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Original Article

Pharmacology Section

A Retrospective Analysis of Reporting of Adverse Drug Reactions in a Tertiary Care Teaching Hospital: One Year Survey

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ABSTRACT

Introduction: Pharmacovigilance (PV) is related to detection, assessment, understanding and prevention of Adverse Drug Reactions (ADRs) which are incurred when drug is made available in the market and used in different physiological conditions. In many countries, ADRs ranks among the top ten leading cause of morbidity and mortality. There is a lack of formal culture for monitoring and reporting of ADRs in India, with ADR reporting rate being only 1% as compared to 5% in world. This type of academic detailing activity helps to create awareness of ADR reporting in the institutions.

Aim: This study was planned to evaluate and analyse the incidence and patterns of ADRs in various inpatient and outpatient departments of hospital.

Materials and Methods: This was an observational, retrospective and record based study conducted by analysing the spontaneous ADR forms, collected over a period of 12 months (September 2014 to August 2015) at Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India.

Results: During the period of one year, 292 ADR forms were collected from 4,34,965 patients attending OPD and inpatients of the hospital. Incidence of ADR was 0.67 per thousand patients and average of around 24 ADR collected per month. Male:Female ratio was 1.30. Adolescent (16-30 yr) was the most common age group affected. Department of Skin and VD reported the maximum number of ADRs (33.22%), followed by the Departments of Oncology (18.84%). Antibiotics were the most common drug implicated followed by anticancer drugs.

Conclusion: ADR reporting is an ongoing and continuous process. Studies from the institute helps to identify and rectify the problems related to ADR reporting. Pitfalls can be addressed by creating awareness among physicians and the patients to achieve finally the goal of Pharmacovigilant India.

Keywords: ADR reporting, Drugs, Pharmacovigilance, Pharmacovigilance program of India

INTRODUCTION

India is a country with large ethnic variability, variable disease distribution and practicing several different systems of medicine ranging from ancient, traditional to the modern and scientific systems of medicine. There is wide gap in affordability of Indian population owing to its variation in socioeconomic status [1]. Indian pharmaceutical industry values around $18 billion dollar, one of the largest in the world, growing at the rate of 12-14% per annum and exporting 40% of generic medicine to the world [2]. Globally Indian pharmaceutical industry ranks fourth, represented by over 6000 licensed drugs and still increasing day by day [3]. But there is lack of a formal culture for monitoring and reporting of adverse drug reactions (ADRs) in India, with ADR reporting rate being only 1% as compare to 5% in world [4]. Thus proactive Pharmacovigilance (PV) throughout the life cycle of drug is need of the hour. PV deals with the detection, assessment, understanding and prevention of ADRs [5]. It is related to the protection of public health and monitoring of ADRs which are incurred when drug is made available in the market and used in different physiological conditions.

Reporting of ADR in India is not new as the formal approach to monitor and report ADR was started almost 30 years back in 1986 by some physicians from academic institutions [6]. They highlighted the potential adverse effects of prescription medicines and stressed the need of rational prescribing. Thus first ADR monitoring programme was started with 12 regional centers, each covering a population of 50 million. But indeed this could not attain success and remained idle for more than a decade. India joined the WHO ADR Monitoring Program Uppsala, Sweden in 1997 and three centers were started in medical colleges at New Delhi, Mumbai and Aligarh. However, this attempt could not get any success. The new year of 2005 brings some good news for Pharmacovigilance in India as on 1st January 2005, the WHO sponsored and World Bank funded National PV Program (NPVP) for India was made operational and India became member of WHO Programme for International Drug Monitoring managed by the Uppsala Monitoring Centre (UMC), Sweden. Footsteps of this programme paved the way for improved ADR monitoring system in India and in July 2010, a nationwide revised ADR monitoring programme was launched and named as Pharmacovigilance Programme of India (PvPI) under the aegis of Health Ministry, Government of India. Initially AIIMS, New Delhi was made the National Coordination Centre (NCC) for this programme and later in April, 2011, it was shifted to Indian Pharmacopoeia Commission (IPC), Ghaziabad. Under this programme, till date over 150 AMCs (ADR Monitoring Centers) are formed in Indian medical colleges covering the entire country. Each AMCs is responsible for collecting ADR reporting forms filled by the clinician in their college and nearby hospitals and to upload these reports in net- based software used for ADR reporting called as vigiflow as well as performing the follow-up of the reported cases as per their Standard Operating Procedure (SOP) [7].

ADRs is any harmful or unpleasant response to a medicinal products which is unintended and which results at doses normally used for diagnosis or treatment of disease and its future administration to the patient warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product. ADRs are of six types. Type A is dose-related, Type B is non-dose-related, Type C is dose-related and time-related Type D is time-related, Type E is withdrawal and Type F is failure of therapy [8]. It accounts for increased patient suffering, hospitalization and economic burden to the patient and has considerable negative impact on quality of life for patient and one of the reasons for poor drug compliance. In many countries, it ranks among the top ten leading cause of

cause of morbidity and mortality in both ambulatory as well as hospitalized patients [9]. Due to this reason it has become the integral part of drug therapy and voluntary reporting of ADR is being promoted aggressively.

Till date over one lac Individual Case Safety Report (ICSRs) have been submitted in WHO-vigibase [7]. This large number becomes very tiny when we consider this in world scenario as India is home to over 15% of world population but with increasing number of new drugs in the market and lack of a formal culture for monitoring and reporting of ADRs in India; our share is meagre 1.8% of total ADR reported worldwide. Our ADR reporting rate being only 1% as compared to 5% in world [10]. So voluntary reporting is the need of the hour and not only voluntary but also passive reporting from consumers are being promoted.

Study by Tandon et al., suggests several reasons for under reporting of ADR in India. These include complacency, fear of litigation, guilt, ambition, ignorance, lethargy, lack of awareness, motivation, training and most importantly, time among health care providers [11]. So while the exact epidemiological data from government institutions remains to be known in India, a productive, institutional reporting can be instrumental in providing valuable information regarding the potential problems of drug usage in this institution.

The main goal of this initiative is to ensure that the benefits of use of medicine should outweigh the risks as drugs are popularly said as a double edge weapon having potential to cause benefit as well as harm [12]. Till now there is not a single study available on this important aspect of treatment from our institution. Thus, one of the aims of the study is to create awareness among clinicians of this institution and with this we can move forward to inculcate the culture of ADR reporting. Therefore, this study was planned to evaluate and analyse the incidence and patterns of ADRs with the help of the reports collected from various inpatient and outpatient departments of the hospital as well as to study the drugs and organs involved in ADR and to create awareness of ADR reporting. Regional data generated from this study will also help in planning the institute/ state health policy.

MATERIALS AND METHODS

This was an observational, retrospective, record based study conducted by analysing the spontaneous ADR forms, collected over a period of 12 months (September 2014 to August 2015) at Indira Gandhi Institute of Medical Sciences, which is a tertiary care reference centre and a teaching hospital located in Patna and is the only super specialty government hospital in Bihar. The ADR monitoring centre of IGIMS Patna is one of the peripheral ADR monitoring centers of the PvPI. ADR monitoring centre is coordinated by the Institute's Department of Pharmacology. The study was commenced after obtaining approval from the Institutional Human Ethics Committee. All spontaneously reported ADR forms collected during Sept 2014 to Aug 2015 were evaluated. The reporting physician was contacted for the collection of any further information when it was necessary. The causality assessment for suspected drug in terms of "certain," "probable," and/or "possible" were done with the help of Naranjo's algorithm [13]. Cases of drug poisoning, medication errors, doubtful causality, and ADR forms with insufficient information were excluded from the analysis.

The data on the reported ADRs were analysed and evaluated under various parameters as:-

Patient characteristics: The patient's age and sex were considered for evaluation.

Reaction characteristics: The individual reactions were classified, depending on the organ system which was affected.

Drug characteristics: The offending drug causing ADR were classified into drug classes and were further classified, based on their route of administration.

Causality assessment: Each ADR was assessed for its causality by using the Naranjo Probability scale as definite, probable and possible [13].

Severity assessment: The ADRs were classified into mild, moderate and severe depending on their severity with the help of severity assessment criteria developed by Hartwig et al., [14].

Outcome assessment: The patient outcomes were reported as one of the following: Fully recovered, Recovering, Unknown, and Fatal.

Management of ADR: The management categories for ADR were abatement of drug, substitution of drug, dose reduction, additional intervention for ADR, or no change in regimen with no additional treatment.

RESULTS

Characteristics of the patients

During the period of one year Sept 2014 to August 2015, total number of patients attending the hospital were 4,34,965 this included OPD and inpatients. During the same period total number of ADR reported spontaneously from various departments of the hospital were 292. The number of ADRs reported was variable, with an average of around 24(24.33%) reports generated per month with maximum reporting in the month of June(29) and minimum reporting in the month of November(16) [Table/Fig-1]. Incidence of overall ADR in the hospital during study duration was 0.67 per thousand patients.

Males experienced more ADRs (165, 56.51%) than females (127, 43.49%). Male: Female ratio was 1.30 [Table/Fig-2].

The maximum number of reported ADRs were found in the adolescent (16-30 y) group (99, 33.90%), followed by the adult group (81, 27.74%) and the older group (51, 17.47%), while pediatric and elderly group had around 10% ADR each [Table/Fig-3]. The youngest patient was a one-year-old male child and the eldest was 98-year-old male.

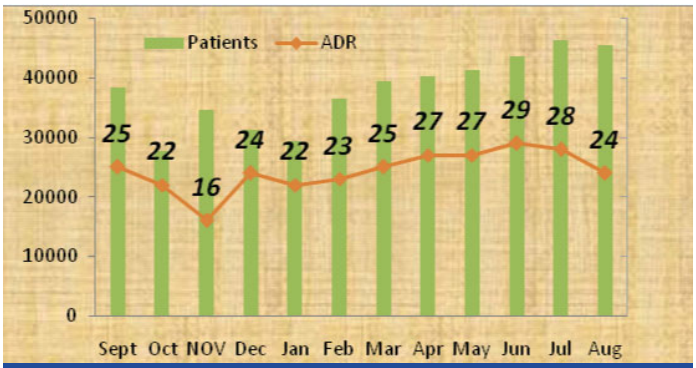
ADRs

The Department of skin and VD reported the maximum number of ADRs (97, 33.22%), followed by the Departments of oncology (55,18.84%), Department of general medicine followed with 41 (14.04%) reports [Table/Fig-4]. Some ADR, 5 (1.71%) were also reported voluntarily by patients through the toll free number, these were labeled separately as "Self". This small number was also very encouraging for us as these it was generated passively so it would help to broaden the coverage of data collection. It was evident from the data that over two third of the ADR reported from the above said three departments, while the rest 15 contributed only one third of cased of ADR.

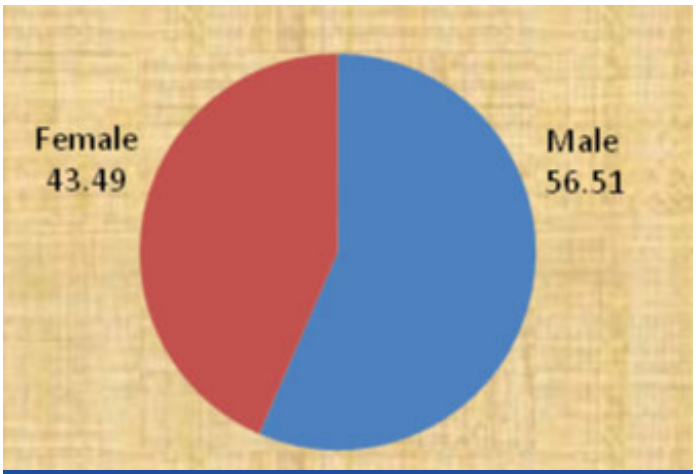
The intravenous route was responsible for the ADR causation in 161 (55.14%) cases as compared to the oral 112 (38.36%) [Table/Fig-5]. Other routes like Topical, intramuscular, subcutaneous, intradermal, and nasal routes together constituted only 6.5% of ADR cases.

Among the drugs, the antibiotics were implicated in the maximum number of times (129, 44.18%), followed by anticancer (39, 13.36 %), blood and other products (34, 11.64%) and autacoids (27, 9.25%). The comprehensive information which depicted the drugs and percentage of ADR as was seen during the study is shown in [Table/Fig-6].

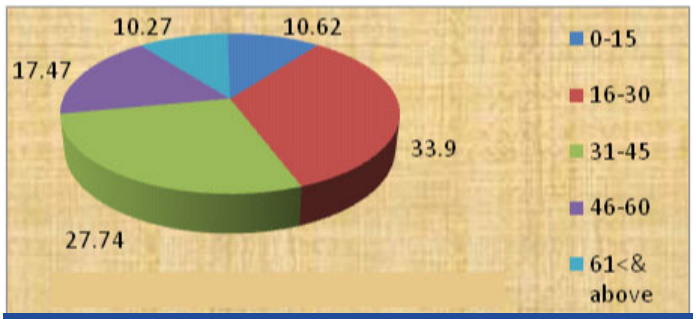
Most of the ADRs were categorized as "Type B" 235(80.47%) against "Type A" 57(19.52%). Of all the ADR reported, possible ADR 154(52.73%), were more than probable 127,(43.49%) and very small ADRs were found to fall in the in definite one 11(3.76%). 256(87.74%) patients were completely recovered and 34(11.64%) were in the process of recovery. Outcome was fatal in two cases.



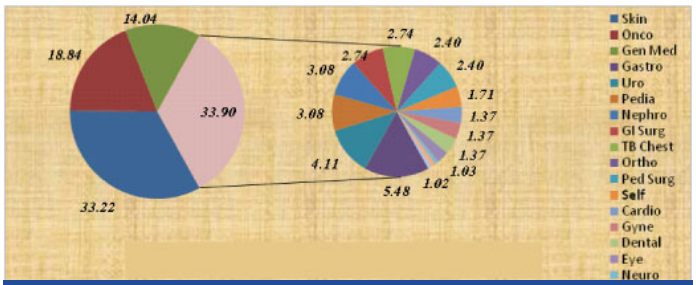
[Table/Fig-1]: Hospital patient data (in no.)



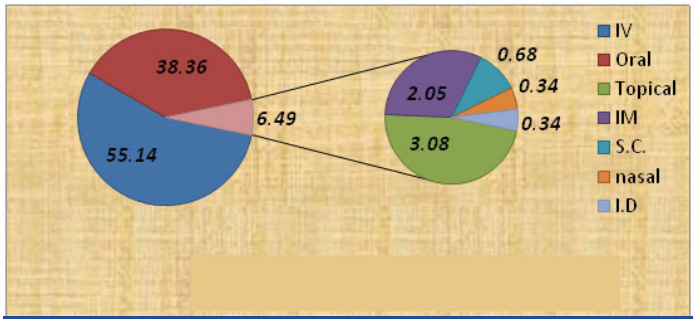
[Table/Fig-2]: Sex distribution (%).



[Table/Fig-3]: Age distribution of patients with ADR (in %).

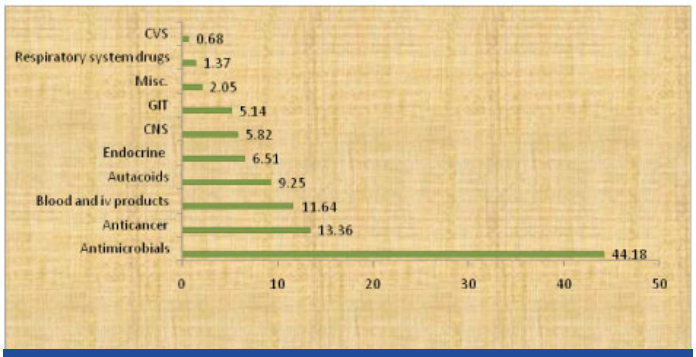


[Table/Fig-4]: Dept. wise distribution of ADR (%).



[Table/Fig-5]: Routes of Admn (%).

The offending drug was abated in 150 (51.36%) cases, substituted in 66(22.60%) cases, other drug was added in 21(7.19%), dose was decreased in 7(2.39%) and no change was made in 48(16.13%) cases.



[Table/Fig-6]: Drug distribution according to organ system involvement (%).

DISCUSSION

ADRs are common in clinical practice but these are often missed by the clinician and even if they are recognized and reported by patients or clinician they are under-reported as many physicians are unaware that clinically important ADRs should be reported to ADRs monitoring centers. In our study we found 292 ADR in the study duration of year, of which we lost two patients unfortunately, however these were also reported by our clinicians bravely. Incidence of ADR was higher than the study by Bhabor et al., where the incidence was 0.25 ADR per thousand patients [15]. Average ADR collected per month was higher than the study done by Arulmani et al., (20/month) in south India [16]. Our study show the striking resemblance to the study by Tandon et al., that in both the study least number of ADR was reported in month of November [11]. This signifies the role of human resources and this can never be overlooked as major festivals, holidays, exams etc grossly affect the consistency in ADR monitoring and reporting due to obvious reasons.

Demographic data showed higher incidence of ADR in males and this was similar to study of Sharma H et al., and differs from other studies where female gender was considered as a risk factor for ADR [17]. Adolescents showed higher frequency of reaction which differs from previous studies where incidence of ADR was high in elderly [6].

ADR

Majority of ADR in our study was related to intravenous route. This was in contrast to the study by Sharmna et al., where oral route was the major contributor [9]. However, intravenous and oral routes together constituted over 93% of ADR. Similar to the study by Khobragade A, our study also reported highest number of ADR from dermatology while gynaecology, ophthalmology and ENT reported least or no of ADR [12].

Every second ADR in this study was related to either antimicrobials or autacoids. Such high incidences of ADR with these drugs were also seen in some previous studies [16]. Logically these two are the commonly encountered drug class in clinical practice. Over 50% reactions in our study, causality assessment was “probable” also the incidence of type B reaction i.e. non dose related or bizzare in our study, this was similar to study by Khobragade A [12]. 60% of ADR cases in our study recovered completely. This was similar to a study done by Arulmani et al., [16]. Offending drug was discontinued in (51.36%) of ADR. This was similar to previous studies [17] but in our study anticancer drugs were continued later once the reaction was abated due to limited options with these drugs.

LIMITATION

Present study is more or less in accordance with the previous studies but also had certain lacunae like issues with polypharmacy, difficulties in causality assessment as re-challenge test was attempted rarely (ethical concerns) and recovery was unknown in some cases due to difficulty in follow-up needs further evaluation.

CONCLUSION

ADR reporting is essential for drug safety evaluation in the post marketing phase. It is an ongoing and continuous process. Studies from the institute helps to identify and rectify the problems related to ADR reporting. Certainly there are some obstacle in reporting the ADR like problems with polypharmacy, diagnosis of ADR, problems with lack of time and high workload on physicians etc. Considering the need to create awareness and to promote the reporting of ADR amongst doctors we in our institute are taking steps to improve the ADR reporting by organizing seminars, workshops for clinicians and paramedical staffs, one to one contact with the clinicians, our technical associate is also working tirelessly round the clock to collect ADR reports. We have facilitated an easy contact and quick access to the hospital ADR monitoring centre with the help of tollfree number displayed over OPD prescriptions. We are also organizing one workshop on ADR reporting exclusively for budding healthcare professionals the interns in our institute as they are the future clinicians as well as the backbone of our healthcare systems and by training them we are creating "agent of transformations" in the field of ADR reporting and Pharmacovigilance.

By this study we conclude that pitfalls in ADR reporting can be addressed by creating awareness among physicians and the patients to achieve finally the goal of Pharmacovigilant India.

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