the severity as shown in table and figure explain that most of ADR were moderate in severity followed by mild and severecases.

Table 9: Severity of Adverse drug reaction

S.NO	Severity	No.of ADR'S
1	MILD a)LEVEL-1 b)LEVEL-2	 1 4
2	MODERATE a)LEVEL-3 b)LEVEL-4A c)LEVEL-4B	 5 2 4
3	SEVERE a)LEVEL-5 b)LEVEL-6 c)LEVEL-7	 1 0 0
TOTAL		**17**

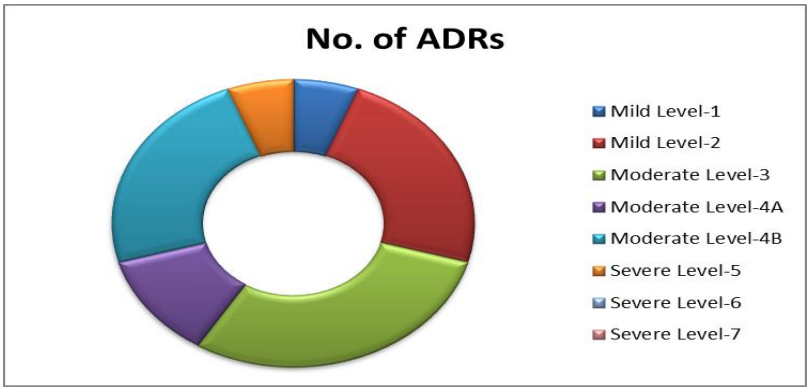

Figure 8: Severity of Adverse drug reaction.

In our study the preventability of the ADR‟s was assessed by using Modified Shumock and Thornton Criteria. The results were revealed that 35% are definitely preventable, 18% are probably preventable and 47% were not preventable**.**

Table 10: Preventability of ADR's.

S.NO	PREVENTABILITY	NO.OF ADR'S	PERCENTAGE
1	DEFINITELY PREVENTABLE	6	35.30%
2	PROBABLY PREVENTABLE	3	17.65%
3	NOT PREVENTABLE	8	47.05%
4	TOTAL	17	100%

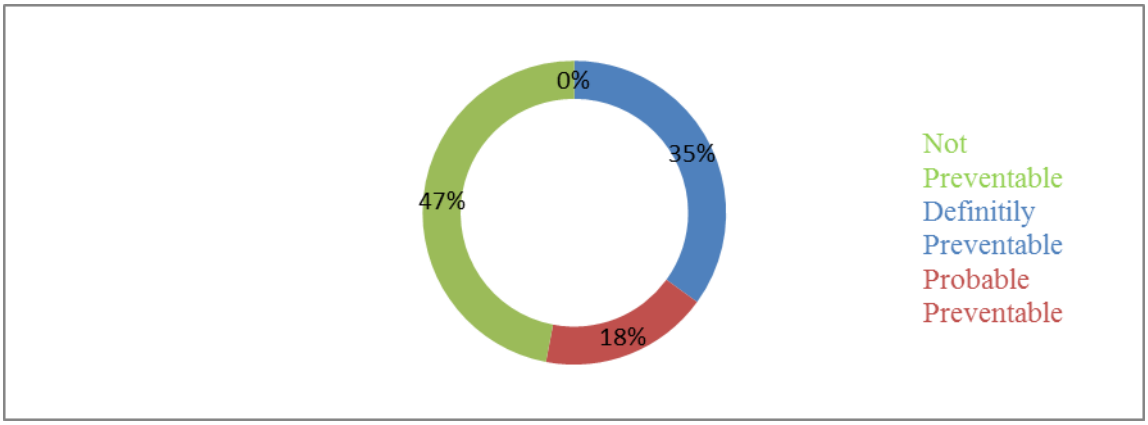

Figure 9: Preventability of ADR'S.

In our study out of 17 patients, in 8 patients suspected drug was discontinued, in 7 patients the drug has been not changed, dose reduction was done in the 2 patients.

Table 11: Fate of Suspected Drug.

S.NO	ACTION TAKEN AGAINS SUSPECTEDDRUG	NO.OF ADRS
1	Drug discontinuation	8
2	Drug replacement	0
3	Drug reduction	2
4	None	7

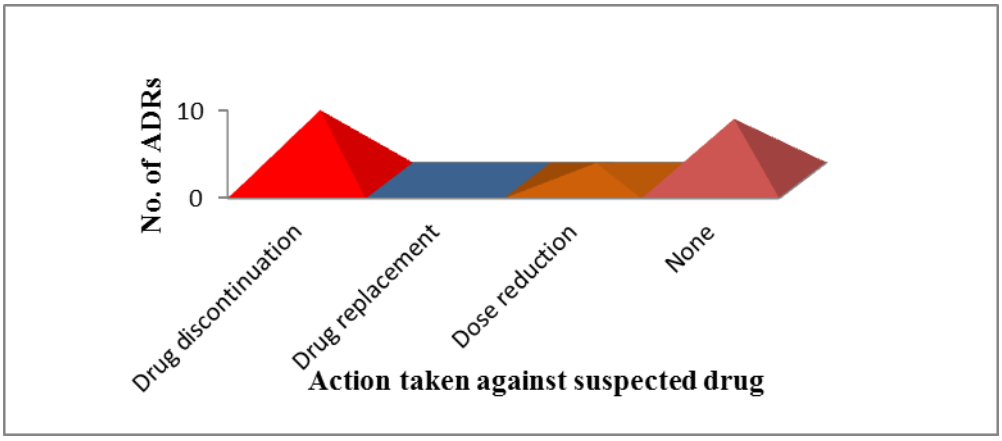

Figure 10: Fate of Suspected Drug

DISCUSSION

In this study we focused on the screening of adverse drug reactions (ADRs) in the dermatology department. During the study period a total of 500 patients were screened in the department of dermatology for adverse drug reactions (ADR). Out of which 17 patients encountered ADR, 6 ADRs are identified during the treatment, 5are ADR related hospital admission and 6 ADRs identified when patient referred from other department. The suspected ADRs were reported to the ADR monitoring center located at Kurnool medical college. In the present study, the incidence of adverse drug reactions in the department of dermatology was 3.5% which was Similar to the other study reported 3.78% by Gohelet al.[9]

In the present study, findings showed that more ADRs were reported in the age group of 51-60 years (n=7) followed by 31-40 year age group (n=3), 41-50 year age group (n=3),21-30 year age group (n=2), 18-20 year age group (n=1) and 61-65 year age group(n=1). The study states that females (64.71%) gender predominance over males (35.29%) in ADRs occurrence which is similar to RuchikaNandha et al[10-12]. This is due to women in comparison to men have lower body weight and organ size, more body fat and different gastric motility and glomerular filtration rate. Due to this difference there is change in pharmacokinetics and pharmacodynamics of drugs in women. In the present study Type-A reactions were 35.30% and Type-B reactions were 64.70%. Most of the reactions were not predictable and were in the Type-B category which was similar to other studies conducted by Bhabhoret al. In the study anti-convulsant (carbamazipine) induced Stevens Johnson syndrome occurred which was similar in the study conducted by the Devi et al.[13]

In this study, corticosteroids and antiretrovirals were implicated for the majority of adverse drug reactions (23.52%). Antiepileptics and antibiotics are the second most therapeutic class of drugs leading to adverse drug reactions (11.76%) which is similar to other studies conducted by Faiyazet al[14] The most common systems associated with ADR in our study were dermatological (64.70%) followed by CNS (11.78%), hematology (5.88%), respiratory system (5.88%), cardiology (5.88%) and nephrology (5.88%). In the study conducted by the Rajesh et al[15] also more dermatological ADRs occurred. On evaluation of severity of ADRs by the modified Hartwig and Siegel severity assessment scale, it was evident that most of ADRs reported in the study were of moderate severity.

In the study preventability is evaluated by the Shumock and Thornton Criteria and it was found to be 47% ADRs were not preventable which was similar to the studies conducted by Padmavathiet al[16] In our study out of 17 patients, in 8 patients suspected drug was discontinued, in 7 patients the drug has been not changed, dose reduction was done in the 2 patients which is not similar to the other studies where there is no change in therapy. In our study predisposing factors responsible for ADRs are age, gender and poly-pharmacy. Patients who are on multiple drugs, on newer drugs or who are at risk of developing reactions are to be kept under close observation. By promoting proper diagnosis, immediate withdrawal of incriminated drug, early referral to a

specialized centre, aggressive management, and good supportive care with fluid and nutritional support, multidisciplinary team work, and control of infection are crucial in minimizing the morbidity and rate of mortality. Knowledge of these drug reactions, the causative drugs and the prognostic indicators is essential for clinicians for diagnosis and prevention of adverse drug reactions.[17]

CONCLUSION

From the results it was concluded that steroids and anti-retrovirals are most common implicated drugs responsible for adverse drug reactions and most effected organ system is skin and a wide clinical spectrum of ADRs ranging from mild maculopapular rash to serious stevens jonson syndrome and toxic epidermal necrolysis were observed. Moreover less ADRs are encountered in the dermatology department which implies that rationalize therapy was following in the RIMS hospital. However in order to prevent ADRs, it is recommended to advise patients to carry a card or an emergency identification of offending drugs in their wallets that list the drug allergies, and intolerances[18-19] By providing the information about same class of offending drug as chances of occurrence of ADRs, such drugs were not to be used in the related groups of affected patient due to cross sensitivity.

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