EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 12
220-226
Year: 2018

A PROSPECTIVE AND OBSERVATIONAL STUDY OF ADVERSE DRUG REACTIONS IN DERMATOLOGY DEPARTMENT OF TERTIARY REFERRAL AND TEACHING HOSPITAL OF MYSORE

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Article Received on 15/10/2018 **Article Revised on 04/11/2018** **Article Accepted on 25/11/2018**

ABSTRACT
Background: To study the cutaneous adverse drug reactions with regards to causality, severity, preventability, predictability. **Materials and Methods:** Study was carried out at Dermatology department in Mysore Medical College & Research Institute; K R Hospital, Mysuru, India, for 1 month (September 2018). A total of 11 patients were enrolled as per inclusion and exclusion criteria. Patient's data were collected by using suspected adverse drug reaction reporting form and causality of ADR's were assessed by using WHO-UMC scale, severity by Modified Hartwig and Siegel Scale, preventability by Modified Schumock and Tornton Scale and preventability scales were used. **Results:** The majority of patients reported with ADR were in the age group of 41-30 years. Fixed drug eruptions were the most commonly seen as ADR. Using WHO UMC scale for causality assessment 45.5% were probable, 54.5% were possible. Moderate reactions accounted for 54.56%, 27.8% severe, and 18.2% for mild reactions. The preventability assessed using the modified Shumock and Thornton method showed 27.3% definitely preventable, 54.5% preventable and 18.2% not preventable. Finally the outcome of the detected reactions requires intervention in 63.3%, 18.2% were hospitalized, 9.1% was recovered. In 9.1% the outcome was unknown. **Conclusion:** The main aim of studying adverse drug reactions is to establish a system of rational use of drugs and the need of more concern from health care professionals towards ADRs and their reporting.

KEYWORDS: WHO (World health Organisation), Adverse drug reaction (ADR), WHO-UMC (WHO- Unfair mean cases).

INTRODUCTION
Drug is a chemical entity intended to use for the diagnosis, prevention, treatment and as prophylaxis of diseases. But it is sometime observed that these drugs can cause some adverse drug reactions. These reactions changes from person -to- person based on their response to the drugs. Even at therapeutic doses, any individual can develop adverse effects.

World Health Organisation (WHO) defines an Adverse Drug Reactions (ADR)"As a response to a drug which is noxious and unintended and which occurs at doses normally used for the prophylaxis, diagnosis, or therapy of diseases or for the modification of the physiological function".[1]

Adverse effects have been classified in many ways. One may classify them into two categories: predictable (Type A or Augmented) reactions and unpredictable (Type B or Bizarre) reactions. Not all ADRs fit into type A and type B categories; therefore, additional categories have been developed which includes type C (continuing), type D (delayed use), and type E (end of use) reactions. Susceptibility to ADRs is influenced by age, gender, disease states, pregnancy, ethnicity and polypharmacy. Drug safety is reliant on nurses and other healthcare professionals being alert to the possibility of ADRs, working with patients to optimise medicine use and exercising vigilance in the reporting of ADRs through the Yellow Card Scheme.

ADR account to 3.4% of hospital admissions and 1.8% mortality in India[2] and 4th leading causes of death in world are by ADR.[3] Pharmacovigilance is the pharmacological science dealing with the detection, assessment, understanding and prevention of adverse effects and promotes safe use of drugs.[4] Central Drugs Standard Control Organisation (CDSCO), New Delhi, under the aegis of Ministry of Health and Family Welfare (MOHFW) has initiated the PvPI in July 2010. Initially National coordinating centre (NCC) was AIIMS, New Delhi but it was shifted to Indian Pharmacopoeia

commission (IPC). Ghaziabad (U.P), in April 2011. The vision of PvPI is to improve patient safety in Indian population by monitoring drug safety and thereby reducing the risk associated with the use of medicines.[5]

For the assessment of causality between drug and suspected ADR, various causality assessment scales been used. Most commonly used causality assessment scales are Naranjo ADR probability scale and WHO-UMC causality categories. A drug reaction was classified as certain, probable/likely, possible, unlikely, conditional/unclassified and Unassessable/unclassifiable according to the "WHO-UMC causality assessment scales". Probability via naranjo scale is assigned by a score termed definite, probable, possible or doubtful.[6]

MATERIALS AND METHODOLOGY

The study was conducted at both outpatient and inpatient dermatology department of KR hospital, Mysuru. This was a prospective observational study were data was collected from both inpatient and outpatient setting. The study was carried out for 1 month (September 2018).

Inclusion criteria

- Both inpatient and outpatients were included
- Patients of all age group and either sex were included
- The ADR filled by the health care professionals was considered.

Exclusion criteria

- The use of alternative system of medicine such as Ayurveda, homeopathy, unani etc. was excluded.
- Patients with drug overdose were excluded.
- Patients who were mentally retarded, drug addicted or consumption of drug in the influence of alcohol was also excluded.

Sources of data

Patient case records, patient or patient caretaker (s) interview, Treatment chart, Communication with prescribers.

Method

Patient enrolment

Patient fulfilling the study criteria were enrolled into the study after obtaining their consent. Patients were enrolled from inpatient as well as outpatient setting.

Data collection

All relevant details of the enrolled patients were obtained from both inpatient and outpatient record. The data's were documented in suspected adverse drug reporting form of CDSCO and was subsequently assessed for causality assessment with WHO-UMC causality assessment scales. For the purpose of assessment of the recorded ADRs various questionnaires were used.

Assessment scales used

- WHO-UMC scale (Causality)
- Modified Hartwig and Siegel Scale (Severity)
- Modified Schumock and Tornton Scale (Preventability)
- Preventability Scale

Scores were given according to the answers given by the patient. For each question there were 3 possible answers, except for preventability there were only 2 answers. The documented findings were subjected to statistical analysis.

RESULTS

Demographic details

Table 1: Incidence of ADR in male and female groups.

Gender	Frequency	Percentage
Male	9	81.8%
Female	2	18.2%

Table 2: Age wise distribution of patients with ADR's.

Age in years	Number	Percentage
41-50	5	45.4%
51-60	4	36.3%
61-70	1	9%
71-80	1	9%

Types of ADR's identified

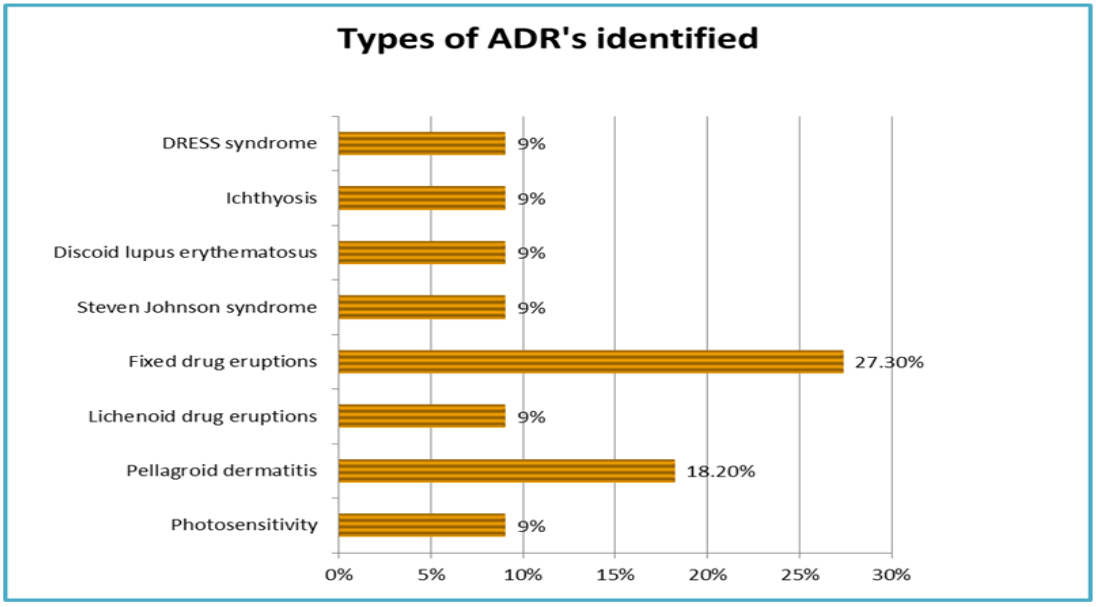

Figure 1: Type of ADR identified.

Causality assessment

Table 3: Causality assessment of ADR's (WHO-UMC Causality assessment scale).

CAUSALITY	FREQUENCY	PERCENTAGE
Certain	0	0
Probable / likely	5	45.5%
Possible	6	54.5%
Unlikely	0	0
Conditional/ unclassified	0	0
Un-assessable/unclassifiable	0	0

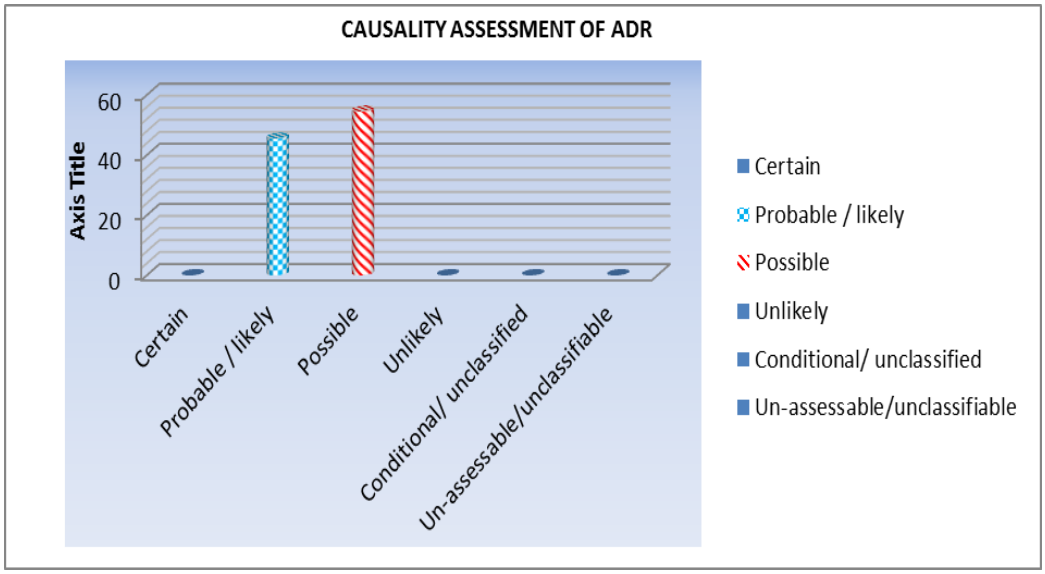

Figure 2: Causality assessment of ADR's.

Severity of ADR

Table 4: Severity of ADR (Using modified Hartwig and Siegel Scale).

SEVERITY	FREQUENCY	PERCENTAGE
MILD	2	18.2%
MODERATE	6	54.5%
SEVERE	3	27.8%

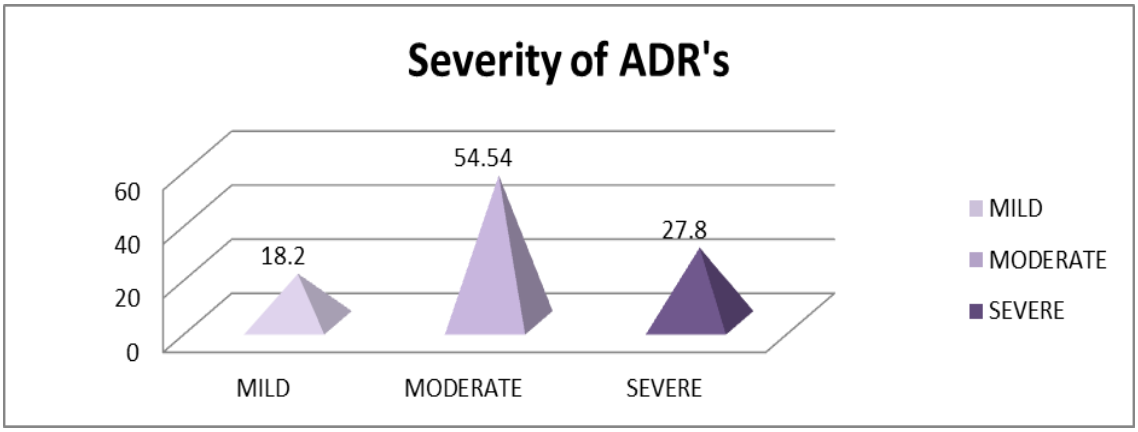

Figure 3: Severity of ADR.

Preventability of ADR's

Table 5: Preventability of ADR's (Using modified Shumock and Thorton method).

PREVENTABILITY	FREQUENCY	PERCENTAGE
DEFINITELY PREVENTABLE	3	27.3%
PROBABLY PREVENTABLE	6	54.5%
NOT PREVENTABLE	2	18.2%

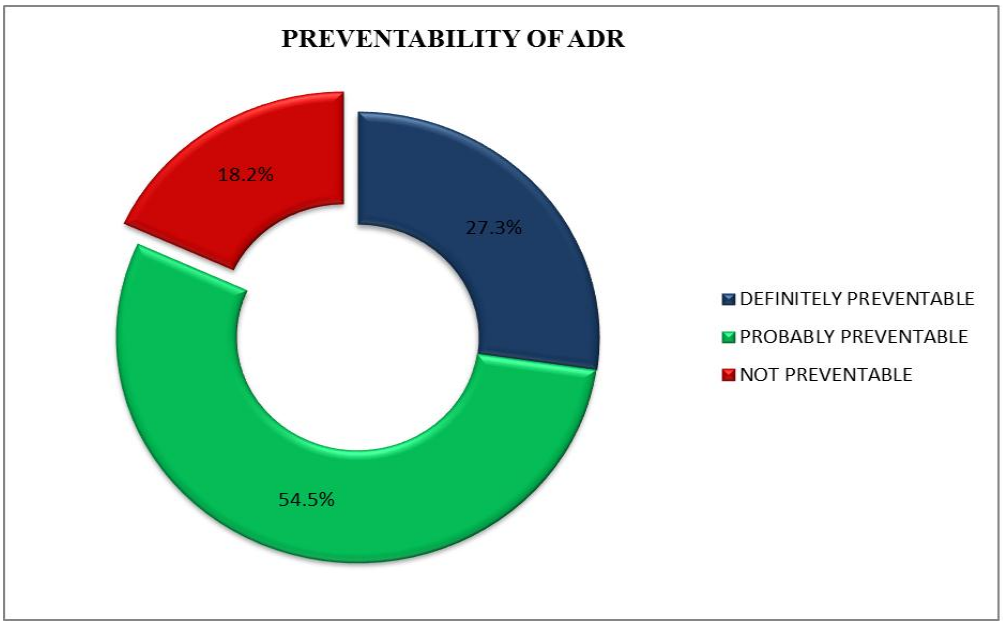

Figure 4: Preventability of ADR's.

Predictability of ADR's

Table 6: Predictability of ADR's.

PREDICTABILITY	FREQUENCY	PERCENTAGE
PREDICTABLE	4	36.4%
NOT PREDICTABLE	7	63.4%

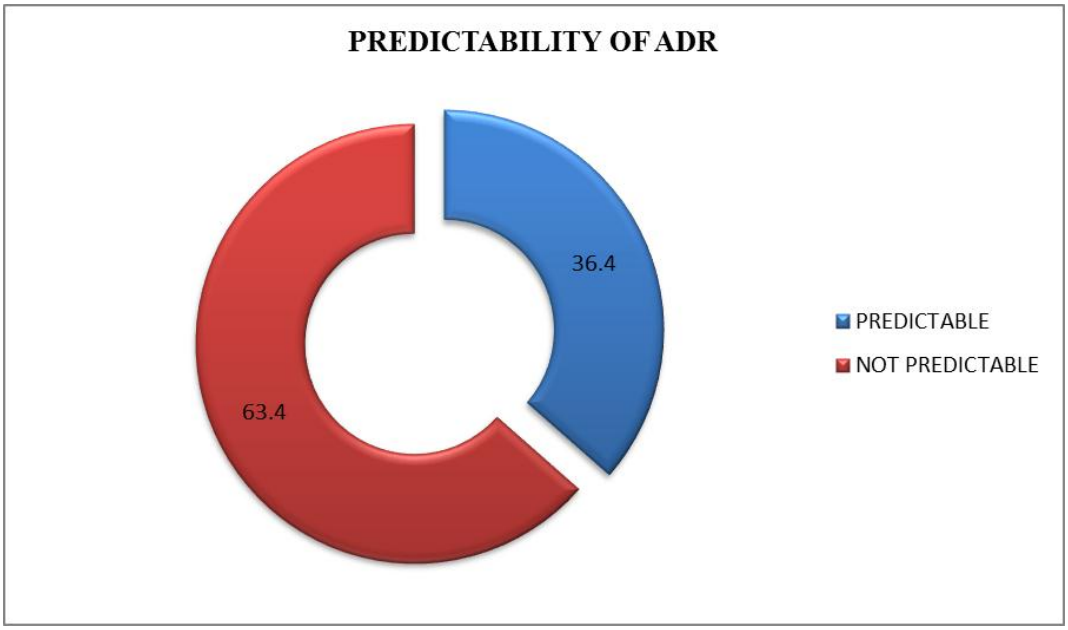

Figure 5: Predictability of ADR's.

Outcome of ADR's

Table 8: Outcome of ADR.

Sl No.	Outcome of ADR	Frequency	Percentage
1.	Recovered	0	0
2.	Recovering	1	9.1%
3.	Hospitalized	2	18.2%
4.	Require Intervention	7	63.6%
5.	Unknown	1	9.1%
6.	Death	0	0

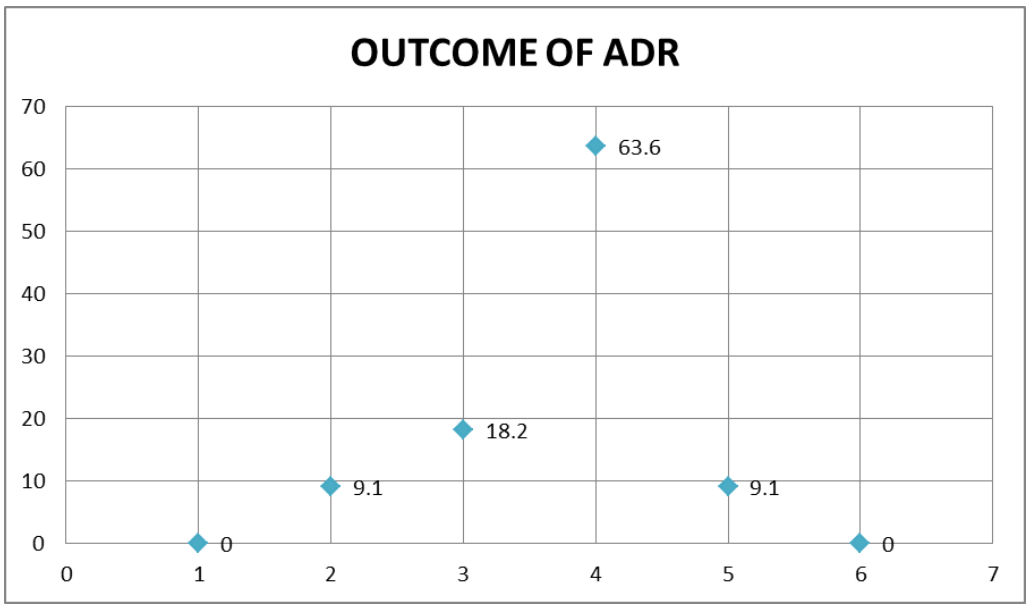

Figure 6: Outcome of ADR's.

Table 1 shows that, out of 11 patients, it was found that the incidence was higher in male patients -81.8%(9 out of 11) than female patient -18.2%(2 out of 11). The table 2 explains, the majority of patients reported with ADR were in the age group of 41-30 (45.4%) and the least number of patients were shared among the age groups of 61-70 (9%) and 71-80(9%); the greater proportion to patients aged between 40's and 50's.

In figure 2, out of those reaction types reported, about 3 patients (n=3) (27.3%) were reported with fixed drug eruptions characterising oval patches of redness and

swelling of the skin ,and a case of surmounted blister were seen. The next majorly reported ADR was pellagroid dermatitis which were found in 2 patients(18.3%) and DRESS syndrome, ichythyosis, discoid lupus erythematosus, stevens Johnson syndrome, photosensitivity were accounted for 9% of the total patients.

The table 3 & figure 2 denotes the assessment of causality by WHO-UMC scale, and shows 5(45.5%) were probable/likely, 6(54.5%) were possible. The table 4 & figure 3 shows the severity of reaction were moderate reactions accounted for 6 (54.45%) patients, followed by severe 3 (27.8%) reactions and mild categorized 2 (18.2%) reactions. The table 5 & figure 4 includes the assessment of preventability by using the modified Shumock and Thornton method showed that 23 (27.3%) definitely preventable, while 6 (54.5%) definitely preventable and 2 (18.2%) not preventable.

The table 4 & figure 3 shows the assessment of predictability; a major share was not predictable (63.4%), only 4 i.e., (36.4%) was found to be not predictable. Finally in table 5& figure 4 shows the outcome of the detected reactions which require intervention in a majority of patients (63.6%), and were hospitalised for (18.2%) of patients due to severe reactions. 1(9.1%) of the patients was recovered. In 9.1% of the reactions, the outcome was unknown. During the study period there were no deaths reported.

DISCUSSION

ADRs significantly diminish quality of life, and thus increase hospitalizations, prolong hospital stay and increase mortality. The recent trends available today are likely to expose more people to ADRs. Although various strategies and systems are being used worldwide, in general, most suffer from problems of under detection and / or underreporting. Therefore the exact incidence of specific ADRs is unknown. Patients receive inadequate and poorly understandable information about ADRs. Reports directly from patients, the individuals who actually suffer the consequences of ADRs, are often not conveyed by health professionals to established monitoring centers or to the regulatory authority. Added to this, is the difficulty in causality analysis of ADRs which often discourages health professionals from reporting.

The present study was carried considering the above issues. The data collected through patient interviews and case report reviews, were well documented, tabulated and statically analysed. This method clearly resulted in the identification of more ADRs. The main objective of my study was to assess the toxicity of various drugs, detect the pattern of ADR reported in dermatology department and finally assess each reaction for the purpose of obvious results, which aids in alleviation or complete diminution of these reactions, and provide an awareness of these reactions among general population.

In this study only 11 individuals were reported to experience ADR from dermatology inpatient and outpatient setting.

- ***Incidence of ADRs***

The incidence of ADRs in dermatology department was found to be higher in male population (81.8%) while comparing female population (64.6%). However, one study identified no difference between men and women in the incidence of ADRs.[7]

- ***Demographic variables***

High incidence of ADRs was observed in patients under the age group of 41-50. (range 40-80) i.e., elderly patients encountered majority of the ADRs. Similar results of incidence in elderly groups were seen in studies carried out by, Jose J et al.[7], and Roughead et al.[8] The reason could be that in elderly patients, the metabolizing capacity and the excretory functions are generally diminished leading to accumulation of drugs in the body and thus increasing the risk of ADRs (Bates and Leape, 2000).[9]

- ***Total number of ADRs***

A total of 11 ADRs were detected in that 8 different types of ADRs were reported.

- ***Pattern of ADRs***

Fixed drug eruptions, was found to be the commonest ADR (27.3%) in the study. Next common ADR was found to be pellagroid dermatitis accounted for 18.2%. The other least common were Photosensitivity reaction, Lichenoid drug eruptions, discoid lupus erythematous, stevens johnson syndrome, DRESS syndrome and icthyosis which were accounted for 9% each.

Patient with pellagroid dermatitis was on Anti-tuberculosis treatment, wasn't supplemented with pyridine (vitamin B6). In a study by Snider DE jr.[10] states the importance of pyridoxine supplementation to prevent development of peripheral neuropathy.

Gohel D et al.[11] and Sowmyanarayan S et al.[12] shows comparable results associated with NSAIDS and fixed drug eruptions(FDE),whereas Santra R et al.[13] shows 20 cases of NSAIDS induced FDE over a period of 6 months in paediatric population.

- ***Assessment of ADR***

The study assessed the causality, severity, preventability and predictability of ADRs. Causality assessment of ADRs was done using WHO-UMC scale. 54.5% ADRs were found to be possible and 45.5% ADRs were probable. This result is comparable to the study of Gohel D et al.[14]

Severity of the assessed reactions showed that 54.5% reactions were moderate; followed by 27.8% of severe and 18.2% of mild. While this result had difference when

comparing Santra R et al.[13], which showed mild to moderate reactions in higher magnitude.

Preventability criteria were assessed using the Shumock and Thornton scale.[14] 54.5% of reactions were probably preventable, while 27.3% were definitely preventable reactions. The remaining 18.2% reactions were not preventable. This result was against the results showed by Santra R et al. were it showed 90% probable preventability.

A high percent (63.4%) of reactions were not predictable, and the remaining 36.4% was predictable. The results were in connection to results of Madagoni et al.[15]

CONCLUSION

From the results revealed from this study it was concluded that reporting of Adverse Drug Reactions from dermatological provides an insight of pattern of occurrence of these reactions and pinpoints the essentiality of awareness for better diagnosis ,drug safety and prevention. The dermatological ADR varied in appearance, duration, causality, severity and preventability. NSAIDS induced fixed drug eruptions and INH induced pellagroid dermatitis were the most reported ADR in this study. After an ADR, the drug was withdrawn and symptomatic treatments were given whenever significant. Re-challenge was not performed in any individual. Most of the ADRs get underreported due to lack of interest and knowledge or unable to identify it as drug induced condition. Pharmacist plays a crucial role in the contribution to patient safety and rational use of drugs by collecting, assessing, monitoring, reporting and treatment of ADRs. So their exist a revampment in health care system for spontaneous reporting of dermatological adverse drug reactions to pharmacovigilance centres directly or via ADR-PvPI application to ensure the safety of drugs.

REFERENCES

1. Geneva: World health organization; 2002. World health organization. Safety of medicine-A guide to detecting and reporting adverse drug reactions-Why health professionals need to take actions. Available at: http:apps.who.int/medicinedocs/en/d/jh2992e/6.html.
2. Charu Bahri (2016); How india tackles adverse drug reactions by ignoring data. *India Spend*, Doi: 08-02-2016.
3. Lazarou J, Pomeranz B, Corey PN(1998); Incidence of adverse drug reactions in hospitalized patient; *JAMA*; 279: 1200-1205.
4. Jeetu G et al; Pharmacovigilance: A worldwide master key for drug safety monitoring; J Young Pharm, 2010; 2(3): 315-320.
5. Subash C (2017); Evolution of pharmacovigilance programme: Present status in india; *Pharma Times*, 49(5): 31-36.
6. Mahesh N et al; A study of agreement between the naranjo algorithm and WHO-UMC criteria for causality assessment of adverse drug reactions*; Indian J Pharmacol*, 2014; 46(1): 117-120.
7. Jose J, Rao PG. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital, Journal of Italian Pharmacological society, *Pharmacol res*, 2006 Sep; 54(3): 226-33.
8. Roughead EE et al. Adverse drug events and medication errors in Australia. *Int J Qual Health Care*, 2003; 15 suppl 1: i49-59.
9. Bates DW, Leape L(2000) Adverse drug reaction, Morreli's clinical pharmacology (4th Edn), McGraw-Hill. New York, USA.
10. Snider DE jr. Pyridoxine supplementation during isoniazid therapy. *Tubercle*, 1980; 61(4): 191-6.
11. Gohel D et al. Evaluation of dermatological adverse drug reactions in the outpatient department of dermatology at a tertiary care hospital. *Indian J Dermatol*, 2014; 3: 42-49.
12. Sowmyanarayan S et al. Adverse drug reactions in the department of dermatol-ogy at a tertiary care hospital: A prospective study. *Int J Basic Clin Pharmacol*, 2017; 7(1): 162-166.
13. Santra R et al. Nonsteroidal anti-inflammatory drug (NSAID) associated fixed drug eruption (FDE) in children attending dermatology OPD of a tertiary care hospital of Eastern india: a cross-sectional observational study. *Int J Basic Clin Pharmacol*, 2018; 3(1): 211-214.
14. Schumock GT, Thorton JP. Focusing on the preventability of adverse drug reactions. *Hosp Pharm*, 1992; 27(6): 538.
15. Madagoni K, Ramu B.A case study on adverse drug reactions(ADR's) monitoring in dermatology patients centre of tertiary care S.V.S.Medical college & Hospital. *Der Pharmacia Sinica*, 2015; 6(5): 22-27.