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A Prospective Study on Assessment and Reporting of Adverse Drug Reactions in a Tertiary Care Hospital

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ABSTRACT: Adverse drug reactions (ADRs) are unintended responses to a medicinal product. This scoping study seeks to offer a thorough map of the most frequent ADRs seen in a tertiary care clinical setting. The aim of this interventional study was to detect, analyze and report ADR in a tertiary care hospital. In addition, to derive a possible pattern of distribution in ADRs in different genders, drug classes, organ system etc., as well as assess its severity, preventability and trigger factors. A total of 179 subjects played an active role in this interventional study. Patients were examined in several departments of a tertiary care hospital for the development of ADR. ADRs were gathered from several clinical departments and evaluated for distribution patterns, trigger tool-based detection, and drug safety alerts-based detection of ADR. A total of 189 ADRs were listed, and most of the subjects studied were female. Approximately, 148 patients (82.6%) experienced adverse drug reactions during hospital stay. The majority of ADRs were reported to the general medical department 161(89.9%) followed by emergency 10 (5%) and cardiac department with 4(2%). Most common medical history showing the highest rate of ADR was hypertension 130(72%), followed by diabetic mellitus 116(64.8%) and infections 81 (45%). The high number of ADRs occurred in the 192(75.8%) oral route followed by the intravenous drip 19(7.5%) and intravenous Bolus 18 (7.1%). Most drug reactions due to oral medications were severe. The most common type of drug adverse reaction reported was type B 113 (63.12%) followed by type A 55 (30.72%). Out of 69 medication given for safety alert 25 medications were used in the hospital which produced ADRs. The Indian system for pharmacovigilance has a reporting pattern that is insufficiently utilised. Our research raises awareness of the problem of adverse medication responses in hospital patients and suggests alternate trigger use techniques as well as drug safety.

KEYWORDS: Pharmacovigilance, Adverse Drug Reactions, PvpI, Individual Case Safety Report, Signal dectection, Drug safety, Uppsala Monitoring Center.

I. INTRODUCTION

All pharmaceuticals have therapeutic effects, but none of them are entirely nonintrusive; as a result, prescribing them should be done with caution and a favorable risk-benefit ratio in mind. Adverse drug reactions (ADR) are more common in hospitalized patients who have a severe and complex disease or are subjected to polypharmacy, which might lead to drug interactions (1). The World Health Organisation (WHO) in 1972 defined Adverse drug reactions as "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 modification of physiological function". However, this term has been redefined over time in accordance to post marketing surveillance (2). In 1995 during the International Conference Harmonisation, a slight modification in the definition of ADR was made as "all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions" (2,3). Pharmacovigilance is defined as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems"(7).The Pharmacovigilance Programme of India (PvPI) is a key player in obtaining drug safety data and reporting it to the World Health Organization's database. PvPI meets the WHO's minimal requirements for any functioning national pharmacovigilance system. PvPI's national coordinating centre is the Indian Pharmacopoeia Commission (IPC). An assessment of the likelihood that a medication was the causative agent of reported ADRs is known as causality assessment. The goal of establishing a causal link between an event A (in pharmacovigilance; the drug) and an event B (the ADR) is to show that A precedes and causes B. This link is difficult to establish and is

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dependent on the facts provided. Recognizing ADRs and establishing a statistical correlation between the medication and the adverse event is critical (13). The WHO has defined a signal as "Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending on the seriousness of the event and the quality of the information" (17). A signal is also a relationship that is thought to be significant enough to examine further. A signal might relate to new information about an existing relationship.

II. OBJECTIVE

To detect, assess and report the pattern of distribution of adverse drug reactions in a NABH accredited Tertiary Care Hospital through WHO-ADR database.

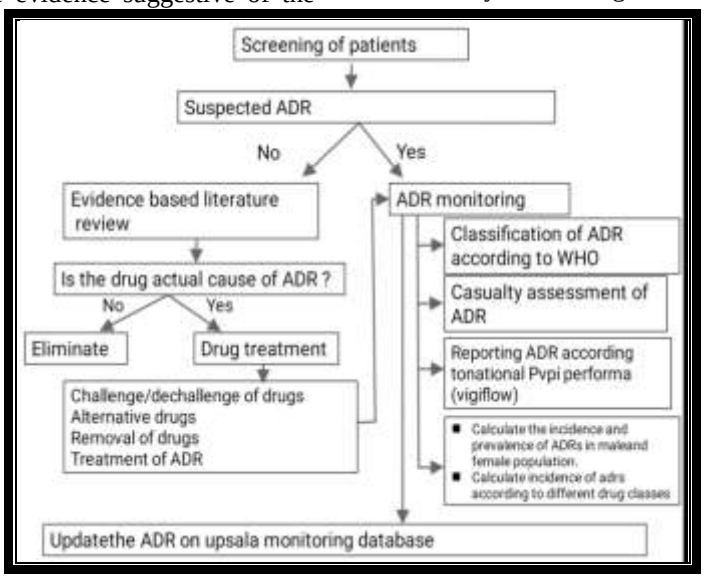
III. METHODOLOGY

In this method, the respective ward or department visit was done and the necessary details were collected. In active vigilance, a medication history interview was done with the patient just as he/she was admitted to the ward. During this interview, if it was found that the patient was having any reaction due to the test dose or overdose, those patients were excluded from the study. If the patient did not fulfill these criteria, then daily follow up with the treating doctors was done in which any subjective or objective evidence suggestive of the patient experiencing the ADR was noted, and such patients were further followed up. Detailed analysis, evaluation, and discussion with the consultant were done in the case of a strongly suspected ADR.

A step by step causality assessment was done with suitable tools and instruments. The suspected drug was investigated to identify if the use was off-label, the suspected reaction was studied. The distribution of adverse drug reactions was studied between male and female patients in order to identify if there is any association between adverse drug reactions and the patient gender. The drugs causing the ADRs were recorded, and their classes were identified according to the classes of drugs that cause ADRs more frequently.

OPD visits were made daily, where the out-patient case files were studied. The patient's complaints in each visits were reviewed for detection of possible acute and chronic ADRs. The ADRs were then suspected and reported. The suspected drugs were then examined, and any necessary dose reduction or dechallenging was done. The detected ADRs were then updated in the Vigiflow database.

After the complete assessment of the ADR, these were then reported to adverse drug reaction monitoring centers (AMCs) in Bangalore Baptist Hospital. These ADR were then discussed in the physician and therapeutic committee (PTC) to help them with the administrative decision whether to continue with the same products or change the brand by withdrawing the drug from the hospital formulary and finding a suitable replacement.



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IV. OBSERVATIONS

Distribution of ADR According To Seriousness:

Results in death 0 (0%), Disabling/incapacitating 8 (4%), Life threatening 19 (10%), Congenital anomaly/ birth defect 3 (1.5%), Caused/ prolonged hospitalization 114 (60%), Other medically important condition 45 (24%)

Seriousness of ADR	Number of ADR	Percentage
Results in death	0	0 %
Disabling / incapacitating	8	4 %
Life threatening	19	10 %
Congenital anomaly / birth defect	3	1.5 %
Caused / prolonged hospitalization	114	60 %
Other medically important condition	45	24 %

Distribution of ADR according to Modified Hartwig Severity Assessment Scale (Levels):

Level 1-15 (8 %), Level 2-40 (21 %), Level 3-30 (16%), Level 4(A)-51 (27 %), Level 4(B)-35 (19 %), Level 5-11 (6 %), Level 6- 7 (3.7 %), Level 7-0(0 %)

Modified Hartwig Severity Assessment Scale	Number Of ADR	Percentage	Modified Hartwig Severity Assessment Scale
Level 1	15	8 %	Level 1
Level 2	40	21 %	Level 2
Level 3	30	16%	Level 3
Level 4(A)	51	27 %	Level 4(A)
Level 4(B)	35	19 %	Level 4(B)
Level 5	11	6 %	Level 5

Distribution Of ADR According To Modified Naranjo's Algorithm :

Definite 11(6 %), Probable 129(68%), Possible 49(26 %), Doubtful 0(0 %)

Modified Naranjo's Algorithm	Number Of ADR	Percentage
Definite	11	6 %
Probable	129	68 %
Possible	49	26 %
Doubtful	0	0 %
Total	**189**	**100 %**

Distribution Of ADR According To WHO Casualty Assessment Scale :

Certain 11(6%), Probable 129(68 %), Possible 49(26 %), Unlikely 0(0 %), Unclassified 0(0%), Inaccessible 0(0%)

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WHO Casualty Assessment Scale	Number Of ADR	Percentage
Certain	11	6 %
Probable	129	68 %
Possible	49	26 %
Unlikely	0	0 %
Unclassified	0	0%
Inaccessible	0	0%
Total	**189**	**100 %**

Modified Thornton & Schumock's Preventability Assessment Scale :
Definitely Preventable 3(2 %), Probably Preventable 17(9 %), Not Preventable 169(89 %)

Modified Thornton & Schumock's Preventability Assessment Scale	Number Of ADR	Percentage
Definitely Preventable	3	2 %
Probably Preventable	17	9 %
Not Preventable	169	89 %
Total	**189**	**100 %**

Distribution Of ADR According To Will's And Brown Classification:
Type A 55(29 %), Type B 113(60 %), Type C 14(7 %), Type D 7(4 %), Type E 0(0 %)

Will's And Brown Classification Of ADR	Number Of ADR	Percentage
Type A	55	29 %
Type B	113	60 %
Type C	14	7 %
Type D	7	4 %
Type E	0	0 %
Total	**189**	**100 %**

V. DISCUSSION

In a study conducted by **Inamdar et.al** an analysis of reported ADR types revealed that the highest number of ADRs were type A (34%) (68%) followed by type B with 14 (28%) followed by type F of 2 (4%)) but in our study the most common type of drug adverse reaction reported was type B 113 (63.12%) followed by type A 55 (30.72%) third type common as type C 14 (7.8%) and lastly, type D 7 (3.9%) as the most common adverse drug side effects reported. The distribution pattern varies because the drug used varies in both settings, therefore, the ADR type pattern will vary.

The casualty assessment tests were performed using the NARANJO scale algorithm. As mentioned in other studies **C. Dilip et al, Nathan et al, JM. Lucca et al**. caused by Naranjo's algorithm was probable in this study (41) (42) most ADRs had a specific causality.

Post Marketing safety markers have made the casualty assessment test very important. But in our study of 179 adverse drug responses it was noted that 129 (72.06%) of them were probable, followed by 49 (27.37%) possible and while 11 (6.1%) were definite.

The casualty assessment tests were performed using the WHO casualty assessment scale. In a our case study we found that of the 179 drug reactions of 129 (72.06%) of them were probable, 49 (27.37%) possible, 11(6.1%) certain. **Makedo et al** has shown that probable and possible to be the most common casualty assessment test (68%) of ADR tests on the WHO scale. The ADRs test using the WHO-causality scale in a study conducted by **Garg et.al** found that 80% cases were probable, 27% were possible and 3% were uncertain.

Assessment of severity is also important to take the necessary steps in drug progression. The severity of the drug side effects reported during the study was determined using the modified Hartwig test assessment scale. The results of the severity assessment tests suggested that the highest rate of adverse drug reactions was found to be level 2 - 79(44.13%), level 1 - 31(17.31%), level 3 - 30(16.75%), level 4(B) - 19(10.61%), level 4(A) -

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12(6.7%), level 5 - 11(6.1%), level 6 -7(3.9%). Out of 179 adverse drug reactions reported in our project it was recorded that the severity of most reactions were Moderate 116(61 %), followed by Mild 55(29 %) and lastly, Severe 18(10 %).

A severe ADR " any untoward medical occurrence that at any dose results in death, requires hospital admission or prolongation of existing hospital stay, results in persistent or significant disability/incapacity, or is life threatening" according to one of the studies by **IslamLJ Et.al**.In a study conducted by **S.inamdar et.al** to assess the severity of the reported ADRs Hartwig scale used, which revealed that an moderate of 26 (52%) cases, 17 mild cases (34%) and 7 (14%) severe cases, similar to a study by **Padmavathi S et al**. The majority of patients receiving multidrug therapy have developed a more severe response than others.

The modified Thornton and Schumock's preventability scales were used for adverse drug reaction tests. Most of the side effects of the drug were Not Preventable 169(89.4%), Probably Preventable 17(8.9%), Definitely Preventable 3(1.5%). These results are different from other studies. In one of the studies conducted by **S.Behra et.al** most ADRs were tested for safety followed by preventable and safe exactly the results of **Tiwari et.al**, which also tested many probably preventable ADRs (95%) followed by definitely preventable(5%). The very high number of ADRs in the probably preventable category indicates a wide range of advances in current prescribing practices. A non preventable reaction may be unpredictable and may occur after a single dose, caused by an allergic reaction (allergy to drugs), genetic abnormalities (idiosyncrasy). Methods for reducing the severity of non preventable ADRs are the use of appropriate rehabilitation and support mechanisms and rapid ADR identification such as taking appropriate drug history, studying patient case records, choosing alternative therapies with different chemical properties, and patient treatment symptoms.

Multiple Adverse drug reactions required ADR interventions to prevent permanent damage. Out of 189 drug reactions, most of the reactions Caused / prolonged hospitalisation 114(60.3%), Other medically important condition 45(23.8%), Life threatening 19(10%), Disabling / incapacitating 8(4.2%),Congenital anomaly / birth defect 3(1.5%).

VI. CONCLUSION

According to this study, there is a great need to simplify the hospital-based ADRS reporting and monitoring system to create awareness and promote ADRS reporting among health professionals. Drug reactions are unavoidable with the use of modern medicine. Adverse drug reactions are one of the major drug-related problems in a hospital setting and are a challenge to ensure drug safety. Our study data will provide an understanding of the pattern of ADRs occurring in tertiary care hospitals with an equal pattern of patient statistics, intelligent data distribution and drug use for intelligent drug response reporting.

The Pharmacovigilance Indian system has an inadequate reporting pattern. Limited comprehensive awareness programs are aimed at health workers at each level. Improving patient safety reduces the likelihood of drug reactions. There are a variety of advanced methods that receive drug reporting. Our study draws attention to the problem of drug reactions patients in hospitals suggest alternative trigger use methods and drug safety.

Pharmacists, doctors, and volunteers in reporting ADRS .They can reduce ADRs and provide better health for patients. This can provide benefits to the organization, pharmacists, other health professionals, and patients. Although the current study has some limitations, this study will inevitably provide insight into the ADRS pattern in a health care institution in a tertiary institution and may help increase awareness of additional pharmacovigilance studies.

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