

An observational study to monitor cutaneous adverse drug reaction profile in Dermatology Department of tertiary care teaching hospital**Janaki R. Torvi, S. G. S. Rajesh Reddy V.***

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ABSTRACT

Background: Incidence of cutaneous adverse drug reactions (CADRs) in developed countries is 1 to 3% and in developing countries, it is much higher i.e. 2 to 6%. 1 in 1000 hospitalized patients will develop severe cutaneous adverse reaction. Maculopapular rash represents majority of cutaneous drug reaction followed by urticaria. Most frequently elicited CADRs are associated with antimicrobials and NSAIDs. This study was designed to monitor Cutaneous adverse drug reaction profile of tertiary care teaching hospital.

Methods: This is a prospective observational study of 6 months' duration to monitor cutaneous adverse drug reactions in dermatology department of tertiary care teaching hospital. CADRs were analysed with respect to demographic details, suspected drugs and type of reaction. Causality assessment is by Naranjo algorithm. Data is represented in tables and graphs. Data is analyzed in Microsoft excel 2007.

Results: Total 57 cases of cutaneous adverse drug reactions were reported. Among them, 57.9% were in males and 42.1% were in females. Majority of CADRs were due to antiretroviral drugs (38.5%) followed by antibacterial (28%) and antiepileptics (14%). Maculopapular rash is most common CADR (35%). Causality of 74% CADRs were probable according to Naranjo algorithm.

Conclusions: CADRs are more commonly associated with antiretroviral therapy (ART), antibacterial drugs and antiepileptic drugs. In case of ART, antiepileptic drug and drugs used in chronic illness compliance plays a major role in the success of therapy. Adverse drug reactions lead to problem of non compliance and failure of therapy. Cutaneous adverse reactions like FDE heal with hyper pigmentation leads to cosmetic problem. Stevens Johnson syndrome (SJS) is life threatening that requires prompt withdrawal of drug and intensive medical management. Many drugs are available without prescription in India leading to problem of misdiagnosis of CADRs. So, data obtained from this study helps in proper diagnosis and treatment of CADRs.

Keywords: CADR, Cutaneous adverse drug reaction, Maculopapular, SJS

INTRODUCTION

Incidence of cutaneous adverse drug reactions (CADRs) in developed countries is 1 to 3%.¹ In developing countries it is much higher 2 to 6%. 1 in 1000 hospitalized patients will develop severe cutaneous adverse reaction. A study found drug induced adverse skin reactions to be 2.6% at dermatology outpatient setting.² Different forms of skin reaction are 1) morbiliform 2) fixed drug eruptions 3)

phototoxic 4) urticaria 5) exfoliative dermatitis 6) Stevens Johnson syndrome (SJS) 7) Toxic epidermal necrolysis.

Maculopapular rash represents majority of cutaneous drug reaction (95%) followed by urticaria.³ In a study by Thappa et al most common eruptions were fixed drug eruptions (31.1%). Although virtually any drug is capable of eliciting an adverse reaction. Most frequently elicited are antimicrobials and NSAIDs.⁴

The relative risk of Stevens Johnson syndrome and toxic epidermal necrolysis perhaps most important severe cutaneous reactions has been quantified in an international case control study and case series sulfonamide antibiotics, amine antiepileptic (phenytoin and carbamazepine), lamotrigine, oxicam NSAIDs are associated with highest risk.⁵ This study was designed to monitor Cutaneous adverse drug reaction profile of tertiary care teaching hospital.

The objectives of current research work are to study patient characteristics presenting with ADR and to study common drugs implicated in CADR. Also, to study different types of cutaneous adverse drug reactions.

METHODS

A prospective observational study. All outpatients and inpatients of Dermatology Department KIMS, Hubli. This study was conducted from August 2015 To January 2016 (6months). This study was conducted at KIMS Hospital, Hubli, Karnataka, India.

Method of collection of data

After obtaining approval and clearance from Institution Ethics Committee, 57 cutaneous ADRs reported from dermatology department KIMS, Hubli over a period of 6 months were included in study. Written and informed consent was obtained from all study subjects. To collect data ADR reporting forms were distributed in Dermatology department and requested them to report suspected ADRs to department of pharmacology. We also actively monitored ADRs by attending Dermatology OPD and inpatient rounds along with dermatologists twice in a week. The demographic data of patients reporting CADR and brief description of event, suspected drug(s) were collected during the study period.

The pattern of cutaneous CADR reported were analyzed. The causality of reactions was analyzed by Naranjo causality scale. Severity of CADR was assessed using modified Hatwig and Siegel scale. Confidentiality of patients was maintained throughout and after study.

Statistical analysis

Data was analyzed using frequency and percentages. Data was described in the form of tables and graphs. Data was entered in Microsoft excel 2007.

RESULTS

A total of 57 CADR were reported over 6 months. Of these, 57.9% were in males and 42.1% were in females (Figure 1).

Maximum number of CADR reported in young adults of age group 18-39 yrs (40%) followed by people with age

groups 40-59yrs (29.8%), 59yrs (17.5%) and <18yrs (12.2%) (Table 1).

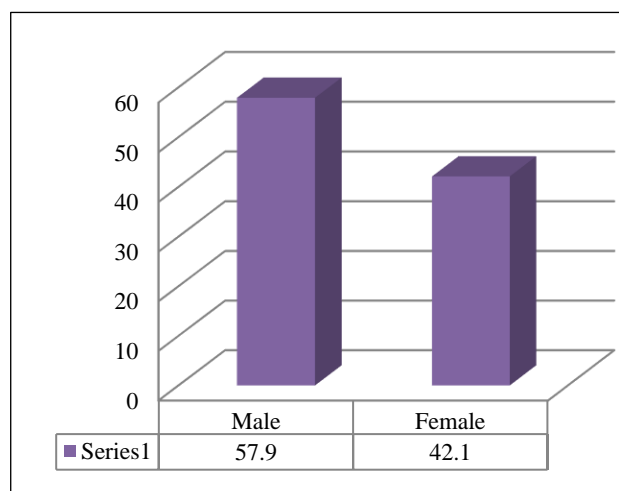


Figure 1: Sex wise distribution of CADR.

Table 1: Age wise distribution of CADR.

AGE	No of CADR	Percentage
<18yrs	07	12.2
18-39yrs	23	40
40-59yrs	17	29.8
>59yrs	10	17.5

Among the suspected drugs causing ADRs, antiretroviral agents accounted for 38.5% of the total CADR followed by antibacterial drugs (28%), antiepileptics (14%), NSAIDs (5.2%), anticancer drugs (5.2%), antihypertensives (3.5%), local anesthetics (1.7%), antidiabetic (1.7%) and antipsychotic drugs (Table 2).

Table 2: CADR in various drug classes.

Drugs	No of CADR (57)	Percentage
Antiretroviral	22	38.5
Antibacterial	16	28
Antiepileptic	08	14
NSAIDS	03	5.2
Anticancer	03	5.2
Antihypertensive	02	3.5
Local anesthetic	01	1.7
Antidiabetic	01	1.7
Antipsychotic	01	1.7

Among CADR maculopapular rash (35%) is most common followed by Fixed drug eruptions (14%), urticaria (10%), exfoliative rash (9%), erythematous plaques (9%), Stevens Johnson Syndrome (7%), type 2 lepra reaction (7%), alopecia (5%), erythema multiforme (1%) and lichenoid drug eruption (1%) (Figure 2).

Assessment of ADRs using Naranjo's causality assessment scale showed that 74% of CADR were

probable, 26% were classified as possible and none of CADR were definite and doubtful (Table 3).

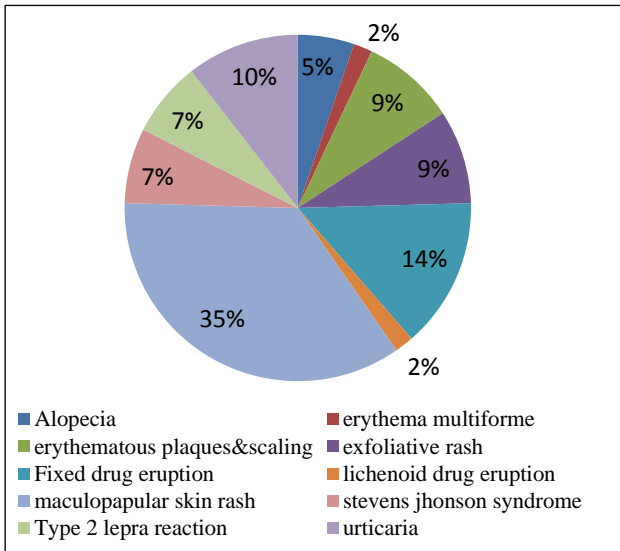


Figure 2: Types of CADR.

Table 3: Causality assessment using Naranjo algorithm.

Causality	No of CADR	Percentage
Definite	00	00
Probable	42	74
Possible	15	26
Doubtful	00	00

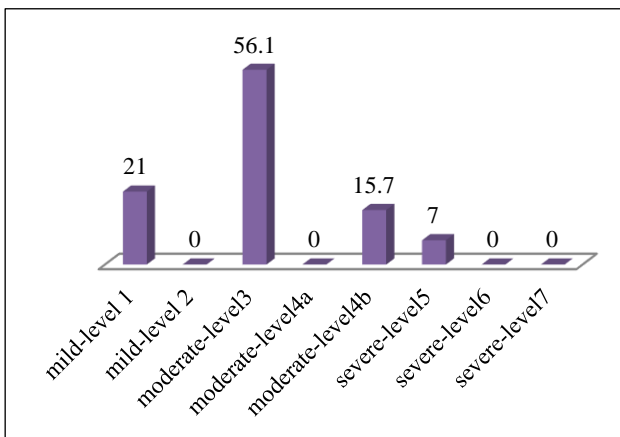


Figure 3: Severity of CADR assessed by modified Hatwig and Siegel scale.

According to modified Hatwig and Siegel scale 21% of ADRs were mild level 1. These ADRs are self-limiting and don't require drug discontinuation. But these ADRs should also be followed up for increase in severity. 56.1% of ADRs were moderate level 3 these ADRs require medical treatment and need change or withdrawal of drug. 15.7% of ADRs were moderate level 4b these were reasons for hospital admission. 7% of ADRs were severe level 5 requiring intensive medical treatment.

DISCUSSION

In our study 57 Cases of CADR were reported. Out of which 33 (57.9%) were males and 24 (42.1%) were females. So, percentage of CADR in males was higher than in females.

Our study result was similar to studies done at Chandigarh where male predominance was seen.^{6,7} This result differs from studies done in South India which reports almost equal incidence (0.87:1).⁸ As all these studies were institution based, this difference in demographic profile can be accounted by the difference in the demography of the patients attending the clinic.

In our study ADRs most commonly occurred with antiretroviral drugs (38.5%), antibacterial drugs (28%) and antiepileptic drugs (14%). In our study most common skin reaction was maculopapular rash (35%) followed by fixed drug eruption (14%) and urticaria (10%).

One case of erythema multiforme is seen with phenytoin. One case of lichenoid drug eruption is seen with carbamazepine. Cases of fixed drug eruptions with doxycycline, ciprofloxacin and diclofenac. Stevens Johnson Syndrome seen with HAART in our study.

A study conducted in Manipal reported that antimicrobials (30%) were most commonly implicated in CADR.⁹ Another study reported that maculopapular rash (50%) and urticaria (21.5%) were most common CADR.¹⁰ Another study in inpatients also reported that maculopapular rash is most common CADR in hospitalized patients and antimicrobials were most common drugs.¹¹

CONCLUSION

CADR are more commonly associated with antiretroviral therapy (ART), antibacterial drugs and antiepileptic drugs. In case of ART, antiepileptic drug and drugs used in chronic illness compliance plays a major role in success of therapy. Adverse drug reactions lead to problem of non compliance and failure of therapy. Cutaneous adverse reactions like FDE heal with hyper pigmentation leads to cosmetic problem. Stevens Johnson syndrome (SJS) is life threatening requires prompt withdrawal of drug and intensive medical management. Many drugs are available without prescription in India leading to problem of misdiagnosis of CADR. So, data obtained from this study helps in proper diagnosis and treatment of CADR.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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