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Original Research Article

A retrospective and observational study of the adverse drug reactions reported in a tertiary care hospital

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ABSTRACT

Background: Adverse drug reaction (ADR) is considered a common cause of prolonged hospitalization and death among patients. Pharmacovigilance is essential in the surveillance of adverse drug reactions. The responsibility of a healthcare professional is to report any adverse reaction that occurs with the use of drugs. This helps in providing a database and improving the safety of patients. The aim of the study was to determine the incidence of ADR, assess causality, severity, and preventability of the submitted adverse drug reactions, increase the awareness of preventability of adverse drug reactions in health care professionals by conducting regular workshops on ADR, and document occurrence of a rare ADR.

Methods: A retrospective observational study was conducted to assess the ADR reported to the ADR monitoring Centre, for the past 6 years included in the study. The data were entered into Microsoft excel and analyzed using descriptive statistics. Mean and standard deviation were calculated for the categorical data. Drugs were classified according to the class. Reactions were analyzed using scales and presented in descriptive statistics.

Results: A total of 95 ADR reports were received and reported. These ADRs were associated with a total of 108 drugs that were prescribed- the occurrence of ADRs dominated among females 60% (57). Antimicrobials were causing the highest number of adverse reactions 21 (19.44%) and antituberculosis drugs and radiocontrast media were associated with the following larger number of the ADRs 19 (17.59%). Intravenous at 40% was the most common route related to the development of ADR. The most common ADR caused by antimicrobials was rash (9), antitubercular therapy commonly caused hepatitis, and chills and rigors were more common with radiocontrast media. Most of the reactions observed in the patients were moderate reactions at 52.63% with 3.16% fatal ones.

Conclusions: In this study, the predominant causative drugs associated with ADR were antimicrobials, antitubercular drugs, and radiocontrast media. The number of ADRs reported though was less there was a wide range of drugs causing ADR that were reported which gave a broader spectrum for analysis. There is a requirement for active monitoring of ADRs to understand the occurrence as well as help in prevention.

Keywords: Adverse drug reaction, Pharmacovigilance, Drug safety, Causality, ADR reporting pattern

INTRODUCTION

WHO defines 'pharmacovigilance' as the science and activities relating to the detection, assessment, and prevention of adverse effects or any other possible drug-related problems, including herbal medicines.[1] Adverse drug reactions (ADR) is one of the common causes of prolonged hospitalization and death among patients. Pharmacovigilance plays a key role in the surveillance of adverse drug reactions. Around 10% of hospital admissions are estimated to be due to ADRs and about 5-20% of hospitalized patients experience a serious ADR.[2] It is the responsibility of a drug regulatory authority to ensure the quality, efficacy, and safety of all marketed products.

Data obtained from preclinical and clinical trials helps in understanding the efficacy and safety to some extent but does not help in detecting rare ADR delayed ADRs or effects from long-term exposure.

Given this, pharmacovigilance plays a prominent role in establishing the safety profile of marketed drugs pharmacovigilance is an important and integral part of the safe practice of medicine.[3] Only a small proportion of the ADR are reported to the central monitoring center. Most of the ADR's go unrecognized in the guise of a disease or a symptom of a disease. Hence there is a need for better reporting of ADRs and the creation of a database that allows feedback and drug alerts by the central agency (PvPI) and better management of patients. Even though India started participating in the WHO PvPI program a few years ago, monitoring and reporting of ADRs is still in its infancy.

The main objective of ADR monitoring is to identify the frequency of ADRs and their risk factors. It is not enough to report the ADRs, but an analysis of the reported ADRs helps us to understand the preventability also. Causality assessment is the method by which the extent of the relationship between a drug and a suspected reaction is established. Several algorithms or decision aids have been published including the Jones algorithm the Naranjo algorithm the Yale algorithm the Karch algorithm the Begaud algorithm the ADRAC the WHOUMC and a newer quantitative approach algorithm.[4-11] In this study we have used the WHO causality assessment scale. Severity can be classified as mild, moderate, and severe depending on the amount of intervention, which was required during management. For assessment of severity most commonly used instrument is the Hatwig SC, Seigel et al, and Schneider et al categorized ADRs into seven levels, levels 1 and 2 fall under the mild category whereas levels 3 and 4 under moderate, and levels 5, 6 and 7 fall under the severe category.[12] The Schumock and Thornton criteria were established for assessing the preventability of ADRs. The modified form of this criterion has been used in various studies.[13-15] It has three sections preventable, probably preventable, and non-preventable.

A study of ADR documentation helps in the periodic assessment of the data obtained and helps provide a database for reference purposes. This study aimed to study the incidence of ADRs, assess the causality, severity, and preventability of the submitted ADRs, and increase the awareness of the preventability of ADRs in health care professionals by giving feedback and documenting any rare ADR occurrence.

METHODS

A retrospective observational study was conducted to assess the ADR reported to the ADR monitoring Centre of Terna Medical College, Nerul, Navi Mumbai. Institutional ethics committee approval was taken before conducting the study.

The ADR forms (Version 1.2 initially and latest 1.4) recommended by the PvPI unit, CDSCO, India were used. ADRs voluntarily reported by the physicians received at the ADR Monitoring Centre during the period 2017-2023, which were entered on the Vigiflow were assessed.

Inclusion criteria

ADRs reported to the ADR monitoring center (i.e., Department of Pharmacology, Terna Medical College, Nerul) for the past 6 years (2017-2023) were included in the study.

Exclusion criteria

ADR forms that were incomplete, and those that were not entered into the Vigiflow system were excluded.

Reports were analyzed according to the following parameters- (1) demographic data of the patient- age, sex (2) ADR was analyzed into type, number, percentage, and causality by using the WHO probability scale, severity by using modified Hartwig's and Siegel scale, and preventability by Schumock and Thornton scale, (3) drugs causing the ADRs were classified and described as number and percentage.

The data was entered into Microsoft excel and analyzed using descriptive statistics. Mean and standard deviation were calculated for the categorical data.

Drugs were classified according to the class. Single drugs were kept as such. The type of ADRs could not be grouped separately as each drug caused more than one symptom.

RESULTS

ADR reports received at the AMC from 2017-2023 which were reported to the PvPi in vigiflow were analyzed. A total of 95 ADR reports were received and reported. These ADRs were associated with a total of 108 drugs that were prescribed. Table 1 shows the Gender distribution and age distribution of the reported ADRs. The occurrence of ADRs dominated among females 60% (57) than male patients 40% (38). The maximum number of ADRs was reported among patients aged between 21 and 40 years at 46.32% (44).

The mean age of the patients was calculated after excluding the patients who were less than 1 year old (n=6, 6.32%). The mean age was 37.9101 with an SD of 17.6517. The drugs causing the ADRs were grouped according to classes the single drugs were kept as such.

As seen in Figure 1, of a total of 108 drugs that were implicated in causing the ADRs, Antimicrobials were causing the highest number of adverse reactions 21(19.44%) and antituberculosis drugs and radiocontrast media were associated with the next largest number of the ADRs 19 (17.59%). The list of drugs that were most

frequently associated with the ADRs and the symptoms seen is presented in Table 2. The most common ADR caused by Antimicrobials out of 21 cases was rash (9), the antitubercular therapy commonly caused hepatitis (n=12 out of 19), and chills and rigors were more common with radiocontrast media (n=11 out of 19).

Figure 2 shows the distribution of the routes of drug administration associated with the ADRs. The most common route associated with the development of an ADR was Intravenous at 40% next was the oral route of drug administration at 39%. Table 3 shows the grouping of the reactions according to the Hartwig and Seigel scale.

The ADRs were mostly moderate in severity i.e., the suspect drug was stopped, and the reaction required treatment but there was no increase in length of stay (LOS).

The analysis using the Schumock and Thornton scale for the preventability of the ADR revealed that all the ADRs in our study were not preventable.

53.68% of the reactions received medical treatment, the common drugs which were given being injection pheniramine and injection hydrocortisone.

Table 1: Showing demographic data as N (%).

Variables	N (%)
Age (years)	
0-1	6 (6.32)
1-20	10 (10.53)
21-40	44 (46.32)
41-60	30 (31.58)
60 and above	5 (5.26)
Total	95
Gender	
Male	38 (40)
Female	57 (60)
Total	95

Table 2: Distribution of drugs as N (%) and the ADRs associated with them as N (%).

Class of drugs/drug	N (%)	Type of ADR
Antimicrobials	21 (19.44)	Maculopapular rash (9), anaphylaxis (1)-death, angioedema (2), fever with rigors (5), convulsions (1), itching and redness (1), swelling (2)
Radiocontrast media	19 (17.59)	Chills and rigors (11), itching and rash (8)
Antitubercular therapy	19 (17.59)	Hepatitis (12), itching (3), hyperuricemia (1), ototoxicity (1), hematemesis (1), swelling of face and limbs (1)
Antipsychotics	8 (7.41)	Extra pyramidal syndrome (6), tremors (1), weight gain (1)
Vaccine	8 (7.41)	Induration (5), swelling (5), superficial and deep petechiae (1), convulsions (1), death (1)
NSAID's	6 (5.56)	Itching, rash wheals, bronchospasm, chills
Iron preparations	6 (5.56)	Shivering, palpitations, itching, swelling, thrombophlebitis, breathlessness
Local anesthetics	3 (2.78)	Altered behavior (1), itching(1) and rash at the site of injection(1)
Antiepileptics	3 (2.78)	Tremors (1), vesicle (1)
Opioids	3 (2.78)	Itching, rash
Antidepressants	2 (1.85)	Dry mouth (2)
Anticholinergic	2 (1.85)	Itching and rash (2)
PG analogues	1 (0.93)	Breathlessness, chest pain, cough (1)
Topical corticosteroid	1 (0.93)	Hypopigmentation (1)
Azathioprine	1 (0.93)	Bone marrow suppression (1)
Topical antiseptics	1 (0.93)	Rash (1)
IV globulin test dose	1 (0.93)	Hypotension, bradycardia (1)
Allopurinol	1 (0.93)	Stevens-Johnson syndrome (1)- death
Antiemetic	1 (0.93)	Extra pyramidal syndrome (1)
Sulfasalazine	1 (0.93)	Rash, angioedema, palpitations (1)
Total	108	

Table 3: Distribution of severity of the ADR using Modified Hartwig and Seigel scale.

Severity of the ADR	N (%)
Mild	39 (41.05)
Moderate	50 (52.63)
ADRs requiring emergency treatment	3 (3.16)
Death	3 (3.16)
Total severe ADR's	6 (6.32)
Total of all ADRs	95 (100)

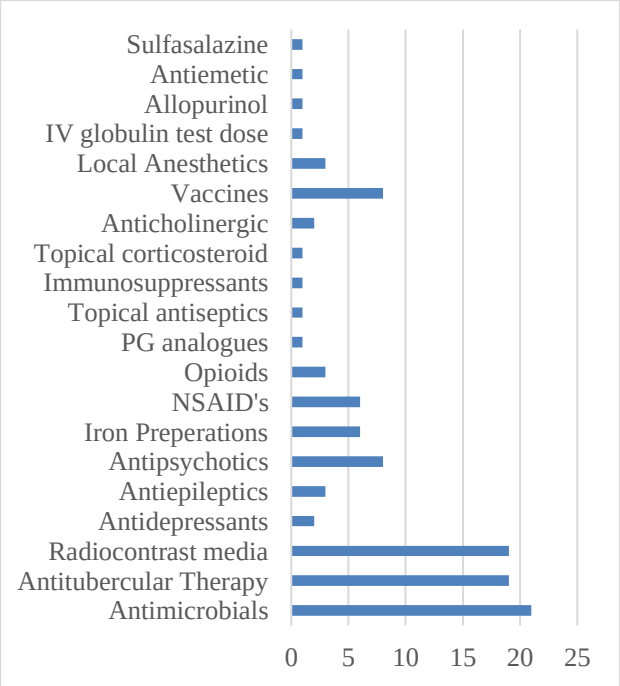

Figure 1: Drugs involved in development of ADR grouped as class.

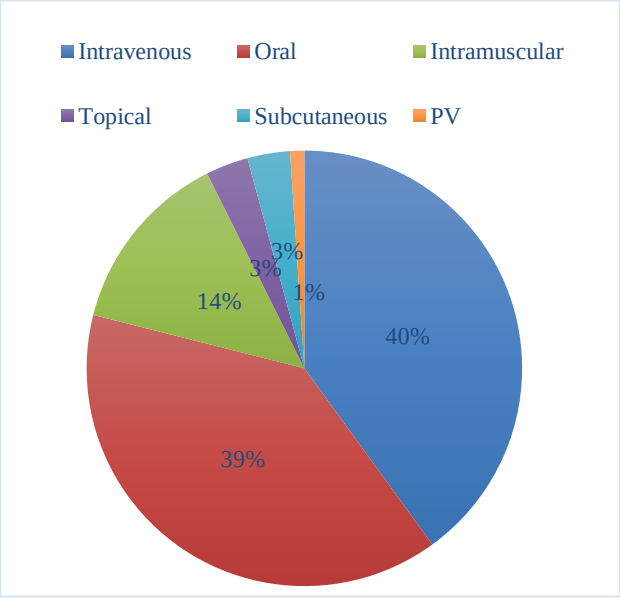

Figure 2: Routes of administration of the drugs involved in development of ADR.

DISCUSSION

According to WHO, pharmacovigilance is a set of practices aiming at the identification, understanding, and assessment of risks associated with drugs. A productive hospital-based reporting program can be instrumental in providing valuable information regarding problems of drug usage in an institution, which results in continuous improvement of patient care periodic evaluation of ADRs reported in a hospital helps in characterizing the pattern of ADRs and thereby helps in designing steps to improve the safety of drug use in the daily routine set up.

ADR are a common occurrence but are under-reported as many physicians are unaware that even commonly expected ADRs should be reported to an ADR monitoring center. In our study, the ADRs received over 6 years were only 95. This could have been more considering the ADR occurrence is quite common. Most of our reactions were because of antimicrobials at 19.44%. This was like other studies done before by Padmaja et al, Gor et al, and Leapa et al.[18-20] Though the percentage was different. It was noted that 46% of ADRs were caused due to antimicrobials in a study done by Ramakrishnaiah et al.[21] This could be because of the number of cases reported by the physicians. In contrast to the other studies, our study had the antitubercular therapy and radiocontrast media at a close second in reported ADRs. This could be explained by the awareness and reporting done more by these departments in comparison to the other places. Most of the reactions observed in the patients were moderate reactions at 52.63%, while 6.32 % had serious reactions and of them 3.16% were fatal. Though the Antitubercular therapy consisted of four drugs all were considered under one heading. The most common ADR caused by these was Hepatitis. This is well documented in the literature.

Most of the patients (92.63%) developed the ADR graded as 'probable', since in all these cases the time from taking the drug correlated with the ADR, the patient recovered on stopping the drug and the events were not explained by the patient's disease. In 7.37% of the cases of adverse drug reactions, they were designated as 'possible in nature' since although the time sequence between the administration of the drug and reaction was reasonable, and the events could have been a result of the patient's disease as was seen in other studies.[22] In this study, the patients did not have any documented evidence of the allergy, nor was any drug requiring drug monitoring or plasma levels calculated. Hence all the reactions were considered as not preventable according to the Modified Schumock and Thornton scale in contrast to the study done before.[23] The adverse cutaneous reactions in this study were mostly erythematous rash and itching, n=36 (33.33%). These were mostly associated with antimicrobials. The other studies had urticaria and fixed drug rashes as the most common reaction types.[24,25] In this study the drugs suspected to be causing ADR were discontinued and the data regarding the replacement drugs was not available hence that part was not analyzed.

CONCLUSION

The ADRs reported to the AMC, of Terna Medical College, ranged from mild reactions such as skin rashes, and itching to moderate reactions prolonging the hospital stay of the patients. Three fatalities due to ADR were reported. The predominant causative drugs were antimicrobials, antitubercular drugs, and radiocontrast media. The antipsychotics and vaccines were also associated with some of the moderately severe and severe ADRs. The majority of ADRs were probable in causality and moderate in severity. However, the preventability assessment was a challenge for the data of this study. There is a necessity to increase awareness of the importance of ADR reporting among healthcare professionals.

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