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Original Research

A retrospective and prospective study on Adverse Drug Reactions in a rural medical college hospital in Himachal Pradesh

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ABSTRACT:

Background: All drugs can produce adverse effects, and whenever a drug is prescribed for the benefit of a patient a risk is also taken. The risk and benefit ratio decides whether to use or not to use a particular drug in a given patient. Many times adverse drug reactions remain undetected due to lack of awareness and knowledge of Pharmacovigilance. The present study was undertaken to evaluate ADRs of various drugs used in a rural medical college & Hospital of Himachal Pradesh, India. **Method**: We performed observational study to evaluate ADRs reported by patients due to various medicines. The study was conducted in two phases: In the first phase, a retrospective study on the clinical records of patients admitted during the past 1 year was studied and in the second phase, a 3 month prospective study was conducted on the inpatients and outpatients. The association between drug and ADR evaluated using Naranjo scale and severity of ADR was assessed by Karch & Lasagna classification. **Result**: A total of 117 ADR cases were found out of the 1800 patients screened in retrospectiveand prospective phases of 1 year, and 3 months respectively. Overall prevalence of ADRs was 6.5%, cases related to skin were 46, followed by GIT cases 33. Antimicrobial related ADRs were 55, NSAIDS related 16, and anti- hypertensives related 20. **Conclusion**: Health care professionals should have knowledge and awareness about the Adverse Drug Reactions and they should act promptly to treat and report to ADR Monitoring centre (AMC).

Key words: Adverse drug reactions, Drugs, Naranjo scale, reported.

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INTRODUCTION:

Drugs are used to diagnose and treat health problems though they may produce adverse drug reactions (ADRs). It is now recognized that clinical trials however thorough cannot be guaranteed to detect all the adverse effects likely to be caused by a medicine and hence, necessitating post marketing surveillance of adverse effects of the drugs[1]. Adverse drug reaction (ADRs) may develop immediately, or after prolonged medication required for chronic diseases or even after stopping the drug therapy. An incidence of 10-25% ADRs has been reported in various clinical settings[2]. The FDA has further estimated that 300000 preventable adverse events occur annually in hospitals of USA, many as a result of confusing medical information[3]. World Health Organization (WHO) has defined ADR of a drug; as a response of a drug which is a noxious and unintended and that occur at doses normally used in human beings for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function in man[4]. ADRs should be carefully looked for and treated immediately to prevent the harmful effects of drugs to the patients. In early 1960s first reports of deformed infants born to pregnant women were identified because of Thalidomide drug taken by them for the treatment of morning sickness[5]. ADRs are classified into 9 types viz. A, B, C, D, E, F, G, H and U according to Wills and Brown classification[6]. Multiple factors are involved in ADR susceptibility of patients like polypharmacy, age of patient, chronic diseases, co-morbid conditions, and allergy to drugs including their metabolites or inert component used for making formulation of drugs due to re-exposure of an agent subsequent to prior interaction between patient and disease[7]. Early detection and treatment/intervention of ADRs may prevent temporary/permanent disability of patients, even save lives of patients, and reduce economic burden on the family as well as at nationallevel[8]. The

knowledge and awareness of ADRs and their immediate interventions will ease the health care system[7, 8].
Pharmacovigilance programme of India (PvPI) is highly helpful for the safe and effective medication of patients and also to prevent development of multidrug resistance.It deals with detection, assessment, understanding and prevention of adverse drug effects and promotes the safe use of drugs[9].The causality assessment of suspected drug is done with the help of naranjo scale[10].
ADR is a broad term and it includes all kinds of noxious effects—trivial, serious or even fatal'' suspected to be due to a drug. Severity of adverse drug reaction has been graded as:
Minor for which no therapy, no antidote or no prolongation of hospitalization is required.
Moderate it required change in drug therapy, specific treatment or prolongs hospital stay by atleast one day.
Severe which is a potentially life- threatening, causes permanent damage or requires intensive medical treatment.
Lethal which directly or indirectly contributes to death of the patient[1].
It is imperative to enhance the awareness regarding early detection, documentation, reporting, management and further prevention of ADRs and to ensure the drug safety and quality of life. Present study was conducted to evaluate the prevalence of adverse drug reactions in MM Medical College & Hospital, Kumarhatti, Solan, Himachal Pradesh, India.

MATERIALS AND METHODS:
The present study was an open, non-comparative and observational study. We had randomly examined a total of 1800 patients for ADRs who came for their treatment in Maharishi Markandeshwar Medical College & Hospital, Kumarhatti, Solan, Himachal Pradesh, India. This study was approved by the institutional Ethical Committee. The ADRs were reported spontaneously by the patients or by their attendants to the doctor on duty or topara-medical staff and were brought into the notice of the concerned physician. The particulars of patient having ADRs were recorded in the patient proforma and description of reaction or problem was entered at the site mentioned in the proforma. Prior to filling theproforma, a written consent was taken from the patients with ADRs or their legally acceptable representatives in their vernacular language for enrolling them in the study. The purpose of the study was explained to them and they must fulfil the inclusion and exclusion criteria were enrolled in the study. ADR alert card was filled and given to the patients for follow up of the outcome and future use of the record regarding ADR of the suspected drug. The causality assessment of ADRs due to suspected drug was evaluated using the Naranjo scale while their severity grading was assessed by Karch & lasagne classification.

Inclusion criteria:
1) Patients with age between 18 to 80 years
2) Patients either sex (Male & Female patients) with ADR

Exclusion criteria:
1) Drug addicts
2) Mentally retarded
3) Pregnant females
4) Patients with Drug overdose

Data collection: Clinical meeting regarding Pharmacovigilance Programme of India (PvPI) were arranged for doctors and para-medical staff (staff nurses and pharmacists) to sensitise them for reporting ADRs and providing knowledge and awareness of ADRs. The health care professionals were motivated to develop rapport with the patients and ask them to report any adverse effects related to medication. The contact number of principal investigator and drug safety associate of adverse drug reaction monitoring centre (AMC) of this hospital were displayed in all the OPDs and in the wards at the nursing staff stations for reporting the ADRs. After receiving the information of ADR, the patient was visited and interviewed by the investigator and drug safety associate to record detail of adverse drug reaction encountered and discussed with the concerned physician to identify the suspected drug. Only then the patient with ADR who full filled the inclusion and exclusion criteria was enrolled the study. Patient's proforma was filled completely for data collection of all the necessary information and outcome of ADRs was confirmed by follow ups and entered in the proforma along with the remedial measures taken by the physician.
For retrospective study phase patients admission files of the past 1 year were examined after obtaining the permission from the medical superintendent of this hospital. We noted the particulars of the patients, medication part and day to day progress of the patient. We also noted any new problem if evolved during the medication as ADR and its management along with prolongation of hospital stay of the patient. All the information collected and recorded in the patient proforma. The suspected ADR reporting form attached in the file was also analysed carefully.
Naranjo scale was used for establishing the causal relation between suspected drug and adverse drug reaction[10]. Severity assessment of ADRs was done by using Karch & lasagna classification as minor, moderate, severe and lethal[11].

RESULTS AND OBSERVATION:

Table 1: Distribution of patients with ADRs on the basis of gender

Sr. No.	Gender	No. of patient with ADRs	Percentage of patient with ADRs
1.	Male	66	56.41%
2.	Female	51	43.59%

Total number of ADRs (n) = 117

Table 2: Patients with ADR divided in two groups according to age

Sr. No.	Groups	No. of patient screening	No. of patient with ADRs	Percentage of patient with ADRs
1.	Adult (18-65years)	1744	111	06.36%
2.	Geriatric(>65years)	56	6	10.71%

Total number of ADRs (n) = 117 found out of 1800 patients screened for adverse drug reactions.

Table 3: Complaints of patients because of ADRs encountered in the study

S.No.	Complaints	No. of ADRs	Percentage of ADRs
1.	Nausea, Vomiting, Diarrhoea	6	05.13%
2.	Abdominal Pain, Vomiting	3	02.56%
3.	Anorexia	4	03.42%
4.	Diarrhoea	3	02.56%
5.	Skin Rashes	13	11.11%
6.	Itching/Pruritus	8	06.84%
7.	Itchy Rash	2	01.71%
8.	SJS	2	01.71%
9.	Swelling on face and lips	1	00.85%
10.	Breathlessness, Swelling & discoloration of IV site-hand	1	00.85%
11.	Urticaria	3	02.56%
12.	Abdominal Pain & Blood in vomiting	1	00.85%
13.	EPS	5	04.27%
14.	Erythema	4	03.42%
15.	Maculopapular Rash	3	02.56%
16.	Bronchospasm	1	00.85%
17.	Severe Headache	1	00.85%
18.	Jaundice, Vertigo, Breathlessness	4	03.42%
19.	MDR	1	00.85%
20.	Drug Eruption	5	04.27%
21.	Jaundice	3	02.56%
22.	Urine urgency & Incontinence	2	01.71%
23.	Constipation	3	02.56%
24.	Metallic/ Abnormal taste	2	01.71%
25.	Vertigo	2	01.71%
26.	Hallucination	1	00.85%
27.	Tachycardia &Skin Rash	1	00.85%
28.	Glossitis/ Stomatitis	3	02.56%
29.	Vomiting, Weakness, Anorexia	4	03.42%
30.	Abdominal Pain	3	02.56%
31.	Insomnia	2	01.71%
32.	Vomiting,	2	01.71%
33.	Ototoxicity (Nausea, Vomiting, Ataxia & Difficulty in conversation	1	00.85%
34.	FDE	3	02.56%
35.	Oral thrush	3	02.56%
36.	Anti TB Drug intolerance	1	00.85%
37.	Pedal Edema	4	03.42%
38.	Dry cough	3	02.56%
39.	Bradycardia	3	02.56%

Total number of ADRs (n) = 117

SJS- Stevens–Johnson syndrome

IV-Intravenous

EPS- Extrapyramidal symptoms

MDR-Multi drug resistant

FDE-*Fixed drug eruption*

Table 4: Drugs and their number of ADRs cases

S.No.	Drugs	No. of ADRs cases	Percentage of ADRs
1.	Anti TB Drugs	14	11.96%
2.	InjCeftazidine	1	00.85%
3.	Inj Ciprofloxacin	3	02.56%
4.	Inj Ceftriaxone	9	07.69%
5.	Tab Aciclovir	3	02.56%
6.	Inj Clindamycin	5	04.27%
7.	Tab Dexamethasone	1	00.85%
8.	InjDiclofenac	2	01.71%
9.	PCM infusion	1	00.85%
10.	Tab PCM	7	05.98%
11.	Tab/Cap Amoxicillin with clavulanic acid	3	02.56%
12.	Tab Metformin	1	00.85%
13.	Tab Frusamide	1	00.85%
14.	Inj Metronidazole	6	05.13%
15.	Tab Nitrofurantoin	1	00.85%
16.	FDC Tab Trypsin, Rutozide, Bromlain, Aceclofenac	1	00.85%
17.	Cap Pregabalin with Mecobalamin	1	00.85%
18.	Tab Zolpidem	1	00.85%
19.	Tab Leflunomide	1	00.85%
20.	Tab Azithromycin	2	01.71%
21.	Tab Diclofenac Sodium with PCM	3	02.56%
22.	Tab Ofloxacin with Ornidazole	3	02.56%
23.	Tab Ibuprofen	1	00.85%
24.	FDC Tab Aceclofenac, Serratiopeptidase& PCM	1	00.85%
25.	InjVancomycin	3	02.56%
26.	Tab Levofloxacin	2	01.71%
27.	IV DNS	1	00.85%
28.	Tab Iron with Folic Acid	4	03.42%
29.	Inj Phenytoin	3	02.56%
30.	Tab Amlodipine	4	03.42%
31.	Tab Cotrimoxazole	6	05.13%
32.	Tab Ofloxacin	2	01.71%
33.	Cap Lincosamide	1	00.85%
34.	Tab Haloperidol	3	02.56%
35.	Tab Metoclopramide	1	00.85%
36.	Tab Amlodipine with Telmisartan	4	03.42%
37.	Tab Ramipril	5	04.27%
38.	Tab Propranolol	3	02.56%
39.	Tab GPM-2	3	02.56%

Total number of ADRs (n) = 117
TB-Tuberculosis
PCM- Paracetamol
FDC-Fixed drug combination
GPM- Glimepiride + Metformin + Pioglitazone

Table 5: Group wise drugs and their number of ADRs encountered

Drug group	No. of ADRs	Percentage of ADRs
Antimicrobial	41	35.04%
Antihypertensive	13	11.11%
NSAIDs	16	13.68%
Anti TB drugs	14	11.96%
Antiepileptic	3	02.56%
Antihistaminic	1	00.85%
Diuretics	1	00.85%
Haematinics	4	03.42%
Others	24	20.51%

Total number of ADRs (n) = 117

Table 6: Causality Assessment of ADRs

Causality Parameters	No. of ADRs	Percentage of ADRs
Definite	3	02.56%
Probable	64	54.70%
Possible	50	42.74%
Doubtful	0	0

Total number of ADRs (n) = 117

Table 7: Severity of ADRs

Sr. No.	Severity of ADRs	No. of ADRs	Percentage of ADRs
1.	Minor	30	25.64%
2.	Moderate	77	65.81%
3.	Severe	10	08.55%
4.	Fatal	0	0`

Total number of ADRs (n) = 117

Table 8: Outcome of ADR Patients

Outcome	No. of ADRs	Percentage of ADRs
Fatal	0	0
Recovered	104	88.89%
Recovering	11	09.40%
Unknown	2	01.71%

Total number of ADRs (n) = 117

DISCUSSION:

As all drugs have potential to cause adverse drug reactions, so ADR monitoring is utmost essential for safe use of medicines especially in patients of extreme age, patients with two or more organ failure, comorbidities, polypharmacy for chronic diseases etc. Moreover PvPI urges all government and non-government, teaching, private, district and corporate hospitals to participate in drug safety program of India for the benefits of the patients. Medical college and hospitals are providing specialized services to the patients. Patient safety is one of their major concerns. Thus the present study was undertaken to study the pattern of ADRs in this institute.

The Table 1 shows, gender distribution of patients who had ADRs, the male patients were 66 and females were 51 and their respective percentages were 56.41% and 43.59%. It revealed prevalence of ADRs in male patients is more than female patients. This finding is almost similar to the previous studies[12].

Table 2 shows that total number of patients screened were 1800, out of which adult patients (age between 18-65 years) were 1744 and geriatric (age more than 65 years) 56. Adult patients with ADR were 111 while geriatric patients with ADR were 6. The percentages of adult patients and geriatric patients are 6.36% and 10.71%. This shows geriatric patients suffer from ADRs almost two times as compared with the adults. The reasons for more prevalence of ADRs in elderly patients were the decline of functions of body organs and polypharmacy because of long terms illnesses present in them.[13, 14, 15]

Table 3 shows the complaints of patients due to ADRs of commonly prescribed drugs in this institute. The total number of patients with ADRs was 117. Out of them skin related and GIT related ADRs were 44 and 43 respectively which were the maximum in number as also reported in previous studies[16, 17]. Followed by the ADRs related to CNS were 8, Respiratory related were 4, and others were 17 cases as shown in this table.

Table 4 & 5 show that antimicrobials, NSAIDs, anti TB drugs, and antihypertensives related ADRs were 41(35.04%), 16(13.68%), 14(11.96%) and 13(11.11%) respectively as revealed in previous studies[18]. Followed by haematinics, antiepileptic, antihistaminic, diuretics and others as 4(03.42%), 3(02.56%), 1(00.85%), 1(00.85%), and 24(20.51%) respectively.

Table 6 shows the causality assessment of ADRs as 3(02.56%) cases were certain, 64(54.70%) cases were probable, 50(42.74%) cases were possible out of 117 cases of ADR while no any doubtful case was found. These results are comparable with the previous studies[19].

Table 7 shows, out of total 117 cases of ADRs, as minor 30(25.64%), moderate 77(65.81%) and severe 10(00.55%) while no any fatal case of ADRs was found during the study.

Table 8 shows outcome of ADRs in all (117 cases of ADRs encountered) patients as 104(88.89%) cases recovered completely, 11(09.40%) were recovering and nothing was known about 2 (01.71%) cases while no any death occurred due to ADR during the study.

CONCLUSION:

It is observed in the present study that there is under reporting of the ADRs by the health professionals and patients, due to lack of knowledge and awareness of ADRs. To enhance the ADRs reporting, we need to conduct seminars and workshops on Pharmacovigilance, proper filling of the ADR form and importance of ADR reporting. The doctors and paramedical staff should be

provided newsletters and bulletins regarding ADRs on regular basis to enhance the Pharmacovigilance.

Every hospital should be associated with Adverse drug reaction monitoring centre (AMC) recolonized by Pharmacovigilance programme of India (PvPI). Health care professionals should have knowledge and awareness about the Adverse Drug Reactions and they should act promptly to treat and report ADRs to ADR Monitoring centre.

Early detection and Identification of adverse drug reactions (ADRs) is a first step toward full, safe, accurate and rational drug therapy of the patients. For this, participation of health professionals and patients' awareness is important to minimise adverse drug reactions.

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