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ASSESSMENT OF ADVERSE DRUG REACTIONS OF DRUGS USED IN TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Objective: The purpose of this study was to assess the incidence and pattern of adverse drug reactions reported from different department of Tertiary care hospital. **Methods:** The reports of ADRS were recorded as per the standard guidelines of Pharmacovigilance programme of India (PvPI). Causality, Severity and Types of ADR was assessed by using Naranjo Probability scale, Modified Hartwigs criteria and Rawlins &Thompson classification respectively, Seriousness of ADR was assessed by criteria given by WHO. **Results:** A total 146 ADRs were reported from 126 patients. Majority of the ADRs were Type A reactions, Highest incidence 65.06% of ADRs was observed between (31-60) years of age, 61.11% of patients were female and 38.88% were male. In the assessment of severity mild and moderate were 99.31% and 0.68% respectively and causality assessment 86.98% were probable, 12.32% possible and 0.68% Unlikely. **Conclusion:** A careful attention is needed in monitoring and reporting of ADR because most of drugs have ADRs and in our country ADR reporting is in growing phase. There is need of more work on spontaneous reporting and awareness among health care Professional and practitioner to report all the adverse drug event to Pharmacovigilance center.

KEYWORDS: Adverse Drug Reactions, Pattern of ADR, Pharmacovigilance, ADR Monitoring.

INTRODUCTION

During the diverse periods of clinical trials, the medication are tried for its transient safety and efficacy and after the medication is affirmed by overall population, post marketing surveillance recognize the new adverse drug reactions related to utilization of various medicated formulations. Adverse drug reactions are major cause of morbidity and ADRs related hospitalizations have consistently increased which has caused an economic burden to the developing countries like India.[1]

The WHO defines ADR (Adverse drug Reactions) as any response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiological function.[2]

Studies from overseas as well as India have demonstrated that polypharmacy is associated with increased potential for ADRs[3] and In USA, ADRs are responsible for 3.4 –7.0% of hospital admissions.[4]

ADR monitoring and reporting activity is in its initial phase in India. India rates below 1% in Pharmacovigilance as against the world rate of 5%.[5] India is one of the largest producer of pharmaceuticals in the world. There are more than 6000 licenses drug manufacturers and more than 60000 brand formulations.[6] India is also emerging center for clinical trials. The important reason of less Pharmacovigilance activity is lack of awareness and lack of interest of health care professionals in ADR reporting and documentation.[7]

An active Pharmacovigilance program is the need in all hospitals especially in Indian set up as ADRs cause a significant burden to patient and to economy.

This study is aimed to work in regard to monitor, assess and dissipate the ADR, which ensures patient safety and minimize the cost and improves the knowledge and pattern of ADRs in patients.

MATERIAL AND METHODS

A Prospective data was collected at GSVM Medical College and associated Hospital, Kanpur for last 6 months(Jul 2019 to Dec 2019) from different departments by Patient safety Pharmacovigilance associate of Pharmacovigilance unit in Dept. of Pharmacology and filled all the suspected ADR reporting forms of Indian Pharmacopoeia commission (IPC).For each patient the forms was completed with regard to

- Age of patient

- Gender of patient
- Number of drug prescribed
- Duration of treatment
- Number of ailment the patient was suffering from
- Causality of ADR
- Severity of identified ADR
- Seriousness of case
- Type of ADR

Patient's age and sex were considered for evaluation. Patient were subdivided into four age groups.

- Children (0 – 12 years)
- Young adult (13 – 30 years)
- Adult (31- 60 years)
- Elderly (> 60 years)

The causality assessment of the ADRs was done by Naranjo ADR probability scale.[8]
Severity of ADRs was assessed at different levels using modified Hartwigs Criteria.[9]

- Mild ADR belonged to level 1 and 2
- Moderate ADR belonged to level 3 and 4
- Severe ADR belonged to level 5 and above

Type of ADRs were identified by using Rawlins and Thompson classification.[10]
Seriousness of ADRs was assessed by different criteria given by WHO[11-13] which is as follows

- Death
- Life threatening
- Hospitalization/Prolonged
- Congenital anomaly
- Disability
- Other medically important

For this study prior approval from Institutional ethical committee was taken.

RESULTS

In our study total 146 ADRs were reported from 126 patients.
Out of this 61% were in female and 39% in male. (Fig. 1)

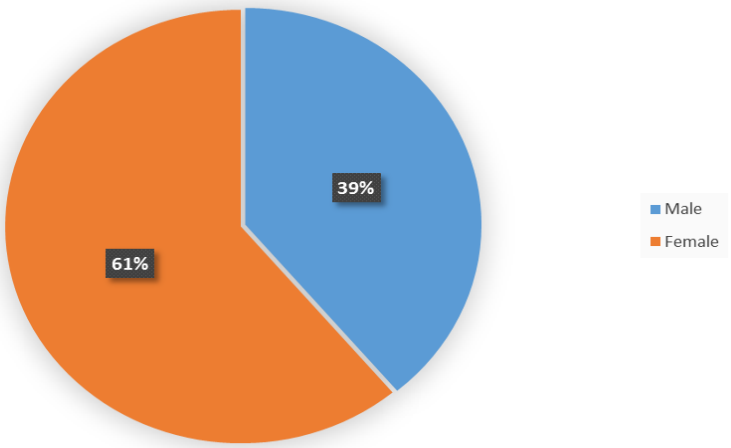

Fig 1: Division of ADRs based on sex of patient.

Maximum ADRs (65.06%) were seen in age group of (31-60 years) (Fig.2)

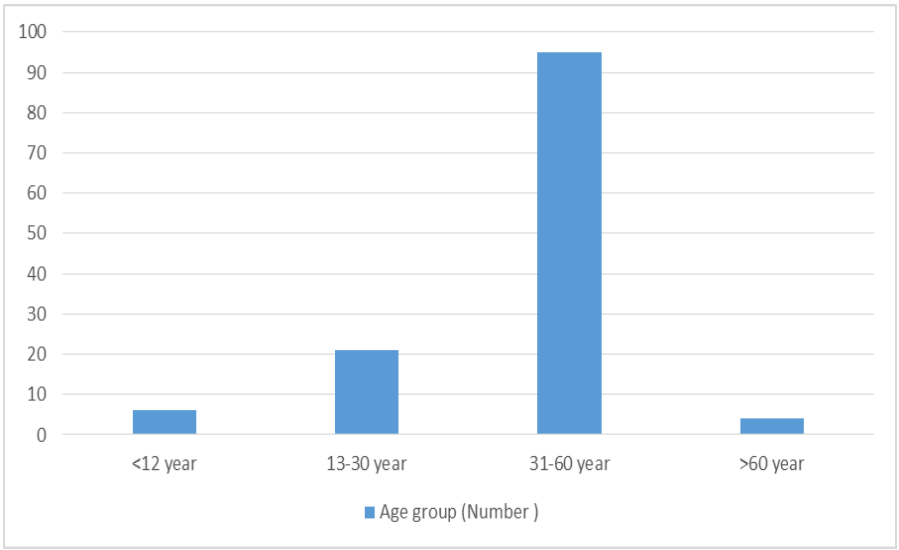

Fig 2: Age group (Number).

In our study maximum ADRs were related to Gastrointestinal disorders (32.88%) followed by skin and subcutaneous disorder (30.13%) (Table 1), most common ADR reported was Rash (14.38%) followed by Anorexia and Diarrhea both (6.16%) (Table 1).

Table 1: Types of ADR with their numbers and suspected drugs.

Reaction/Event	Number (N) (%)	Drugs Involved
Gastrointestinal disorder	**48 (32.88%)**	
Anorexia	09(6.16%)	Carboplatin (2), Paclitaxel(2), Ibuprofen(1), Epirubicin (1), Cisplatin (1), Etoricoxib(1), Gemcitabine + Carboplatin (1)
Diarrhoea	09(6.16%)	Cisplatin (3), Amoxicillin + Clavulanic Acid (3), Clindamycin (1), Cyclophosphamide (1), Iron Sucrose (1)
Vomiting	08(5.47%)	Cisplatin (4), Diclofenac (1), Ranitidine (1), Cyclophosphamide + 5 FU (1), Ceftriaxone (1)
Constipation	06(4.10%)	5 FU (2), Cyclophosphamide (2), Paclitaxel (1), Cisplatin (1)
Mouth Ulcer (Mucositis)	04(2.73%)	Cyclophosphamide + 5 FU (3), Carboplatin (1)
Abdominal Pain	03(2.05%)	Levofloxacin (1), Clindamycin (1), Ibuprofen (1)
Nausea	02(1.36%)	Fluconazole (1), Ibuprofen (1)
Gastritis	02(1.36%)	Etoricoxib (1), Diclofenac(1)
Dry Mouth	01(0.69%)	Diclofenac(1)
Skin And Subcutaneous Disorder	**44 (30.13%)**	
Rash	21(14.38%)	Ceftriaxone(7), Amoxicillin + Clavulanic acid (6),Iodixanol (1), Oflaxacin (1), Curadex(1), Nevirapine(1), Streptomycin (1), Lignocaine (1), Acyclovir (1), Vancomycin (1)
Itching	15(10.27%)	Ceftriaxone (3), Levofloxacin (2), Piperacillin (1), Curadex(1), Metformin (1) Ondensetron(1) Indapamide (1) Streptomycin (1) Azithromycin (1) Efavirenz(1) Cinnarizine (1) Paclitaxel (1)
Pigmentation	04(2.73%)	5 FU (3), Paclitaxel (1)
Alopecia	03(2.05%)	Adriamycin (1), 5 FU (1) and Cisplatin (1)
Urticaria	01(0.69%)	Hosit
Nervous System Disorder	**27(18.50%)**	
Headache	9(6.16%)	Atenolol (2), Losartan (2),Etoricoxib(1), Cyclophosphamide(1), Levokast(1), Sildenafil(1), Ceftriaxone (1)
Lethargy	06(4.10%)	Methyl prednisolone (3), Glipizide(1), Atenolol(1), Tizanidine(1)
Numbness	04(2.73%)	5 FU (2), Carboplatin (1), Paclitaxel(1)
Dizziness	03(2.05%)	Escitalopram (1), Efavirenz(1), Dicyclomine (1)
Drowsiness	02(1.36%)	Diphenhydramine (1), Escitalopram (1)
Tinnitus	01(0.69%)	5 FU (1)
Balance disorder	01(0.69%)	Diphenhydramine (1)
Depression	01(0.69%)	Cinnarizine (1)
Body As A Whole General Disorder	**17 (11.64%)**	
Anxiety	08(5.47%)	Etoricoxib (2),Cefopodoxime (2),Atenolol(1), Losartan (1),Carboplatin (1),5 FU (1)
Fever	03(2.05%)	DNS (2), Levomac (1)
Body pain	02(1.36%)	Sitagliptin (1), Geftinib(1)
Chill	02(1.36%)	DNS (2)
Swelling	02(1.36%)	Etoricoxib (1), Ranitidine (1)
Musculoskeletal Disorder	**5 (3.42%)**	
Limb Pain	04(2.73%)	Cyclophosphamide (2), Carboplatin (1), Irbesartan (1)

Fracture leg	01(0.69%)	Dapagliflozin(1)
Cardiovascular Disorder	**03(2.05%)**	
Tachycardia	02(1.36%)	DNS (1), Biopiper TZ (1),
Hypotension	01(0.69%)	Diclofenac(1)
Blood And Lymphatic Disorder	**01 (0.69%)**	
Anemia (Decreased Hb)	01(0.69%)	Methotrexate (1)
Respiratory System	**01(0.69%)**	
Cough	01(0.69%)	Ibuprofen

In this study Drug class most commonly causing ADR was Antineoplastic agents (40.99%) followed by Antimicrobial agents (23.78%). Amongst the antineoplastic agents 5- FU (10.92%) was the drug most commonly associated with adverse drug events followed by Cyclophosphamide (7.56%). (Table 2)

Table 2: Drug class and Individual drugs most commonly associated with ADRs.

DRUG CLASS	NUMBER OF ADRs reports (%) (N = 122)	DRUG	NUMBER PF ADR REPORTS (%)
Antineoplastic agents	**50(40.99%)**	5FU	13(10.92%)
		Cyclophosphamide	09(7.56%)
		Cisplatin	08(6.72%)
		Paclitaxel	08(6.72%)
		Carboplatin	07(5.88%)
		Adriamycin	01(0.84%)
		Geftinib	01(0.84%)
		Gemcitabine	01(0.84%)
		Methotrexate	01(0.84%)
		Epirabin	01(0.84%)
Antimicrobial Agents	**29(23.78%)**	Ceftriaxone	06(5.04%)
		Levofloxacin	04(3.36%)
		Amoxicillin/Clavulanate	04(3.36%)
		Cefopodoxime	02(1.68%)
		Piperacillin	02(1.68%)
		Clindamycin	02(1.68%)
		Efavirenz	02(1.68%)
		Gentamycin	02(1.68%)
		Streptomycin	01(0.84%)
		Azithromycin	01(0.84%)
		Vancomycin	01(0.84%)
		Fluconazole	01(0.84%)
		Nevirapine	01(0.84%)
Anti-inflammatory Drugs	**11 (9.01%)**	Diclofenac	06(5.04%)
		Ibuprofen	03(2.52%)
		Etoricoxib	02(1.68%)
Antihypertensive agents	**08(6.55%)**	Atenolol	04(3.36%)
		Losartan	03(2.52%)
		Irbesartan	01(0.84%)
Hypoglycemic drugs	**05(4.10%)**	Metformin	02(1.68%)
		Sitagliptin	01(0.84%)
		Dapagliflozin	01(0.84%)
		Glipizide	01(0.84%)
Antihistaminic drugs	**04(3.28%)**	Cetrizine	02(1.68%)
		Levocetrizine	01(0.84%)
		Diphenhydramine	01(0.84%)
Antiemetic Drugs	**04(3.28%)**	Cinnarizine	02(1.68%)
		Ondensetron	01(0.84%)
Antianxiety Drugs	**02(1.63%)**	Escitalopram	02(1.68%)
Miscellaneous	**09(7.38%)**		

In our study Majority of the ADRs were Type A reactions (78.76%), Non Serious (99.32%), mild in severity (99.32%) and on causality assessment 87% were probable, 12.32% possible and 0.68% Unlikely. (Table 3)

Table 3: Assessment of ADRs (N = 146).

Characteristics		Number N (%)
Type of ADR	Type A	115(78.76%)
	Type B	31(21.24%)
Seriousness of ADR	Serious	01(0.68%)
	Non Serious	145(99.32%)
Severity of ADR	Mild	145(99.32%
	Moderate	01(0.68%)
Causality	Unlikely	01(0.68%)
	Possible	18(12.32%)
	Probable	127(87%)
	Certain	00

DISCUSSION

ADRs can have a detrimental effect on a patient's wellbeing and overall health care system[14] and ADR collecting program in a hospital can help to assess the safety of drug therapies, measure ADR incidence rates over time and educate health care professionals of drug effect and increase their level of awareness regarding ADRs.[15]

In our study most of the reactions were Type A reactions (78.76%). But Murphy and Frigo[16] as a part of the ADR reporting program in a teaching hospital recorded a higher percentage of Type B reactions in comparison to Type A reactions. This higher number of Type A reactions may be due to the higher number of reactions reported to oncology medications which usually are Type A in nature. Drug class most commonly involved in the reactions was Antineoplastic agents which are consistent with other studies[17,18] but in other studies antimicrobial or analgesics were most commonly associated[16,17,18,19] In our study in antineoplastic agents 5- FU was the drug most commonly associated with adverse drug events.

Gastrointestinal system (32.87%) was the most common affected SOC (System Organ Class) in our study and Rash (15%) being the most common individual reaction. This was similar to study conducted by Sriram S et al[20] but the study done by Palanisamy et al[21] reported skin and subcutaneous disorder being the most common affected SOC.

Most of the reactions belonged to category "Probable" which is similar to results in study conducted by Prosser TR et al[19] but according to Murphy and Frigo[16] there were more of "Possible" reactions.

Considering the severity of the reactions, majority of the reactions were mild (99.32%) which is in similarity to results of Gonzalez- Martin et al.[22]

Our study has its own limitations firstly the duration of study was short. Lack of awareness to report ADRs combined with busy schedule of the physicians due to lack of manpower in government Tertiary care hospital needs to be taken into consideration while interpreting the data. But our study data would give an insight into the pattern of ADRs which do occur in tertiary care hospitals with a comparable pattern of patient demographics and drug usage. The pattern of ADRs reported in our Hospital is comparable with the results from studies conducted elsewhere in hospital set up. Results of many of the evaluated parameters were similar to other studies[16,19] while some aspects were different from other studies.[22,23]

CONCLUSION

From this study we concluded that most of the ADRs are of Type A of mild severity and Preventable and GIT is the most common system affected due to Antineoplastic agents.

A careful attention is needed in monitoring and reporting of ADR because most of drug have ADRs and in our country ADR reporting is in growing phase. There is need of more work on spontaneous reporting and awareness among health care professional and practitioner to report all the adverse drug event to Pharmacovigilance center.

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