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A SYSTEMIC REVIEW ON ADVERSE DRUG REACTIONS REPORTED IN A PERIOD FROM 2014 TO 2018 IN DIFFERENT PARTS OF INDIA

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ABSTRACT

One of the main causes for the morbidity and the mortality in the world is Adverse Drug Reaction(s) [ADR]. Thalidomide tragedy is the best example for ADR after which international attention to patient safety was gradually increased. There was global occurrence of 10% of ADRs where 2% were reported in India. Major contributors for morbidity, mortality and hospitalization of patients and increasing economic burden of patients are ADRs. CDSCO and Pharmacovigilance play a key role in the identification of ADRS. This study was carried out by collecting different ADRs collected and reported by health care professionals at different places of India. Underreporting was the main problem in reporting an ADR which can be overcome by following spontaneous reporting system. Most vulnerable organs for ADRs are Gastrointestinal tract along with skin & appendages. Antimicrobials are the class of drugs which majorly causes ADRs. Adults and middle aged are common group of people affected due to ADRs. Causality, severity and preventability were calculated using different scales like WHO-UMC causality assessment scale, Naranjo causality assessment scale, Hartwig's severity assessment scale and Schumock and Thornton Preventability assessment scale.

KEYWORDS: Adverse Drug Reaction, ADRs reported in different parts of India, vulnerable organs for ADRs, Most ADR causing drugs.

INTRODUCTION

One of the main causes for the morbidity and the mortality in the world is Adverse Drug Reaction(s) [ADR]. A best example for ADR was Thalidomide tragedy which occurred during late 1950's. An ADR is an untoward effect which can occur even when the drug is given within the therapeutic range.[1]

The most common cause for the medical intervention is drugs, which uses generally for diagnosis or prevention or mitigation. So, the saying goes "Drugs are double edged weapons".[2] One of the important cause for increasing mortality and morbidity in ambulatory and hospitalized patients were Adverse Drug Reactions. [3] Age, gender, co-morbidities, genetic factors are the patient related factors and route of administration, time of administration, duration of therapy, type of drug and dosage of drug are the drug related factors which influences the severity and incidence of Adverse Drug Reaction.[2]

According to World Health Organization (WHO) – ADR is any response to a drug which is noxious, unintended which occurs at doses normally used in man for prophylaxis or diagnosis or therapy of disease or for the modification of physiology of the body.

According to Karch and Lasagna – An ADR is any response to a drug that is noxious and unintended which occurs at doses used in humans for prophylaxis or diagnosis or therapy excluding failure to accomplish the intended purpose.

An important tool for the collection of ADR is to establish a relation between drug and it's reactions. For the betterment of the ADR reporting FDA categorized the serious adverse event into life threatening, initial or prolonged hospitalization, disability, congenital anomaly, required intervention to prevent permanent damage.[1] Proper monitoring of ADRs can prevent the occurrence.[2] Pharmacovigilance and CDSCO (Central Drug Standard Control Organization) are helpful for reducing the preventable adverse drug reactions. [3 & 4] A health care professional (HCP's) plays a vital role in reporting the adverse drug reaction(s). ADRs reported by health care professionals created information to generate new signals which helped in updating the knowledge of other HCP's.[4] There are different scales for the

assessment and monitoring of ADRs. The most commonly used scales are WHO causality assessment scale, Naranjo scale, Hartwig's scale, Schumock and Thornton scale etc.

MATERIALS AND METHODS

Eleven research articles published in different journals were taken. Those studies were held in different places of India. The methodology of the taken studies was as shown in table -1.

Table 1: List of studies with the details of author, year of publication, study design, study period, sample size, data base used.

Study	Author	Year	Study Design	Study Period	Study Settings	Sample Size	Data base
1.	Siavash Shabazi Nia	2018	Prospective Observational	24 months	General Medicine, Intensive Care Unit	385	MS Excel
2.	More Pankaj Daulat	2018	Retrospective Observational	6 months	Complete Hospital	290	Proportion test & R software
3.	R. Vijai Shri	2017	Prospective Interventional	6 months	General Medicine, Surgery, Intensive Care Unit, Respiratory Medicine, Nephrology departments	1138	MS Excel, Medline & Embase
4.	Parvati B. Patel	2017	Prospective Cross-sectional	12 months	Complete Hospital	208	VigiFlow
5.	Ayan purkayastha	2017	Retrospective	12 months	Department of Pharmacology	162	MS Excel using Chi square test
6.	Ratan J. Lihite	2017	Prospective Observational	6 months	Out Patients, In-Patients of Cardiology, Dermatology, Gynecology, Hematology, General Medicine, Opthalmolog, Pediatrics, Psychiatry, Neurology & Respiratory Medicine departments	219	MS Excel
7.	Prashant Shukla	2017	Retrospective Observational	10 months	Complete Hospital	175	MS Excel
8.	Bhabagrahi Rath	2017	Retrospective Cross-sectional	24 months	Complete Hospital	238	MS Excel
9.	Anup Kumar	2016	Retro-Prospective Observational	12 months	Internal Medicine department	2036	MS Excel
10.	Kavita Dhar	2015	Prospective Observational Non-interventional	6 months	Complete hospital	126	MS Excel
11.	Tejas Kamaleshba-hi Patel	2014	Prospective	12 months	Complete Hospital	389070	Graph Pad Prism 6.0 version

RESULTS AND DISCUSSION

Study 1: Among 385 patients 390 ADRs were reported in the study period of 24 months. Majority of cases were reported in Females (221) when compared with Males (164). Among the reported ADRs each 2 reactions were found 5 cases and the remaining 380 cases were reported with single ADRs. Mostly affected age group was 31-40years (109 patients) were reported with ADRs, followed by 41-50years (86 patients), 21-30 years (62

patients), 51-60 years (41 patients), 61-70 years (32 patients), 11-20 (26 patients), 71-80 years (18 patients), 1-10 years (8 patients) and above 80 years (3 patients). Majority of ADR causing drug classes were Antimicrobials (156), Cardiovascular agents (109), Anti-asthamatic agents (28), Anticonvulsants (28), Steroids (21), Analgesics (14), Supplements (13), Anti-anxiety agents (9), Anti-thyroid (6), Anti-depressants (3) and Antacids (3). The most commonly affected systems due different ADRs were Gastro Intestinal Tract (141) followed by Fluid and electrolytes (57), Nervous system (48), Dermatology (44), Endocrine (28), Hematological (26), Cardiovascular (22), Respiratory (10), Renal (9), Musculo-Skeletal (3) and Ophthalmic (2). The most commonly reported ADRs were elevated LFT, diarrhea, itching, hypokalemia, hyponatraemia, hypoglycemia, rashes, drowsiness, vomiting, hyperglycemia, edema, bradycardia and others. Among the suspected ADRs depending upon Naranjo Causality Assessment Scale 215 was probable, 141 were possible and 34 were doubtful. Depending upon Hartwig and Seigel's Severity Assessment Scale mild were 327, moderate were 62 and severe was 1.[6]

Study 2: 290 ADRs were found in 10094 during the time period of 6 months. Among the reported ADRs 146 were found in females and 144 in males. System that was mostly vulnerable to ADRs was gastrointestinal tract followed by central nervous system, skin and appendages, hormones, electrolytes, cardiovascular system, blood and respiratory system. The most common ADR was constipation followed by vomiting, diarrhea, pruritis, headache, rash, blurred vision, sedation, oral candidiasis and angioedema.[7]

Study 3: A total sample size of 1138 were taken out of which 742 were treated by means of single Antibiotic, 576 were treated with two antibiotics, 276 were treated with three antibiotics and 64 were treated with four antibiotics. Among all the patients 143 ADRs were identified. Among the reported ADRs 51.74% were male and 48.25% were female. Based on the departments in the hospital most of the ADRs were seen general medicine followed by Surgery, Pulmonology, Nephrology and Intensive Care Unit. As per age, middle aged persons (45-65years) were mostly affected followed by geriatrics, adults (19-45years), pediatrics (0-8years). The most commonly affected organ was Gastro Intestinal Tract followed by skin & appendages, respiratory system, nervous system, musculoskeletal system, haemopoietic system and cardiovascular system.[4]

Study 4: A total number of 449 ADRs were reported out of which 276 were reported by students and 173 were reported by physicians. Among the reported ADRs 280 were Augmented and 169 were Bizzare. As per causality assessment 1 was certain, 210 were probable, 238 were possible and 25 were serious. Mostly affected organ was gastrointestinal tract followed by skin, appendages, nervous system, urinary tract, respiratory tract and cardiovascular system.[5]

Study 5: Among 162 collected ADR forms 96 were Females and 66 were Males. The age group who were majorly affected was 16- 30 years with 71 ADRs, followed by age group of 31-45years with 65 ADRs, >60 years group with 15 ADRs, age group of 46-60 years with 8 ADRs and age group of 0-15 years with 3 ADRs. Among the reported ADRs 150 were serious and 12 were non-serious depending upon nature on seriousness of ADRs. As per WHO-UMC causality 120 were probable, 42 were possible. Among 162 ADRs 69 were anaphylactic reactions which occurred due to Iron Sucrose (33), Amino-acid derivatives (16), Human Albumin (9), Anti-microbials (9), Blood transfusions (1) and 5% DNS (1). The types of anaphylactic reactions were Maculopapular Rash (15), Erythromatous Rash (10), Utricarial rash(6), Extrapyramidal symptoms (6), Fixed drug eruption (5), Steven Jhonson Syndrome (4), Toxic epidermal necrolysis (3) and others (20) such as fever, vomiting, respiratory discomfort and itching.[8]

Study 6: A total of 303patients were reported with ADRs among which 84 patients s were discarded from the study due to presence of more than one offending drug which causes ADR. Among 219 patients reported with 255 ADRs. ADRs were majorly reported in female (118) when compared to male (101). Out of 219 patients single ADRs were found in 124 patients, two ADRs were found in 73 patients, three ADRs were found 19 patient and four ADRs were found in 3 patients. Out-patients (91.7%) reported with more ADRs when compared to in-patients (8.2%). ADRs were most commonly seen in the age group of 21-30 years (37.4%) followed by the age group of 31-40 years (20.5%), 11-20 years (15.5%), 41-50 years (13.6%), 51-60 years (5.4%), 1-10 years (5%) and above 61 years (2.2%). The departments that reported most of the ADRs was Dermatology followed by Hematology, Psychiatry, General Medicine, TB & Chest, Cardiology, Gynecology, Pediatrics, Neurology and Opthalmology. Depending on the Naranjo Causality Assessment Scale 240 ADRs were classified as possible, 10 were classified as probable and 2 ADRs were classified as definite. According to Hartwig's Severity Assessment Scale mild ADRs were 222, moderate ADRs were 32 and 1 ADR was severe.[9]

Study 7: 288 ADRs were reported in 175 patients from in-patients and out-patients over a time period of 10 months. Among 175 patients 108 were male 67 were female. The major organ system that was affected due to ADRs was skin and appendages followed by Gastrointestinal, Central Nervous System, Respiratory System, Cardiovascular system, Genito-Urinary tract and miscellaneous which includes fever, chills, shivering. Among the 288 ADRs definite were 9, probable were 131, possible were 136 and doubtful were 12 depending on Naranjo Causality Assessment Scale. According to Hartwig's Severity Assessment Scale 230 reactions were

found to be mild, 52 were moderate and 6 were severe. Class of drugs which caused ADR were Antimicrobials followed by IV fluids, analgesics, anti-ulcer drugs, anti-cancer drugs and miscellaneous.[10]

Study 8: A cross-sectional, prospective study was conducted over a period of 2 years and a total of 238 ADRs were collected. Among the ADRs reported 147 were male and 91 were female. The mostly affected age group was 19-60 years followed by 0-18 years and above 60 years. Organ system that was vulnerable to ADRs was skin and appendages, gastrointestinal tract, central nervous system, hematological, cardiovascular system, respiratory, hepatic, musculo-skeletal, genitor-urinary, immunological, ophthalmological and peripheral nervous system. General Medicine department reported more number of ADRs followed by Dermatology, Psychiatry, ART centre, Cancer, Pulmonary medicine, Pediatrics, ENT and Anesthesia. ADRs mostly occurred due to Antiretroviral drugs followed by antimicrobials, antipsychotics, anticancer, antiepileptic, antimalarials, NSAIDs, antihypertensives, anti-tubercular and miscellaneous. According to WHO-UMC Causality Assessment Scale 85 were probable and 151 were possible. Depending upon Hartwig's Severity Assessment Scale severe were 17, 92 were moderate and 84 were mild. Among the reported ADRs 3.36% were definitely preventable, 36.97% were not preventable and 59.67% were probably preventable.[11]

Study 9: Among the total sample size of 6922 patients 526 patients were documented with adverse drug reactions which were screened retro-prospectively. Out of 526 patients 284 were male and 242 were female. As per age, 126 ADRs were found in group of 18-40years, 202 in group of 41-60years, 178 in group of 61-80years, 20 in group of above 80 years. Most commonly ADR causing class of drugs were antimicrobials followed by Non Steroid Anti Inflammatory Drugs (NSAIDs), hypoglycemic agents. In antibiotics the class which was attributed to ADRs was betalactams followed by tetracyclines, macrolides. According to causality assessment scale among the ADRs 12.1% was mild, 74.2% were moderate, 13.6% were severe and there were no lethal cases. Depending on the classification based on the severity, type A ADRs were 63.57%, type B ADRs were 21.63% and type C ADRs were 14.8%.[3]

Study 10: In a total span of six months 126 ADRs were collected and reported. Among the ADRs 52.5% occurred in male patients and 47.5% occurred in female patients. As per age, most of the ADRs were found among adults followed by pediatrics and then geriatrics. The organ which was mostly affected due to adverse drug reaction was Gastro Intestinal Tract followed by respiratory system, skin & appendages, cardiovascular system, nervous system, musculoskeletal system, urinary system and haemopoietic system. Most common type of reactions was abdominal pain followed by dysponea, nausea, vomiting, cough, diarrhea, headache, fatigue, vertigo, joint pains, rashes, tingling sensation, constipation, itching, Inflammation, swelling, anxiety, throat pain, change in stool colour, tinnitus, oral ulcers. According to WHO causality assessment scale Certain were 4.76%, Possible were 61.9%, Probable were 25.3% and unlikely were 7.9%.[2]

Study 11: Among 389070 patients were enrolled in the study in the time duration of 12 months 135 were reported in 120 cases. After exclusion of 23 patients due to doubtful causality while using Naranjo Causality Assessment scale 111 reactions from 97 patients were considered in the study. Among them 23 ADRs from 22 patients were reported as severe reactions. The mean age of the total population was 40. Females were more affected due to ADRs than male population with a ratio of 1.15:1. The most affected organ system was skin and appendages (58 ADRs) followed by Gastro Intestinal Tract (16 ADRs), Central and Peripheral Nervous system (14 ADRs), General Disorders (6), Metabolic and Nutritional Disorders (5), Reproductive Disorders (3), Respiratory Disorders (2), Psychiatry (2), Cardiovascular disorders (2), Renal Disorders (1), Liver and Biliary system disorders (1) and Vision disorders (1). Among all the suspected ADRs the major causative route for the occurrence of ADR was oral (80.56%) followed by Intramuscular route (13.19%) and topical (4.86%). The most ADR causative drug classes were Anti-microbials, Autocoids, Anti-psychotics, NSAIDs, Anti-depressants, Anti-epileptics, Opioids, Benzodiazepines and others. According to Naranjo Causality Assessment Scale definite were 2, probable were 73 and possible were 36. According to Schumock and Thorton preventability criteria definitely preventable were 8, probably preventable was 1 and not preventable were 102.[12]

CONCLUSION

One of the drug related problem in the hospital setting now-a-days are ADRs. Ensuring drug safety is the most important challenge for the health care providers. Among the taken studies both female and male were affected irrespective to their age, disease condition and comorbidities. Age group that was vulnerable to ADRs was adults followed by middle aged, pediatrics and geriatrics. The organ system that was mostly affected due to ADRs in these studies were skin & appendages followed by gastrointestinal tract, nervous system, respiratory system, cardiovascular system, musculo-skeletal system and others which includes haemopoietic system, genitor-urinary system and ENT. The class of drugs that are mostly responsible for causing ADRs include antimicrobials, antiretrovirals, NSAIDs, cardiovascular agents, drugs acting on central nervous system, electrolytes, steroids and others which include antiulcer drugs, anticancer drugs and supplements. Mostly used scales for ADRs assessment are Naranjo Causality Assessment Scale, WHO-UMC Causality Assessment Scale, Hartwig's Severity Assessment Scale, Schumock and Thornton Preventability Assessment Scale. Most of the reported ADRs are possible followed

by probable and definite depending on causality. Based on severity most of the ADRs are mild followed by moderate and very less common are severe.

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CONFLICT OF INTEREST

We have no conflict of interest.

REFERENCES

1. Srinivasan R, Ramya G, Adverse Drug Reaction-Causality Assessment, International Journal of Research in Pharmacy and Chemistry, 2011; 1(3): 606-12.
2. Kavita Dhar, Akanksha Sinha, Preeti Gaur, Rajkumar Goel, V.S Chopra, Umakant Bajaj, Pattern of Adverse Drug Reactions to Antibiotics commonly Prescribed in Department of Medicine and Pediatrics in a Tertiary Care Teaching Hospital, Gaziabad, Journal of Applied Pharmaceutical Science, 2015; 5(4): 78-82.
3. Anup kumar, Dinesh Kansal, Praveen Kumar Sharma, Amit Bharadwaj, Sushma Swaraj, To Study the Pattern of Adverse Drug Reactions Among patients Hospitalized in the Medical Wards of a Tertiary Care Hospital, International Juornal of Basic & Clinical Pharmacology, 2016; 5(5): 1972-7.
4. R. Vijaishri, G. Andhuvan, A Prospective Observational Study on Antibiotics associated Spontaneous Adverse Drug Reaction Monitoring and Reporting in a Tertiary Care Hospital, Asian Journal of Pharmaceutics, 2017; 11(4): 834- 40.
5. Parvati B Patel, Tejas K. Patel, Snehal Anturlikar, Sahila Khatun, Prakash Bhabhor, Manoj Kumar Saurabh, Adverse Drug Reactions Reporting by Undergraduate Medical Students in a Tertiary Care Teaching Hospital of India: Content and Quality Analysis in Comparision to Physician Reporting, Perspectives in Clinical Research, 2017; 8(3): 137-44.
6. Siavash Shahbazi Nia, Shadan Modaresahmadi, Armin Eisa Zaei, Distinguishing Adverse Drug Reactions, the Noxious Effects of Medicines at a Tertiary Care Hospital, International Journal of Pharmaceutical Investigation, 2018; 8: 69-73.
7. More Pankaj Daulat, V.J. Ambika Abhishake, S. Basalingappa, Arun Gopi, A Retrospective Study of Adverse Drug Reractions in a Tertiary Care Centre, International Journal of Basic & Clinical Pharmacology, 2018; 7(7): 1339-44.
8. Ayan Purkayastha, Dolly Roy, Rohit Tigga, Analysis of Adverse Drug Reaction in a Tertiary Care Hospital: A Retrospective Study, Asian Journal of Pharmaceutical and Clinical Research, 2016; 10(1): 2017.
9. Ratan J. Lihite, Mangala Lakhar, Sukirti Das, Debeeka Hazarika, Murali Kotni, Mudasir Kotni, Mudasir Maqbool, Swapna Phukan, A Study on Adverse Drug Reactions in a Tertiary Care Hospital of Northeast India, Alexandria Journal of Medicine, 2017; 53: 151-56.
10. Prashant Shukla, Anita Gupta, Anjleen Kaur, Hema Chhabra, Adverse Drug Reactions Pattern in a Tertiary Level Teaching Hospital: A Retrospective Study, Indian Journal of Pharmacy Practice, 2017; 10(1): 27-31.
11. Bhabagrahi Rath, Sapan Kumar Behera, Sashi Bhushan Biswal, Sabita Mohapatra, Pattern of Adverse Drug Reactions in a Tertiary Care Hospital in Western Odisha, International Journal of Pharmaceutical Sciences and Research, 2018; 9(6): 2471-77.
12. Tejas Kamaleshbahi Patel, Roshini Vahora, Parvati B. Patel, Nimisha Desai, Adverse Drug Reactions in a Tertiary Care Teaching Hospital in India: Analysis of Spontaneously Reported Cases, International Journal of Basic & Clinical Pharmacology, 2014; 3(6): 1078-85.