

Research Article

A Prospective Study of Adverse Drug Reactions at a Private Tertiary Care Teaching Hospital.

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ABSTRACT

Adverse drug reactions (ADRs) are responsible for approximately 5% of hospital admissions and they are potentially avoidable causes for seeking medical care. Most of the ADR are not reported. Hence this study was undertaken to emphasize the need to report ADRs. The study was carried out at Dr. B.R. Ambedkar Medical College and Hospital from July 2014 to July 2015. 40 cases were reported. Informed consent was obtained from each patient and thorough clinical examination was done. All the information was carefully recorded in a pre-designed proforma as per PVPI (Pharmacovigilance Programme Of India). To establish the etiologic agent for a particular type of reaction, attention was given to drug history, temporal correlation with the drug, duration of reaction, associated signs and symptoms, improvement of condition or lesion after withdrawal. Naranjo's Algorithm was used to determine the causality of ADRs.

In the present study, most common age group reported with ADRs was between 25-40 years, with female predominance 26(65%). Type B ADRs 36(90%) were more common than Type A. The most commonly observed ADRs were with NSAIDS 27(67.5%) followed by anti-microbial 9(22.5%) and anti-convulsants 4(10%). The most commonly observed reaction was Fixed drug eruption (FDE) 18(56.25%), followed by impairment of LFT (Liver Function Test) 2(0.8%). Study reveals that most of the reactions were cutaneous in nature. Systemic reactions were under reported. Causality assessment did not reveal strong association because of polypharmacy. So, ADRs are potentially avoidable causes for seeking medical care. ADRs can be prevented by avoiding polypharmacy, knowing previous history of ADR and reporting it for further concern and care of patients.

KEYWORDS

Adverse drug reactions (ADRs), Tertiary care.

1. INTRODUCTION

WHO defines an adverse drug reaction (ADR) as “Any 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 functions”¹.

A meta-analysis of 39 epidemiological studies by Lazarou et al., found that ADRs ranked fourth and sixth leading causes of deaths in USA². Pharmacovigilance programme of India (PvPI) was started in 2010 to emphasize the need for monitoring ADRs which will improve public health³. ADRs are responsible for approximately 5% of hospital admissions. Skin and mucosa is the commonest sites for initial presentation of many ADRs. Cutaneous ADRs contribute to 2-3% of hospitalised patients⁴. The use of herbal supplements has increased dramatically in recent years⁵. There are various predisposing factors for the occurrence of an ADR like extremes of age like in neonates and elderly, the liver and kidney enzymes necessary for drug metabolism and elimination are not optimally functional. Women are expected to have a higher incidence of ADRs than men. Patients with past history of ADRs are more likely to develop an ADR. Genetic factors also play a role for pre-disposition to ADR, examples are drug hypersensitivity syndrome to specific human leukocyte antigen (HLA) antigen-abacavir (HLA B*5701), allopurinol (HLA B*5801), carbamazepine (HLA B*1502) are more susceptible to develop SJS-toxic epidermal necrolysis (TEN). Environmental factors like sun exposure may precipitate severe cutaneous drug reactions. Patient with hepatic disease, renal disease, systemic lupus erythematosus, HIV is prone to develop an ADR⁶. Incidence of suspected ADR reporting in India was found to be 2-3% which is lower than expected.

Spontaneous reporting of ADRs voluntarily by the healthcare professionals has been the core data-generating system of Pharmacovigilance for years. It plays a major role in identifying and reporting of any adverse events to the regulatory authorities. Hence this study was undertaken to emphasize the need to report ADRs. The aim and objective of the study is to do survey of clinical pattern of suspected ADRs in DR. B. R. Ambedkar Medical College and hospital, a tertiary care centre over a period of one year.

2. MATERIALS AND METHODS

2.1. Duration of study- July 2014 to July 2015

2.2. Inclusion criteria

- Diagnosis of ADR was in accordance with definition provided by WHO.
- No alternate explanation for the reaction
- A plausible time relationship between introduction of the drug and onset of a reaction
- Improvement in condition of the patient after withdrawal of the suspected drug.
- All age groups
- Gender – Male and Female
- All the departments of DR. BR Ambedkar Medical College and hospital

2.3. Exclusion criteria

- Cutaneous manifestations of systemic diseases.

- Alternative forms of medicines like – herbal, Ayurvedic, Homeopathic.

2.4. Method

The study was carried out in Dr. B.R. Ambedkar Medical College, Bengaluru from July 2014 to June 2015. Institutional Ethics Committee clearance was obtained. Both inpatients and outpatients were included in the study. Informed consent was taken from study subjects. Information regarding the etiological agent, drug history, temporal correlation with the drug, duration of the reaction, associated mucosal or systemic involvement, improvement of the lesion on withdrawal of drug and laboratory investigations were recorded in a carefully pre-designed proforma. Causality assessment was done by using Naranjo's algorithm scale which consists of 10 questions. Each question was given a score, and the total score was recorded for each patient and graded as definite, probable, possible, and doubtful⁷. Naranjo's algorithm scale has wide acceptability as it is simple to follow and nonspecific. Hence, it was used for causality assessment in this study. All values were expressed in percentages (%).

3. RESULTS AND DISCUSSION

A total number of 40 patients with ADRs were included in the study. There were 14 males and 26 females. Mean age of males was 34± 15years (43.5) and females were 35±15 years (37.5) (Table 1). There were 10 inpatients and 30 outpatients. Majority of the patient were in the age group of 35-45 years. Past history of cutaneous ADR was present in 10(25%) patients (Figure 1). Most common type of ADRs was Type B most commonly cutaneous ADRs (Table 2). In our study was fixed drug eruption (FDE) 18(56.25%) caused by Tab. Paracetamol, followed by erythema multiforme 7(21.88%), drug-induced urticarial 5(15.62%), SJS with TEN 2(6.25%) were seen. The number of cutaneous ADRs associated with individual drug groups were Nonsteroidal anti-inflammatory drugs (NSAIDs) 27 (67.5%), anti-microbials 9(22.5%), anti-convulsants 4 (10%) (Figure 2). In this study, NSAIDs contributed to the largest number of ADRs followed by antimicrobials. Most of the FDE were caused by NSAIDs. Causality assessment was done using Naranjo's scale and 35 (87.5%) ADRs were probably due to drugs, 2(5%) possible, 1(2.5%) doubtful, 2(5%) definite (Figure 3).

In the present study all age groups were affected with ADRs, higher incidence with adult age group between 30-50 years. Few previous studies have shown a higher incidence in 21- 40 years of age^{8,9}. There was female preponderance 26 (65%). The diagnosis of cutaneous ADRs involves analysis of factors such as timing of the drug exposure and the reaction time, the course of the reaction with drug withdrawal/ discontinuation, the timing and nature of eruption on rechallenge history of similar reaction to the suspected drug and previous reports of similar reactions to the same drug¹⁰.

Cutaneous reactions are the most common manifestations of ADRs. Most of the reactions were of type B 36 (90%). Spectrum of cutaneous manifestations ranges from maculopapular rashes to SJS and TEN. Majority were mild to moderate in severity (Figure 4). Incidence of serious ADRs in most studies: 0-20%. In the present Study it was: 12.5%. Cutaneous ADRs were most common 32 (80%) in our study. Amongst the drugs which caused ADR, NSAIDs were most common 27(67.5%). Few studies have reported that NSAIDs were the main group of drugs to cause

different type of skin reactions, thus supporting our study. However previous studies suggest anti-microbial were the most common drugs followed by anti convulsants which cause cutaneous ADRs^{8,11-14}. Few studies suggests anti-microbial were the most common drugs which cause cutaneous ADRs followed by anti convulsants^{15,16}. The most common type of ADRs in our study was FDE 18(56.25%), which is in concordance with some of the studies^{4, 12, 13}. Two definite cases were due to anti TB drugs provided by RNTCP with LFT impairment in the beginning, when rechallenge done with same drugs showed LFT impairment.. Two cases of STEVENS JOHNSON SYNDROME were reported due to Tab. Nimesulide (Image 1, 2), Tab. Allopurinol (Image.3). NSAIDS responsible for ADRs in our study were diclofenac was most common drug followed by paracetamol, Nimesulide, ibuprofen. Anti-microbials were ciprofloxacin, co trimoxazole and sulphonamides. Anti convulsants like carbamazepine, phenytoin. None of our patients had concomitant illness like HIV, viral or autoimmune hepatitis, diabetes mellitus, as incidence of ADRs is more common in immuno compromised patients.

Strategies to prevent ADRs

1. Avoid polypharmacy.
2. Prescribe drugs, which have been known to cause cutaneous ADRS, only if extremely necessary.
3. Obtain history of ADRs in the past.
4. Educate the patients regarding common early symptoms of drug reactions (e.g. erythematous rash, oedema, mucosal erosions, itching etc.) especially during the start of therapy.

4. CONCLUSION

ADRs are potentially avoidable causes for seeking medical care. Study reveals that most of the reactions were cutaneous in nature. Systemic reactions were under reported. Hence, emphasizes the need for setting up a Pharmacovigilance unit in each hospital so that all ADRs are reported. Thus it improves patient care and safety by promoting rational use of medicines and minimizes the ADR incidences. NSAIDs were the most common agents responsible for ADRs in our study. When ADR is suspected, the causative drug must be identified and withdrawn. Depending on the nature of reaction, symptomatic treatment can be accompanied by local skin care and if indicated immunomodulating therapy with corticosteroids to reduce severity. If ADR is severe, admission and proper supportive care is necessary until the patient recovers completely.

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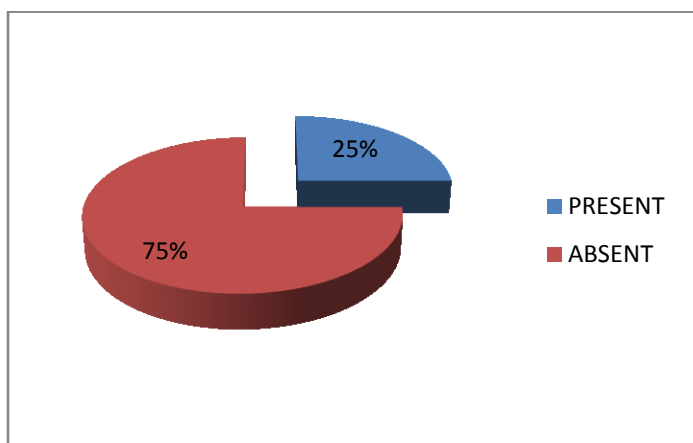


Figure 1: Significant Past History.

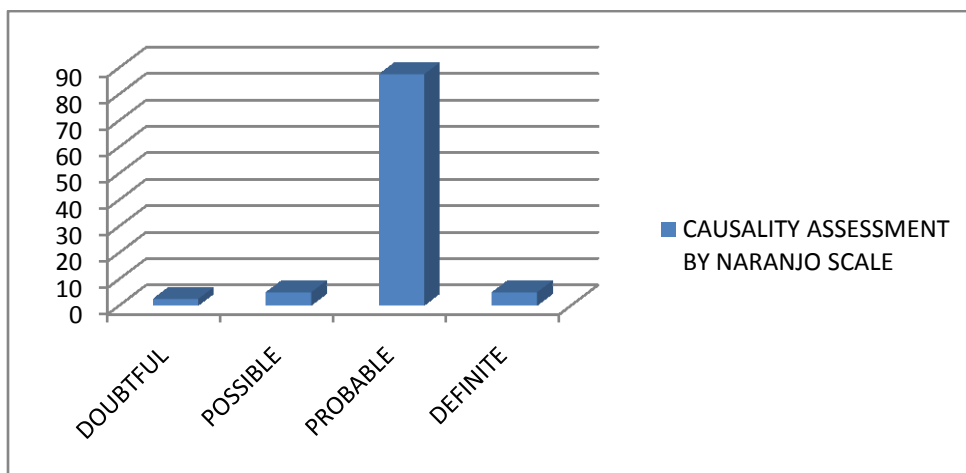


Figure 2: Causality Assessment by Naranjo Scale

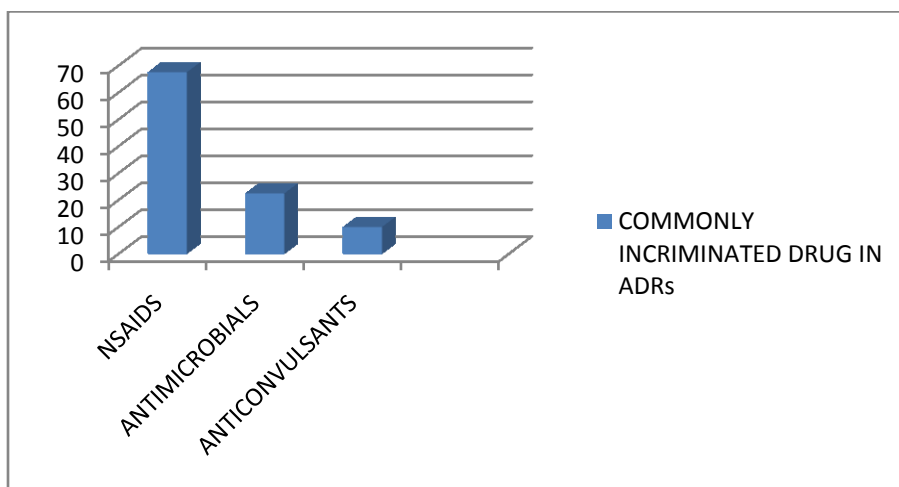


Figure 3: Commonly Incriminated Drug in ADRs.

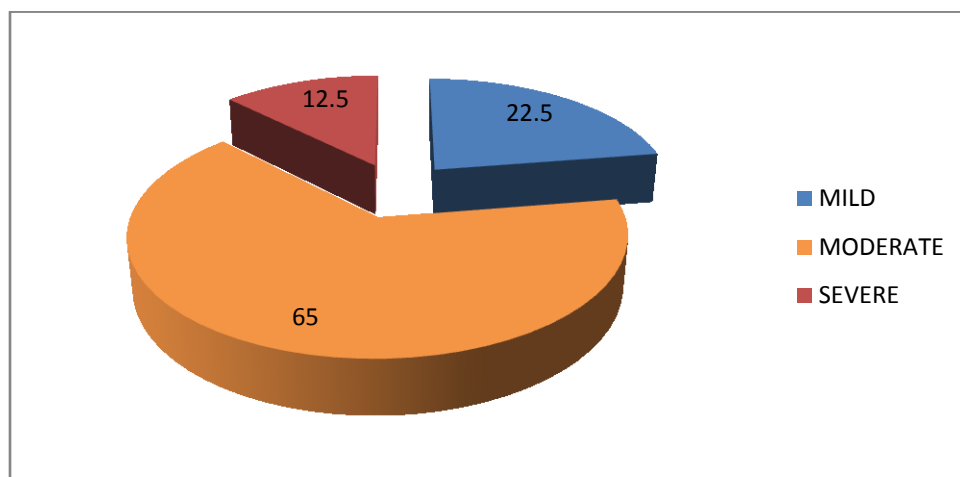


Figure 4: Severity Based Distribution of ADRs.

Table 1: Baseline Characteristics.

AGE	0 – 20 Years: 6 (15%)
	20 – 60 Years: 34 (85%)
MALE: FEMALE (%)	14 (35%): 26 (65%)

Table 2: Types of ADRs.

	NUMBER	PERCENTAGE
TYPE A	4	10%
TYPE B	36	90%
CUTANEOUS	32	80%
SYSTEMIC	8	20%



Image 1



Image 2



Image 3