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Original Research Article

Analysis of voluntary reported adverse drug reactions in a tertiary care hospital

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ABSTRACT

Background: Adverse drug reactions are the major cause for increased hospital stay and it increases the economic burden of the patients. Reporting of ADR helps in signal generation and to ensure safe use of a drug. Present study was conducted to analyse the ADR reporting pattern and completeness of the ADR forms.

Methods: This was a retrospective study conducted for 6 months in a tertiary care hospital. A total of 330 ADR forms were analysed and completeness of ADR forms were assessed.

Results: A total of 330 ADRs were reported. 46% ADRs were reported in 2018, 23% in 2019, 11% in 2020, 8.9% in 2021 and 10.7% in 2022. 177 (53%) were males and 153 (47%) were females. Most occurred reaction was Hyponatremia 22 (6%), followed by Hypokalaemia 18 (5%). Neuropsychiatry cases were 62 (18.78%), Urinary system cases were 45 (13.63%). 122 (88%) patients were taking concomitant drugs whereas only 17 (12%) patients were not taking. Above 80% completeness were seen in 155 (46.96%) forms. Above 70% completeness in 292 (88.68%) forms.

Conclusions: ADRs occurrence was high in male compared to female. Most of the ADRs affected Neuropsychiatry followed by Urinary system. Antimicrobials are responsible for majorly reported ADRs followed by cephalosporins (17.6%) and Penicillin (11.76%). Overall completeness of reported ADR form was 80%, 67.87% of forms were not adequately filled with mandatory fields.

Keywords: Adverse drug reactions, Completeness of ADR form, Pharmacovigilance, Spontaneous reporting

INTRODUCTION

Drugs are intended to produce therapeutic effect in patients; despite the benefit it may cause Adverse Drug Reactions (ADR), even in therapeutic doses.¹ ADR can increase the hospital stay, cost of treatment and also decreases the quality of life. Pharmacovigilance helps in active assessment, monitoring and prevention of ADR. It is important to report and analyse the ADR to identify the potential risks with drugs and to enhance the safety of drug use. Health Care Professionals can spontaneously report the ADRs using Suspected ADR forms. The completeness of the reported ADR form is important because it hastens the process of signal generation.² Inadequate information

or incompleteness in the reported ADR form hinders the analysis of ADR. This study was conducted to evaluate the occurrence, contributing factors of ADR and completeness of the ADR form.

METHODS

The study was conducted in a tertiary care hospital for 6 months. It was a retrospective study. All the ADRs occurred from 2018 to 2022 were assessed. The following data were analysed from the ADR form suspected adverse reaction, suspected medications, seriousness and outcome of a reaction. Completeness of the ADR forms was assessed using scoring method. The suspected ADR

reporting form contains 17 fields classified under four sections (Patient Information-4 fields, suspected adverse reaction-3 fields, suspected medication-8 fields, and reporter information-2 fields). In our study, field no.8 and 16 were further divided into 8 fields (Drug Name, dose, route, frequency, indication, causality assessment, date of therapy started and ended) and 2 fields (Reporter Name and Details) respectively. Hence, a total of 25 fields were taken for completeness assessment. Each field is given a score of 1, if the information is filled.

RESULTS

A total of 330 ADR forms reported during the period of January 2018 to June 2022. Most of the ADRs were reported in the year 2018 (Table 1).

Table 1: Year wise distribution.

Year	Percent ADR reported
2018	46
2019	23
2020	11
2021	8.9
2022	10.7

Table 2: Causality assessment of ADR.

Causality assessment	% ADRs
Certain	14.7
Possible	33.5
Probable/likely	50.7
Unlikely	1

Among the cases, 53% were males and 47% were female. 5% cases were paediatric, 74.2% were Adult, 21% were Geriatric. Most occurred reaction was Hyponatremia followed by Hypokalaemia, Diarrhoea and Hyperglycaemia (Figure 1). From the reported ADR 14.7% was found to be certain, followed by possible 33.5%, probable 50.7%, unlikely 1% in causality assessment (Table 2). Only 4 reactions were identified as non-serious and 292 reactions were serious. 52% ADRs prolonged hospitalization, 27% ADRs required intervention, 13% ADRs were life threatening, 7% ADRs caused disability and 1% ADRs lead to death. Neuropsychiatry cases were 18.78%, Urinary system cases were 13.63%, Gastroenterology cases were 13% and Dermatology cases were 10% (Figure 2). Antibiotics caused a greater number of ADRs 51 (15%), followed by Antihypertensive 37 (11%), Anticonvulsant 27 (8%), Anticoagulant 24 (7%) and Anticancer 20 (6%) (Figure 3). 62% drugs were administered orally followed by 31.5% intravenously. 88% patients were taking concomitant drugs whereas only 12% patients were not taking. Polypharmacy (≥ 5 drugs) was identified in 18 (13%) patients. 51% cases were comorbid.

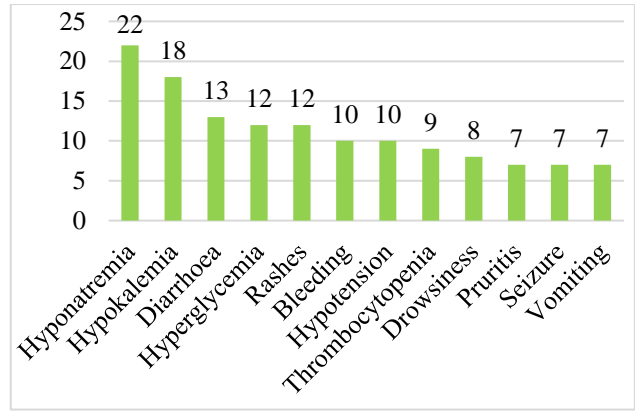


Figure 1: Distribution of ADR.

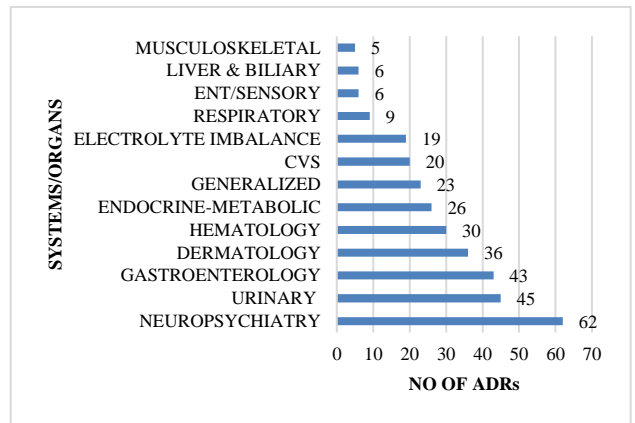


Figure 2: Organ systems affected.

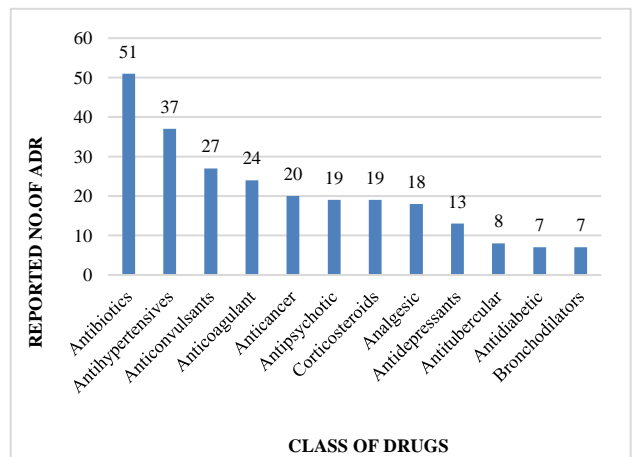


Figure 3: Class of drugs and ADRs.

Reaction was reappeared in 7 (6%) cases, not reappeared in 18 (15%) cases, not known in 42 (34%) and 55 (45%) cases were not applicable. We found an overall completeness of 80.60%. Above 80% completeness were seen in 155 (46.96%) forms. Above 70% completeness in 292 (88.68%) forms. Reaction reappeared after introduction, concomitant medication, Name, weight and date of reaction stopped were the areas identified to be lacking complete information.

DISCUSSION

In our study we were able to calculate occurrence of reported ADRs and highest number of ADR reported in 2018 (46%). In this study mean age of the subjects is 49.50 ± 18.55 (mean \pm standard error of mean of mean) (95% confidence interval, 30.95-68.05 years). There were 177 men and 153 women with a male: female ratio of 1.15: 1. Out of 330 ADRs, 231 were adults (19 - 65) of percentage 50.2% in males and 49.5% in females, ADR rates declined in eighth and ninth decades. In contrast to study conducted by Debilis et al which are in concordance with several other studies by Giardini et al.^{3,4} The occurrence of ADR was more common in male patients 54%. In this study, males are more affected than females like study by Ali et al which are in concordance with several other studies by Giardini et al.^{4,5} No significant differences were found in occurrence of ADR among males (49.2%) and females (50%) in a study conducted by Medal et al.⁶

Our study results do not support that female gender is a risk factor for ADR for development of adverse drug reactions. Our results were contrast to study on gender related differences by Prasad et al.⁷ Comparing the route of administration, no of reactions occurred with the oral 62% followed by IV 31% and others (SC, IM, INH, SL, LA) 6.36%. Which was in congruence with study proposed by Dhivya et al.⁸

The most occurred reaction is Hyponatremia 22 (7%), followed by hypokalaemia 18 (5%) and diarrhoea 13 (4%). Hyponatremia were caused mainly by antihypertensive (45.5%), anticonvulsants (36.36%), (4.5%) by antidiabetic, antidepressants and antineoplastic. These results were consistent with study by Sahay et al and narrative review by Liamis et al that specified certain drugs (e.g., diuretic, antidepressants, anti-epileptics) that cause either symptomatic or asymptomatic hyponatremia.^{9,10} In this study, antimicrobials (15.45%) are the most common causative drug class for high burden of ADR, followed by antihypertensive (11.21%) and anticonvulsant (8%) caused a greater number of ADRs. Of 330 ADRs, 51 were caused by Antimicrobials. In 51 ADRs, 30 were males (16.9%) and 20 were females (13.07%). The frequently implicated classes of antimicrobials in our study were (23.5%) cephalosporins, (13.7%) penicillin, (11.76%) polymyxin, (5.88%) glycopeptide and quinolones, (3.9%) by aminoglycoside and tetracyclines.

This is quite consistent with study carried out by Manju et al Antimicrobial associated ADR profiling a four-year retrospective study: A higher occurrence of antimicrobial associated ADRs were found in this study (54.4%). Penicillin and cephalosporins caused 25.12% and 18.84% of ADRs.¹¹ Enoxaparin (2.7%) was the agent that caused most ADR followed by acenocoumarin (2.4%), (2.1%) heparin. In this study, Neuropsychiatry constituted for the most common system affected, accounting for (18.7%) of total ADRs followed by genitourinary (13.6%), gastrointestinal (13%) and dermatological reactions

(10.9%). In study proposed by Yu et al the highest frequency of ADRs occurred in Gastro-intestinal which was the fourth highest in our study, followed by nervous system and psychiatric disorders.¹² It is because of difference in prevalent causative drugs that are involved (acid related, anti-inflammatory and analgesics) in study.

The causality assessment was done using the Naranjo scale. According to causality relationship, (53%) of the cases were classified as probable and (34%) as possible. The causality assessment in a study done by Raja et al showed the most common one was probable in 62.5% cases, possible in 32.3% cases and 2.5% were uncertain which were in accordance with the present study though we had no cases of uncertain ADRs.¹³

The seriousness of reaction is also essential to take necessary action, which is an important factor in drug use. Among 330 ADRs which were found to be serious 98% and 1.3% were non serious, out of 292 serious ADRs, (35%) required intervention to prevent permanent damage and (51%) increased hospitalization or prolonged hospitalization. In a study conducted by Meda et al also majority of ADRs led to hospitalization/prolonged hospitalization (27.9%) and (31.8%) required intervention.⁶ In this study, most patients were recovered from the incidence (85%), not recovered (9.27%), unknown (4.46%), fatal outcomes (1.03%). Concomitant patient's disease may also influence susceptibility to ADRs. In this study, 51% had comorbidities. The mean number of comorbidities were 3.7. Of 330 forms, concomitant medication column was filled in 139 forms. Out of which 88% were given concomitant medications. Majority received 3 drugs (30.2%).

Multimorbidity and polypharmacy both were associated with incidence of ADR proven in study by Rostami et al.¹⁴ Comorbid conditions and their management are known to predispose to prescribing cascades and therefore polypharmacy. The number and severity of ADRs increases disproportionately as the number of drugs taken increases. We found an overall completeness score of approximately 80.60% with the lowest completeness score of 52% in 2019 and highest score of 100% in 2018. Completeness score was calculated based on 25 components: (name, age, weight, gender, date of reaction started, date of recovery, reaction or problem, generic name, dose, route, frequency, date of therapy started & stopped, indication, ADR management, reaction abated after drug stopped or dose reduced, Reaction reappeared after introduction, concomitant medications, Relevant test, Comorbidities, seriousness of the reaction, outcomes, Reporter details (name & qualification), causality assessment (WHO scale), Report date in suspected ADR form by AMC.

Each of these 25 components were given 1 point and zero to unfilled. Year wise completeness score in number and percentage are listed: 2022 in 8.78%, 2021 in 7.27%, 2020 in 9.08%, 2019 in 18.78%, 2018 in 37.57%. The overall

completeness score was similar to study conducted by Manali et al except that they have also analysed quality along with completeness of ADR forms using NCC instrument.¹⁵ Mandatory fields (patient initials, age at onset reaction, reaction, date of onset of reaction, suspected medication & reporter information) completely filled for 106 forms (32%) out of 330.

CONCLUSION

In this study, ADRs occurrence was high in male compared to female. Most of the ADRs affected Neuropsychiatry (18.78%) and Urinary (13.63%). Frequently occurred ADRs were hyponatremia followed by hypokalaemia, hyperglycaemia and rashes. Antimicrobials are responsible for 15.45% of reported ADRs and the frequently implicated classes were cephalosporins and penicillin. Of 330 ADR reports, Steroid caused only hyperglycaemia, acenocoumarol induced bleeding, levosalbutamol induced hypokalaemia, Enoxaparin induced haematuria and Ceftriaxone induced diarrhoea. Causality assessment of 50.7% reported ADRs were probable/likely. Of all ADRs reported, many of them were probable. Overall completeness of reported ADR form was 80%.

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