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Research Article

IDENTIFICATION AND REPORTING OF ADVERSE DRUG REACTIONS IN THE PHARMACOVIGILANCE CENTER OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: In spite of being the most vital part of the health-care system, medicines can become the reason for hospitalization or prolonged hospital stay if not used with vigilance. Adverse drug reactions (ADRs) have become a major reason for the rise in morbidity and mortality rate. Hence, monitoring of the ADRs and understanding their route cause is utmost important in a clinical setup. This project aims to monitor the ADRs and improve ADR reporting in the hospital.

Methods: The work was carried out at a tertiary care hospital in Pune. Daily visit to different departments was done and patients were screened from admission to discharge during the study period. ADRs occurring due to chemotherapy, overdose, intoxication, drug abuse, accidental/intentional poisoning, and blood/blood products were excluded. The data of ADRs reported in the hospital in the past 3 years were collected and compared with the prospective data to analyze the improvement in ADR reporting in the hospital.

Results: ADRs occurring in males were more than those in females. Adults between the age group of 20 and 59 years were more prone to ADRs. Maximum number of ADRs reported were occurring due to antimicrobial agents. The organ that was commonly affected due to ADRs was skin.

Conclusion: High incidence of ADRs insists on vigilant monitoring to prevent its further recurrence. More studies need to be conducted to know the exact occurrence and prevalence of ADRs in the Indian population. Creating awareness among the HCPs for reporting suspected ADRs will help to improve patient safety. ADR reporting can be enhanced if the involvement of clinical pharmacists is strengthened in health-care centers.

Keywords: Adverse drug reactions, Causality assessment, Pharmacovigilance, Severity scale, Antimicrobial agents, Skin reactions.

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INTRODUCTION

Medicines have become a vital part of the health-care system around the world because they save lives. However, the use of drugs itself may result in illness and death due to their adverse effects [1]. When a new pharmaceutical drug is introduced to the market, certain patients may experience adverse reactions. It is critical to monitor and report adverse drug reactions (ADRs) to determine risk and benefit ratio and ensure the safety and efficacy of medicines [2,3]. In the Indian population, the incidence of ADRs resulting in hospitalization accounts for 5% of all hospital admissions and occurs in 10–20% of hospitalized patients. Approximately 770,000 people bear severe consequences each year as a result of ADRs, accounting for $5.6 million of health-care costs [4]. A study conducted in South India estimated the total cost of ADRs to the hospital as INR 15,67,397. The costs were found to be significantly burdensome for a country where the per capita annual expenditure on health is only about USD 109 [5].

ADRs are classified into six types, i.e., Type A - augmented pharmacologic effects, Type B -bizarre effects, Type C - chemical effects, Type D - delayed effects, Type E - end-of-treatment effects, and Type F - failure of therapy [6,7]. ADRs have a variety of effects, ranging from allergic reactions to permanent damage and even death. Various factors are related to ADRs such as age, gender, genetic factors, polypharmacy, drug interactions, and multiple diseases [8]. Preventable ADRs include the ones occurring due to medication errors (MEs), drug–drug interactions, errors in prescribing or dispensing, underlying allergies, and poor adherence [9]. One-third of MEs result in ADRs [10]. Elderly patients who are exposed to polypharmacy are more prone to ADRs [11]. According to the American Food and Drug Association, ADR is serious and should be reported to the FDA if the outcomes are life-threatening and require intervention to prevent permanent impairment [7,12]. ADRs increase the hospitalization stay and lose the potential benefit of medicine as the patient may discontinue taking medicines. They impact patient's quality of life and confidence in the health-care system [13]. Health-care providers rely on the detection and reporting system of suspected ADRs to identify new reactions. Failure to identify ADRs may lead to unnecessary investigations which add to the financial burden to the patient [14].

Under the guidance of the Ministry of Health and Family Welfare, the Government of India has launched the Pharmacovigilance Programme of India (PvPI) and established ADR monitoring centers (AMCs) [1,15]. Although several regulatory authorities such as Central Drugs Standard Control Organization (CDSCO), Drug Controller General of India (DCGI), and World Health Organization-Uppsala Monitoring Centre (WHO-UMC) are focusing on drug interactions and ADRs, there is inadequate ADR reporting [16]. Causality assessment is a method by which the relationship between a medicine and a suspected reaction is established [7]. Various causal assessment methods are used such as the WHO-UMC system based on expert judgment, algorithm-based Naranjo scale, and Bayesian Adverse Reactions Diagnostic Instrument (BARDI) [17]. VigiBase is the largest database of spontaneous ADR reports in the world [13,15].

MATERIALS AND METHOD

Materials

1. Suspected adverse drug reactions (ADRs) reporting form by the Pharmacovigilance Programme of India (PvPI).

2. Naranjo Algorithm (Adverse Drug Reaction Probability Scale).
3. Hartwig Scale (Severity Assessment Scale).

Methods

The current work aimed to observe the prospective and retrospective data of ADRs reported in a 300-bedded, tertiary care hospital. After taking permission from the Ethical Committee (ABMH/Academics/EC/3613), this observational, single-centered study was conducted among indoor patients of a tertiary care hospital in Pimpri-Chinchwad. Prospective data were collected for a duration of 6 months, and the data of ADRs reported in the hospital in the earlier 3 years (retrospective data) were also collected. Visit to different departments was done daily, and a total number of 876 patients were screened from admission to discharge during the study period. Following the exclusion criteria that consisted of ADRs occurring due to chemotherapy, overdose, intoxication, drug abuse, accidental/intentional poisoning, and blood/blood products, 602 cases were excluded. Total 274 cases were included (patients of all ages and both genders) in the study. Out of the 274 cases, ADRs were found in 29 cases.

All the necessary data which included patient demographics, medical/medication history, details regarding suspected ADR, concomitant drugs, dechallenge/rechallenge, action taken, and reporter's details were collected and noted in a pre-designed ADR reporting form. Other information such as the severity of ADR, organ involvement, and causality assessment was clinically interpreted. The Hartwig Severity Scale was used to assess the seriousness of ADRs, and the Naranjo Algorithm was used to assess the probability of ADR occurrence. The retrospective data were compared with the prospective data to analyze the pattern of ADR reporting in the hospital.

RESULTS

The study was carried out to identify and report ADRs occurring during the 6-month duration of the study (prospective). These data were compared with the data of 3 years that were collected retrospectively. Total 74 ADRs were included in the study. Demographic details of the patients show that ADRs reported in males were more than those in females, as shown in Fig. 1. This does not indicate that ADRs are more prevalent in males because our study population had more number of males than females. Fig. 2 suggests that there was only one definite ADR in prospective and retrospective data each. One doubtful ADR was found in the prospective study. Fifteen possible and 12 probable ADRs were detected in the prospective study, whereas 27 possible and 17 probable ADRs were reported in the retrospective study.

The class of drugs that led to the maximum number of ADRs was the antimicrobial agents in both prospective and retrospective studies (Fig. 3). After antimicrobial agents, analgesics and antipyretics caused a greater number of ADRs. The organ that was commonly affected due to ADRs was skin because the most commonly observed ADRs were rashes and itching that is evident from Fig. 4. Moderate ADRs were more common in the data as the suspected drug was withheld or discontinued and an antidote was required with no increase in length of stay (Fig. 5).

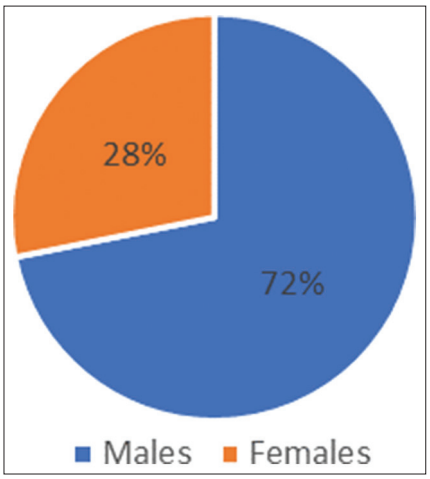

Fig. 1: Distribution of patients based on sex

DISCUSSION

A total number of 876 patients were screened during the study duration of 6 months. Among these, 274 patients complied with the inclusion criteria. ADRs were identified in 29 patients. Retrospective data of 3 years were collected, in which 45 ADRs were reported. Based

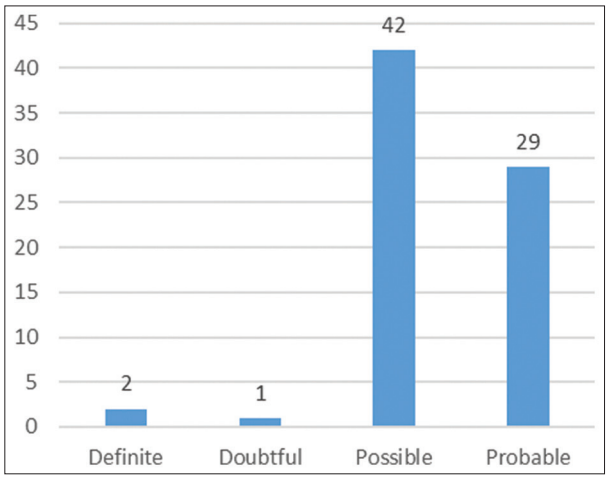

Fig. 2: Distribution of patients based on causality assessment

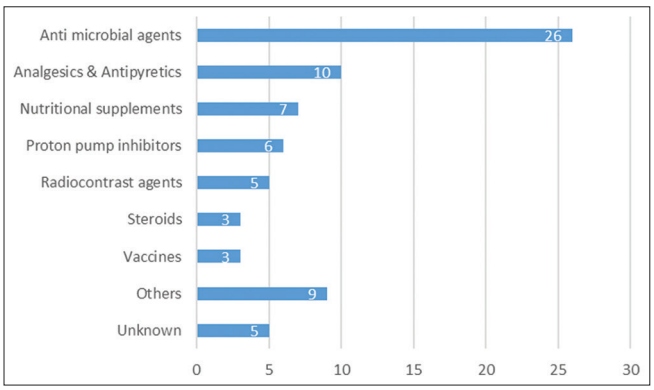

Fig. 3: Distribution of patients based on the class of suspected drugs

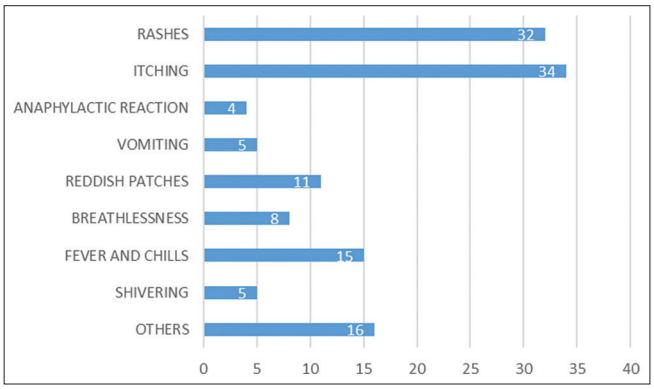

Fig. 4: Distribution of patients based on symptoms of ADR

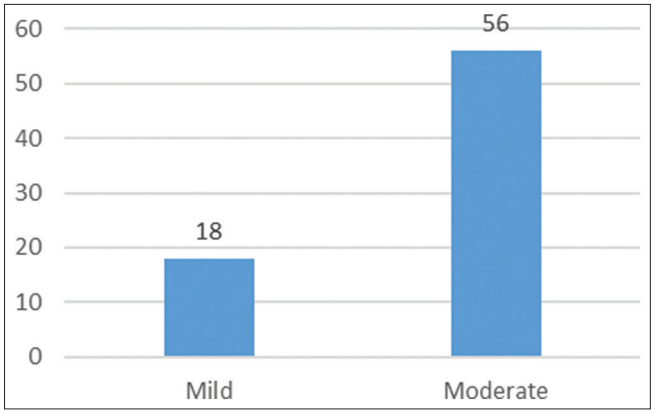

Fig. 5: Distribution of patients based on the severity of ADRs

on the data collected, a comparison was made and improvement in ADR reporting was assessed.

On the basis of demographic details, the male: female ratio for ADR occurrence was 3:1 in the data because a greater number of male populations was included in this study. A study conducted by Shamna *et al.* showed similar results [18]. Some previous studies showed that more females were affected due to ADRs than males. This parameter changed in different studies. According to the Naranjo's Causality Assessment Scale, a greater number of patients in the data were found to have possible relation with the drug, whereas probable, definite, and doubtful were lesser in number. In a similar study by Kalyani *et al.*, Naranjo's Probability Scale-based comparison of causality assessment of ADRs showed that 12.4% were probable, 25.9% possible, 13.8% definite in a total of 14 studies [16].

The clinical spectrum of ADRs ranged from the more common reactions such as skin rashes, itching, nausea, and vomiting to reactions leading to prolongation of the hospital stay. The most frequent ADRs were rashes and itching. According to the anatomical system, the skin was the chief organ system affected. Various previous studies by James *et al.*, Lihite *et al*., and Ramakrishnaiah *et al.* showed the involvement of skin as the chief organ system was affected with the most common complaints of skin rashes [1,8,19].

The predominant causative drugs were antimicrobials, non-steroidal anti-inflammatory drugs, analgesics, and antipyretics. The majority of ADRs were associated with antimicrobial agents. Major antimicrobial drugs causing ADR were revealed to be cephalosporin which accounted for approx. 50% of all ADRs. According to studies done by Ramakrishnaiah *et al.* and Arulmani *et al.* in tertiary care hospitals, maximum ADRs were caused due to antimicrobials [8,20]. This shows that antimicrobial agents are the major cause of ADR occurrence in the patients.

As per the Hartwig and Siegel Severity Assessment Scale, most of the reactions were moderate. Other studies conducted on ADR identification and reporting by Santosh Chandrashekar *et al.* and Darji *et al.* showed similar results, i.e., there were more moderate reactions than mild and very few of the adverse reactions were severe [21,22].

Studies conducted in several parts of India have estimated the incidence of suspected ADRs to be nearly 2–3% among hospitalized patients. There is an increasing need for interventions for the prevention of ADR-related health problems. Vigilant monitoring of ADRs and encouraging prompt reporting of the same can prevent the occurrence of ADRs [3,14]. Most of the ADRs were dose-related and pharmacological reactions that usually subsided with stoppage of drug or reduction in dose. The majority of drugs were withdrawn for the management of ADR and rechallenge was performed in very few patients. Anti-allergic agents such as pheniramine, fexofenadine, and a steroidal agent such as hydrocortisone were used for the treatment of the adverse reactions. No fatalities were observed in this study. All the patients recovered within 1 day to 1 week after detection of ADRs.

CONCLUSION

ADR is a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function. It increases the length of hospital stay, adds to treatment costs, and is a burden on the health-care system of a country. ADRs can be avoided if medicines are used in the right dose for the right patient. The precocious detection of a suspected ADR is a very important procedure for appropriate management of the patient and to avoid exposure to additional drug hazards. Many ADRs may not be well recognized in clinical trials and become apparent during post-marketing surveillance as severe. In such cases, reporting of ADRs in hospitals becomes very crucial. Creating awareness among patients and HCPs will help in reducing the ADRs and their negative impacts.

The Indian scenario shows that the patient inflow is huge and the health-care professionals are overburdened. This leads to a lack of pharmacovigilance activities. There is a need of conducting more studies in the Indian population to know the exact ADR occurrence rate. The clinical pharmacist plays a key role in patient safety and their involvement can strengthen health-care services. Intervention by CPs might improve the reporting and monitoring aspects of ADRs and minimize harmful effects to patients. In this study, it was concluded that the majority of ADRs are caused because of antimicrobial agents. This shows the importance of Antimicrobial Stewardship (AMS) and the need for optimizing the use of antibiotics.

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AUTHORS CONTRIBUTION

The authors confirm their contribution to the paper as follows: TS and ST designed and conceptualized the study. Data collection was done by VS, JS, TS, and ST. VS and JS analyzed and interpreted the data to write the manuscript. Results were reviewed and the final version of manuscript was approved by MK, PJ, and TM.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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