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EVALUATION OF DERMATOLOGICAL ADVERSE DRUG REACTIONS IN THE OUTPATIENT DEPARTMENT OF DERMATOLOGY AT A TERTIARY CARE HOSPITAL – AN OBSERVATIONAL STUDY

Pharma

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ABSTRACT

Background: Drugs, no matter how safe and efficacious, come together with the risk of adverse reactions. Of all organs affected by drug reactions, the skin is most frequently involved. **Aim and Objectives:** To evaluate the dermatological adverse drug reactions in patients attending the Dermatology outpatient department of a tertiary care hospital. **Materials and Methods:** An observational, cross-sectional study was conducted to evaluate the adverse drug reactions in the Outpatient Department of Dermatology in an Tertiary Care Hospital for a period of 1.5 years. The causality of ADRs was evaluated using WHO-UMC Scale, Naranjo's scale, severity was assessed using Modified Hartwig and Siegel's scale, Preventability was assessed using Schumock and Thorton's criteria. **Result:** Total 78 drugs were suspected of 67 ADRs. Most common ADR encountered was Maculopapular rash and most common drug causing ADR was found to be antimicrobials. Causality assessment using Naranjo's scale revealed that 59.70% cases were probable, 34.33% cases were possible, 5.97% cases were definite. Causality assessment using WHO-UMC scale revealed that out of total 67 ADR, majority of cases 40 (59.70%) were probable. 19 (28.36%) cases were possible. 8 (11.94%) cases were certain. On preventability assessment 79.1% ADRs were definitely preventable, 20.9 ADRs were probably preventable. Severity assessment concluded that 67.16% were mild, 29.85% moderate, 2.99 % were severe. **Conclusion:** Proper implementation of ADR monitoring will help to reduce the harmful effects resulting from the use of medicinal products by early detection of drug safety problems in patients.

KEYWORDS

Dermatological adverse drug reactions, Naranjo's scale, Modified Hartwig and Siegel's scale, Schumock and Thorton's criteria.

INTRODUCTION

Adverse Drug Reactions (ADRs) are considered as one among the leading causes of morbidity and mortality (1). WHO defines adverse drug reaction as "a response to a drug that is noxious and unintended and occurs at doses, used in man for prophylaxis, diagnosis, or therapy of a disease or for modification of physiological function."(2).They result in diminished quality of life, increased physician visits, hospitalizations, and even death. In most cases, the presentation is benign to begin with and hence early identification of the reaction and the culprit drug could be the keystone in management and prevention of all kinds of drug reaction (3). Dermatological ADRs still remains a neglected domain from patients and medical professionals' point of view. Only severe or life threatening dermatological ADRs which require admission in indoor facility were reported to surveillance authorities. We have come across very few studies regarding dermatological adverse drug reactions available in developing countries like India. Hence, medical professionals in our country may not get the access to extensive dermatological ADRs database which could have helped them to avoid these ADRs. The incidence of dermatological ADRs among in-patients in developed countries ranges from 1–3% whereas in developing countries such as India it is 2–5 %.(4) Few studies have been conducted which can give us a comprehensive database of ADRs occurring in the outpatient departments. Hence, this study is aimed at evaluating dermatological adverse drug reactions in patients attending the Dermatology outpatient department of a tertiary care hospital.

MATERIALS AND METHODS

The study is a observational, non-interventional, cross-sectional study to evaluate the dermatological adverse drug reactions in the Outpatient Department of Dermatology in an urban Tertiary Care Hospital. The study was conducted in the Department of Pharmacology in collaboration with the Outpatient Department of Dermatology in a Tertiary Care Hospital after taking permission from Institutional Ethics Committee (IEC) and enrolling 67 patients fulfilling selection criteria.

The study was conducted for a period of one and half years.

Inclusion Criteria

1. Patients of all age groups with either gender presenting with dermatological adverse drug reactions confirmed by the dermatologists, attending the dermatology outpatient department.
2. Patients presenting with adverse drug reactions including old and new patients.

Exclusion Criteria

1. Pregnant and lactating mothers.
2. Patients who are not willing to participate in the study.

MUHS, Dean, Institutional Ethics Committee and Institutional Review Board permission was taken before starting the study. Patient participation was voluntary and the participants were explained that they had the right to withdraw from this study, at any time, without giving any reason what so ever, with a guarantee that should this be the case then their disease management and treatment services from the department of Dermatology would not be affected and compromised. Number of drugs prescribed per prescription, use of generic and brand names, drug dose and dosage forms, frequency, duration of treatment were recorded along with the suspected adverse drug reaction, the date when the reaction started and date of recovery.

Total no. patients with ADRs and number of ADRs were calculated. The gender wise and age group wise distribution of the adverse drug reactions were noted in the study population.

Class of drugs causing ADRs and nature of ADRs were analyzed. Causality of ADR was assessed using WHO-UMC Scale, Naranjo's scale. Severity of ADR was assessed using Hartwig and Siegel's scale. Preventability of ADR was assessed using Schumock and Thorton's criteria.

RESULT

Total 78 drugs including single drug therapy (SDT) as well as fixed dose combination (FDC) led to total 67 ADRS. Of these the most common drug class showing highest numbers of ADR was antimicrobial drugs 34 (50.74%), followed by NSAIDs 18 (26.86%). Among antimicrobial drugs, maximum number of ADR were observed with combination of Amoxicillin + clavulanic acid i.e., 10 (14.92%) followed by combination of Rifampicin + Isoniazid i.e., 9 (13.43%). ADRs caused by anticonvulsant drugs were 11 (16.42%) where as those caused by retinoids were 2 (2.99%). ADRs caused by xanthine oxidase inhibitors were 2 (2.99%). The youngest patient in which ADR

was encountered was 11 years and the oldest was 68 years. Majority of the patients, 21 (31.34%) were in the age group of 21 to 30 years followed by 12 (17.91%) in age group of 31 to 40 years. The relative occurrence of ADR in different age groups was, 11-20 years – 14.93%, 21-30 years – 31.43%, 31-40 years – 17.91%, 41-50 years – 11.94%, 51-60 years – 13.43%, 61-70 years – 10.45%. Out of the total 67 patients enrolled, the occurrence of ADR was higher in males i.e., 38 (57%) than in females 29 (43%). The approximate ratio of Male: Female was 1.3:1. Of 30 participants who had social habit of either drinking alcohol or smoking, 10 (33.33%) participants were smokers and 13 (43.33%) participants had a habit of drinking alcohol. 7 (23.33%) participants were both smokers and alcohol drinkers.

The most commonly reported dermatological ADR was Maculopapular rash 20 (29.85%) followed by fixed drug eruption 15 (22.39%). Other reported ADRs were pruritus 4 (5.97%), urticaria 9 (13.43%), erythema multiforme 6 (8.96%), angioedema 4 (5.97%), acneiform eruptions 5 (7.46%), cheilitis. 2 (2.99%), Steven–Johnson syndrome 2 (2.99 %). Among all the single formulations that were prescribed paracetamol 8 (15.09%) was the most commonly prescribed single drug therapy followed by diclofenac 7 (13.21%) and carbamazepine 7 (13.21%). Isotretinoin 2 (3.77%) and Allopurinol 2 (3.77%) were the least commonly prescribed single drug therapy. When it came to fixed dose combinations, the combination of rifampicin plus isoniazid was used in the highest number of cases i.e., 15 (60%). It was followed by amoxicillin plus clavulanic acid combination in 10 (40%) cases.

Out of 78 drugs, 65 (83.33%) were administered via oral route and 13 (16.67%) were prescribed via parenteral route. 48 (61.54%) drugs were prescribed using generic names and 30 (38.46%) were prescribed using brand names. More cases of ADR were reported from other Departments 45 (67.16%), as compared to Outpatient Department of Dermatology 22 (32.84%). 29(43.28%) ADRs occurred in less than 24 hours of drug administration, 22 (32.84%) developed between the duration of 24 hours to 1 week of drug administration whereas16 (23.88%) ADRs developed after 1 week of drug administration. Most common indication for prescription of suspected drug was tuberculosis 18 (23.08%) followed by epilepsy 12 (15.38%). Other indications were Acne 2 (2.56%), body ache 8 (10.26%), dysmenorrhea 4 (5.13%), fever 6 (7.69%), gout 2 (2.56%), HIV 5 (6.41%), migraine 3 (3.85%), respiratory tract infection 7 (8.97%), urinary tract infection 7 (8.97%), vaginal candidiasis 4 (5.13%).

Out of total 67 drugs, 35 (44.87%) drugs were replaced, 25 (32.05%) drugs were discontinued and 18 (23.08%) drugs were continued with co-administration of drug(s) for treatment of ADR.

According to Causality assessment done using Naranjo's scale majority of cases 40 (59.70%) were probable, 23 (34.33%) cases were possible and 4 (5.97%) cases were definite. When Causality assessment was done using WHO-UMC scale 40 (59.70%) were probable/likely,19 (28.36%) cases were possible and 8 (11.94%) cases were certain. Assessment of Preventability was done using Schumock and Thornton Scale. Out of total 67 ADRs, 53 (79.1%) were definitely preventable and 14 (20.9%) ADRs were probably preventable. Severity assessment was done using Modified Hartwig and Siegel scale. Out of 67 total ADR, 45 (67.16%) were mild. 20 (29.85%) ADRs were moderate and 2 (2.99%) ADRs were severe.

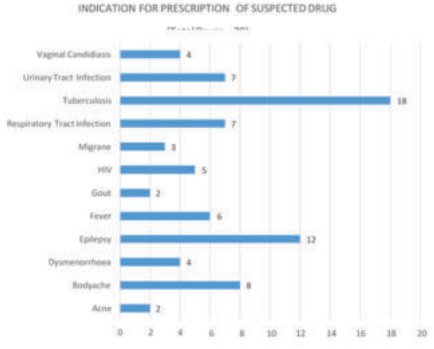

Figure No. 1: - Indications For Prescription Of Suspected Drug (Total Drugs = 78)

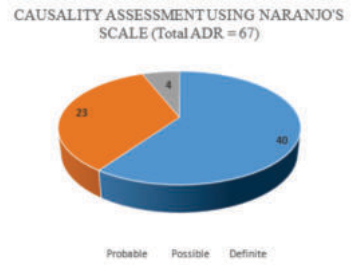

Figure No. 2: - Assessment Of Causality (Total ADR = 67)

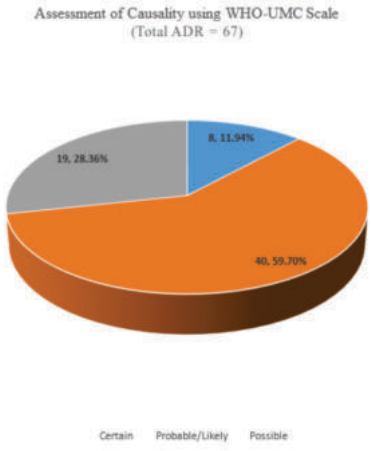

Figure No. 3: - Assessment Of Causality Using Who-umc Scale (Total ADR= 67)

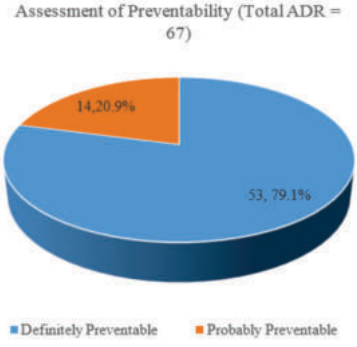

Figure No. 4: - Assessment Of Preventability (Total ADR = 67)

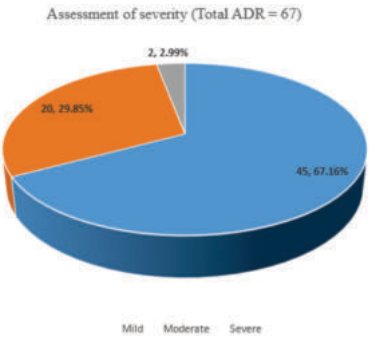

Figure No. 5: - Assessment Of Severity (Total ADR = 67)

Table No. 1: - Adrs Caused By Various Classes Of Drugs In Study Population (Total ADR=67)

Class of drug	Sr. No.	Name of individual drug	ATC CODE	No. of ADR	Total ADR	Percentage (%)
Anti-microbials	1.	AKT (Rifampicin + Isoniazid)	J04AM02	9	34	50.74
	2.	AKT (Kanamycin)	J01GB04	3		

	3.	Nevirapine	05AG01	5		
	4.	Amoxicillin + Clavulanic acid	01CR02	10		
	5.	Norfloxacin	J01MA06	4		
	6.	Fluconazole	J02AC01	3		
NSAIDs	1.	Paracetamol	N02BE01	7	18	26.86
	2.	Diclofenac	M01AB05	6		
	3.	Nimesulide	M01AX17	5		
Anti-convulsant Drugs	1.	Carbamazepine	N03AF01	6	11	16.42
	2.	Phenytoin	N03AB02	5		
Retinoids	1.	Isotretinoin	D10AD04	2	2	2.99
Xanthine oxidase inhibitor	1.	Allopurinol	M04AA01	2	2	2.99
TOTAL					67	100

Table No. 2: - Nature Of Adr In Study Population (Total ADR = 67)

Nature of ADR	Frequency	Percentage (%)
Maculopapular Rash	20	29.85
Fixed Drug Eruption	15	22.39
Acneiform Eruption	5	7.46
Pruritus	4	5.97
Cheilitis	2	2.99
Steven Johnson Syndrome	2	2.99
Erythema Multiforme	6	8.96
Urticaria	9	13.43
Angioedema	4	5.97
TOTAL	67	100

Table No. 3: - Measures Taken Against Suspected Drug (Total Drugs = 78)

Measures taken against suspected drug	Number	Percentage (%)
Drug replacement	35	44.87
Drug discontinuation	25	32.05
Continuation of the drug with simultaneous treatment for ADR	18	23.08
TOTAL	78	100

DISCUSSION

Adverse drug reaction (ADR) is defined as "an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product." (5)

Of all organs affected by drug reactions, the skin is most frequently involved.

Adverse Drug Reactions may result in decrease in quality of life, increased visits to physician, admission in hospitals, and even death. The incidence of dermatological ADRs among in-patient in developed countries ranges from 1–3% whereas in developing countries such as India it is 2–5 %. The incidence of drug-induced adverse skin reactions is found to be 2–15% at a dermatology outpatient setting. (6)

In India, Central drugs standard control organization (CDSCO) has mandated all medical institutions to report ADRs originating from their hospitals. (7)

In this study titled "Evaluation of Dermatological Adverse Drug Reactions in The Outpatient Department of Dermatology at A Tertiary Care Hospital – An Observational Study", an attempt has been made to survey different dermatological adverse drug reactions.

In our study, patients of all age groups with either gender presenting with dermatological adverse drug reactions confirmed by the dermatologists, attending the dermatology outpatient department were included, the youngest patient was 11 years and the oldest patients was 68 years. Majority of the cases, 21 (31.34%) were in the age group of 21 to 30 years followed by 12 (17.91%) in age group of 31 to 40 years.

This finding is in accordance with study conducted by Sharma et al., (8) in which maximum number of cases were in the age group of 21–30 years (30.6%) followed by 31–40 years (26%).

In the present study, out of the total 67 patients enrolled, the occurrence of ADR was higher in males i.e., 38 (57%) than in females 29 (43%). The approximate ratio of Male: Female was 1.3:1.

Similar results were observed in a study conducted by Gohel et al., (9) in which 54.90% cases were males and 45.09% were female with male: female ratio of 1.21:1.

In a study conducted by Mittal et al., (10) male comprised of 68% of the population and female comprised of 32% of the population.

This finding is in contrast with the study conducted by Bhanushali et al., (11) in which females comprised of 54% cases and male comprised of 46% cases.

In our study, the drug class showing highest numbers of ADR was antimicrobial drugs 34 (50.74%), followed by 18 (26.86%) of NSAIDs.

ADRs caused by anticonvulsant drugs were 11 (16.42%), by retinoids were 2 (2.99%) and by xanthine oxidase inhibitors were 2 (2.99%).

This is in conformity with the study conducted by Sharma et al., (13) in which antimicrobials were responsible for 40% ADR followed by NSAIDs 35.3% ADR.

In another study conducted by Rajendran et al., (12) in which antimicrobials (30.1%) were noted to be the most common offending drugs, followed by antiepileptics (18.1%), analgesics and antipyretics (11.1%).

In this study, 22 (32.84%) ADRs were reported from the outpatient department of Dermatology and 45 (67.16%) ADRs were reported from other departments.

Similar finding was observed in the study conducted by Sharma et al., (13), in which 25.81% cases of ADR were reported from outpatient department of Dermatology and 74.19% cases were referred from other departments.

Out of total 67 ADRs, most commonly reported dermatological ADR was Maculopapular rash 20 (29.85%) followed by fixed drug eruption 15 (22.39%).

Out of total 67 ADRs the frequency of occurrence of pruritus was 4 (5.97%), urticaria 9 (13.43%), erythema multiforme was 6 (8.96%), angioedema was 4 (5.97%), acneiform eruptions were 5 (7.46%), cheilitis was 2 (2.99%), Steven–Johnson syndrome was 2 (2.99%).

This is in accordance with the study conducted by Shubham et al., (14) in which maculopapular rashes was the most common ADR reported in 38.97% cases, urticaria was reported in 19.12% cases, fixed drug eruptions were reported in 15.44%, acneiform eruptions were reported in 10.29% cases, erythema multiforme was reported in 5.88% cases, Stevens-Johnson syndrome-toxic epidermal necrolysis was reported in 4.41% cases.

In contrast to finding of our study, in a study conducted by Parvin et al., (15) it was found that Stevens-Johnson syndrome was the most commonly observed ADR in 22.2% cases, followed by rashes in 16.7% cases.

Out of total 78 drugs, 35 (44.87%) drugs were replaced, 25 (32.05%) drugs were discontinued and 18 (23.08%) drugs were continued with co-administration of drug(s) for treatment of ADR.

In a study conducted by Sharma et al., (13) 1.61% drugs were continued with the same dose, 0.8% drugs were continued at reduced dose, 37.9% drugs were discontinued with no treatment required and 59.68% drugs were discontinued and treatment was given.

In our study, out of total 67 ADR, majority of cases 40 (59.70%) were probable, 23 (34.33%) cases were possible, 4 (5.97%) cases were definite. This is in accordance with the study conducted by Gohel et al., (9) 74.23% cases were probable, 21.65% cases were possible and 4.12% cases were definite. In another study conducted by Shubham et al.,(14) 79.41% cases were probable, 16.18% cases were possible and 4.41% cases were definite.

Causality assessment using WHO-UMC scale revealed that 40

(59.70%) ADRs were probable, 19 (28.36%) were possible and 8 (11.94%) were certain.

This finding is in accordance with the study conducted by Anjaneyan et al. (16),in which 70% ADRs were probable, 21% were possible and 9% were certain.

Assessment of Preventability was done using Modified Schumock and Thornton Scale.

Out of total 67 ADRs, 53 (79.1%) were definitely preventable, 14 (20.9%) ADRs were probably preventable.

This finding is in accordance with the finding in a study conducted by Sharma et al.,(8) 91.1% cases were definitely preventable and 8.87% cases were probably preventable.

In a study conducted by Gohel et al.,(9) maximum cases 72.16% were probably preventable and 27.84% cases were definitely preventable.

Severity assessment was done using Modified Hartwig and Siegel scale, out of 67 total ADR, 45 (67.16%) were mild, 20 (29.85%) were moderate, 2 (2.99%) were severe.

This is in accordance with the study conducted by Kumar et al., (7) in which 72.3% cases were mild, 15% cases were moderate and 2.6% cases were severe.

Limitations Of The Study

1. This research was limited by the size and site of the study population as this was a single centric study, so the results obtained may not be reflective of the entire community. A larger sample size and that too, from different sites and locations, can give a better and more reliable outcome.
2. Since the study was conducted in an urban tertiary care hospital, the data collected represents the ADR pattern in an urban area which cannot reflect ADR in the rural areas.
3. Rechallenge was not tried because of ethical issues.

Acknowledgment

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CONCLUSION

From this study we can conclude that, use of 78 drugs led to 89 ADRs. Majority of the patients (31.34%) were in the age group of 21 to 30 years. Occurrence of ADR was higher in males than in females. Most common ADR observed was maculopapular rash (29.85%). Most common class of drug responsible for ADR (50.74%) was antimicrobial drugs. Majority of ADRs occurred within 24 hours of drug administration. In majority of the cases (44.87%), suspected drug was replaced. Causality assessment using Naranjo's scale revealed majority of cases (59.70%) to be probable. Causality assessment using WHO-UMC scale revealed that majority ADRs (59.70%) were probable. Assessment of Preventability using Schumock and Thornton Scale, revealed maximum cases (79.1%) to be definitely preventable. Severity assessment using Modified Hartwig and Siegel scale revealed that majority of the cases (67.16%) were mild.

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