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Pharmacovigilance Studies Of Commonly Encountered Adverse Drug Reactions Reported From M.K.C.G. Medical College& Hospital, Berhampur"

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ABSTRACT

Background: The relevance of Pharmacovigilance to adverse drug reaction(ADR) detection is highlighted worldwide. Pharmacovigilance starting from the tip of clinical trial in industries up to post -marketing surveillance is essential to ensure the drug safety. As newer drugs are entering market at a rapid pace pharmacovigilance with special attention to monitor and report adverse drug reaction is today's need.

Objective: This study on adverse drug reaction monitoring and reporting was carried out in collaboration the departments of dermatology, psychiatry, pediatrics, radiotherapy of MKCG Medical College, Berhampur. Data obtained from this study may throw some light in the network of pharmacovigilance and bring a change in the safety data profile of established as well as upcoming drugs

Methods: This was a prospective, observational study, carried from January 2013 to October 2014 in collaboration with department of dermatology, psychiatry, paediatric and radiotherapy of MKCG Medical College and hospital (tertiary care hospital). Incidence rate for occurrence of adr were calculated using MS office excel 2010. Column statistics expressing mean, standard deviation, median, range, confidence interval, for different parameters of ADRs were calculated using a statistical software, Graphpad prism version 5.0.

Results: Out of 237 ADR cases 90 were cutaneous ADRs. Among the various patterns of Cutaneous adverse drug reactions (CADRs), the major presentations were exfoliative dermatitis (n= 17; 18.89%), Fixed drug eruption (n= 17;78%) and 15.56% of them were urticarial rashes. Drugs suspected to cause CADR in the study population were broadly classified in 10 groups. Among them 26.67% of CADR were caused by various NSAIDs. In this study, a total of 9900 patients attending psychiatry OPD were screened for ADR. Out of which 60 patients were suspected at least one ADR (0.61%). Seven major different kinds of psychotropic drugs were used for different kind of psychiatry illness. Extrapyramidal side effects was the commonest ADR (n=41; 34.17%) reported followed by weight gain (n=35; 29.17%). Anticholinergic side effects and sedation were observed in 16.17% and 10.83% of cases respectively. In this study period total 57 paediatric patients reported with different ADRs. Among them 61.40% patients were male and 38.60% were female. The commonest drug to develop ADR was ofloxacin (26.28%) followed by diclofenac (14.04%). Only 12.28% of ADR were with Ceftriaxone and metronidazole. During this study period a total 326 patients received different cancer chemotherapeutic agents among which 30 patients (9.22%) developed various ADRs. The most common ADR was nausea and vomiting (53.33%), hematological ADR (40%), hepatotoxicity skin rash and diarrohea were least to occur.

Conclusion: The patterns of the adverse drug reactions and the drugs which caused them, varied in our study according to the different pattern of the drug intake, the associated illness and the susceptibility of the patients. This study was able to recognize the ADRs within a short period and was limited to a solitary institute. Yet, the results convincingly prepare for the edifice to lead us to further long term active surveillance in early detection of ADRs and drug safety. Further study in collecting ADRS with drugs used in special situations, population and drug interactions is an immense need.

Keywords: *Adverse drug reactions, Cutaneous adverse drug reactions, Pharmacovigilance, cancer chemotherapeutic agents, Psychotropic drugs*

1. INTRODUCTION

Modern medicines have changed the trend of management and control of diseases. Despite all the benefits, evidences show that mounting adverse reactions of medicines are rampant, sometimes causing illness, disability and even death. In some countries ADR ranks among top ten leading cause of mortality. The overall incidence of ADR in hospitalized patients is estimated to be 6.67% and fatal ADR is 0.32%. [1]. So to minimize the suffering of patients from ADR its earliest detection ADRs earliest and to establish the causality that assesses the relationship between drug treatment and occurrence of adverse events is the key. This is the important component of pharmacovigilance by which risk-benefit profile of a medicine is assessed in a better way encouraging their safe, rational and more effective use including cost effectiveness. [1]. Cutaneous adverse drug reactions (CADR) are the most frequent of all manifestations of drug sensitivity. Cutaneous ADR patterns and the drugs causing various reactions are changing every year, which may be due to the emergence of newer molecules and changing trends in the use of drugs. [2]. . In most of psychiatric illness long term pharmacotherapy is a norm and most of those drugs are associated with ADRs. Very often patients not responding to initial therapy require several trials with different medications. [3]. Very few reports are published in this context and the ADR incidence to SSRI, antipsychotics, antidepressant vary to a large extent. Hence identification and reporting of potential ADRs to these drugs (including antiepileptic) is important in psychiatry. [4] .

The safety of drugs used in patients of an adult age group cannot be extrapolated to a pediatric age group. The actual information regarding the frequency, severity and types of drugs most frequently causing adverse reactions in the pediatric age group is lacking. An active drug surveillance system is needed to capture risk information in children. [5]

Cancer chemotherapeutic drugs very often show ADRs. Nausea, vomiting, myelosuppression, mucositis etc. are very common ADRs due to cancer chemotherapy. There is paucity of data regarding the safety profile of cancer chemotherapy in Eastern India. [6] Hence the present study was undertaken to evaluate the pattern of ADRs reported in the department of dermatology, psychiatry, pediatrics, radiotherapy of MKCG Medical college hospital (tertiary care teaching hospital).

2. MATERIALS AND METHODS:

This was a prospective, observational study, carried from January 2013 to October 2014 in collaboration with department of dermatology, psychiatry, paediatric and radiotherapy of MKCG Medical College and hospital (tertiary care hospital).The study protocol of the present investigation was approved by Institutional ethics committee. Prior to the investigation the written informed consent was obtained from the participants and patient attendants. The detailed patients history viz; age, sex, presenting complaints, duration of illness, type of drug intake, past history of drug allergy, past history of illness were recorded in a predesigned case record form.The physical examination findings of the reaction, laboratory investigation reports if any for cutaneous ADR morphology of the reaction, site of involvement were recorded in ADR reporting form (CDSCO). The reaction details and treatment details were recorded as per expert opinion of the treating physician. All the ADR data were subjected for causality assessment using WHO-UMC scale. [7] the categories of causality association with the suspected drugs were established by a pharmacologist, experts of the concerned departments and a medicine specialist. Severity of the ADRs was assessed by Modified Hartwig and Siegel Scale. [8]

1. For patients having cutaneous ADRs [2]

a. Inclusion criteria
Both gender of age group between 15-80 years
Visible skin reactions to suspected drug**.**

b. Exclusion Criteria**:**
Suspected drug could not be traced.
Reactions due to disease.
Reaction to indigenous/ ayurvedic drugs

2. ADRs in patients on drug therapy for psychiatry illness. [3]

a. Inclusion criteria

In this study irrespective of their psychiatry diagnosis all the patients attending psychiatry OPD were screened for ADR. The screening was carried by a senior psychiatrist and a pharmacology resident trained in the psychiatry department for interviewing mental patients. Patients and their attendants were interviewed as well as past prescriptions and case notes if available were also reviewed. Laboratory investigations were advised if indicated clinically. Immediately the patients were followed up for the details of the reactions and the drugs. ADR monitoring was done till the discharge of the patients from the hospital and a follow up was conducted on repeat visits.

b. Exclusion criteria:

- pregnant woman having psychiatry illness with ADR
- patient with known substance abuser
- psychotic subjects not accompanied by family care giver because proper information could not be elicited

3. Paediatric patients showing ADRs-[5]

a. Inclusion criteria

- All patients of age group equal to or less than 14 years of either gender were screened for development of ADR if any.
- Paediatric in patients, out patients, intensive care units were included for screening.

b. Exclusion Criteria:

- Suspected drug could not be traced
- Reactions due to overdose of drugs or administration error.
- Non compliance of the drug

4. Patient with ADRs due to chemotherapy drugs-[6]

a. Inclusion criteria

- Patients of all age group of either gender receiving chemotherapy, attending in radiotherapy department during the study period were included
- Patients who developed at least one ADR due to chemotherapy including alopecia were considered.

Statistical analysis

- Incidence rate for occurrence of adr were calculated using MS office excel 2010. Column statistics expressing mean, standard deviation, median, range, confidence interval, for different parameters of ADRs were calculated using a statistical software, Graphpad prism version 5.0.

3. RESULTS:

This observational study was conducted over a period of one year and 10 months in OPDs and hospitalized patient of the major departments like dermatology, psychiatry, radiotherapy, paediatrics. Total 258 cases of suspected ADRs were detected out of them 21 cases were excluded for further analysis: 6 patient blamed indigenous medicines of unknown compositions, 11 patients failed to recall the correct name of the medications consumed, In 2 cases the skin reaction were indistinct, in 1 case viral Exanthematous reaction could not be included. 1 patient refused to give consent, hence 237 cases were included in the present study for final valuation.The study population comprised of total 180 adult patients, 43 were of paediatric age group, among the adult patient 99 (55%) were males and 81 (45%) were females. Also among 57children males outnumbered females (61.40% Vs 38.60%).

Figure-1

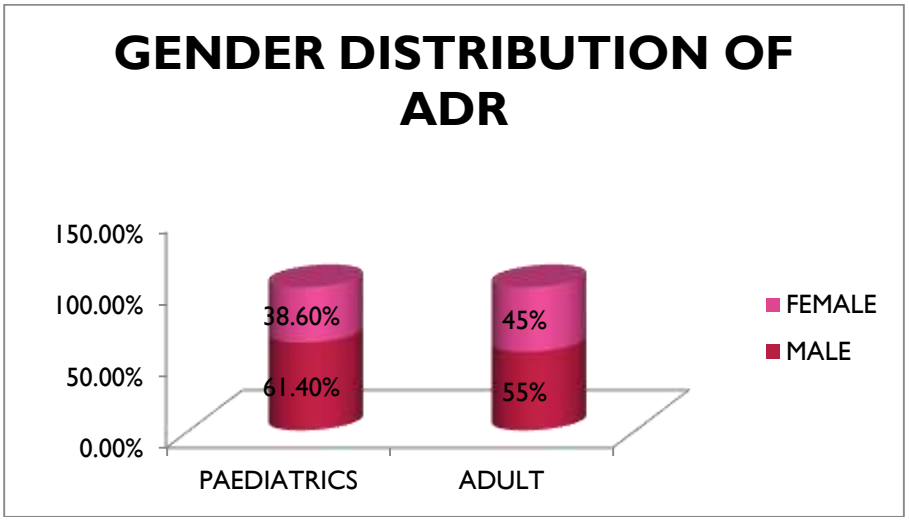

Figure-2

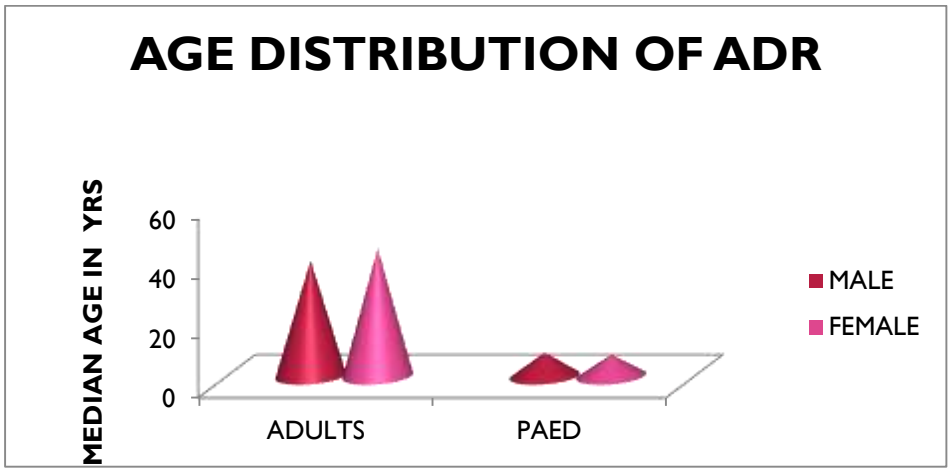

Table-1 COMMON CLASS OF DRUGS SHOWING CUTANEOUS ADVERSE DRUG REACTIONS

DRUGS	NO.OF CASES(%)	URTICARIA(%)	FDE (%)	BDE (%)	ED (%)	MUCOSITIS (%)	MRASH (%)	MPRASH (%)	PRASH (%)	SJS (%)	OTHER(%)
NSAIDS	24 (26.67)	5 (20.83)	2 (8)	3 (12.5)	6 (25)	2 (8.34)	3 (12.5)	1 (4.17)	0	0	2 (8)
FLOROQUINOLONE AND NITROIMIAZOLE FDC	19 (21.11)	0	9 (47)	3 (15.8)	1 (5.3)	2 (10.6)	0	1 (5.26)	0	0	3 (17)
ANTI RETROVIRAL THERAPY	10 (11.11)	3 (30)	0	0	3 (30)	2 (20)	2 (20)	0	0	0	0
B LACTAM ANTIBIOTICS	13 (14.40)	6 (46.15)	0	1 (7.69)	4 (30.76)	0	0	0	2 (15.3)	0	0
FLOROQUINOLONES ONLY	8 (8.89)	0	1 12.5	3 (37.5)	1 12.5	1 (12.5)	0	1 (12.5)	0	0	1 (13)
ANTI EPILEPTICS	5 (5.56)	0	0	0	1 (20)	1 (20)	0	1 (20)	0	0	2 (40)
NITROIMIDAZOLE ONLY	4 (4.44)	0	2 (50)	0	0	1 (25)	0	0	0	1 (25)	0
STEROID	3 (3.33)	0	1 34	0	1 (34)	0	0	0	0	0	1 (32)
SULPHA DRUGS	2 (2.22)	0	1 (50)	0	0	0	1 (50)	0	0	0	0
AZITHROMYCIN	2 (2.22)	0	0	0	0	1 (50)	0	0	1 (50)	0	0
TOTAL CASES	90	14 (15.56)	16 (17.78)	10 (11.11)	17 (18.89)	10 (11.11)	6 (6.67)	4 (4.44)	3 (3.33)	1 (1.11)	9 (10)

N.B BDE—BULLOUS DRUG ERUPTION, ED-EXFOLIATIVE DERMATITIS,M RASH-MACULAR RASH M P RASH-MACULOPAPULAR RASH, P RASH-PAPULAR RASH

Data depicted in this table shows common class of drugs which caused major cutaneous adverse drug reactions. Out of 237 ADR cases 90 were cutaneous ADRs. Among the various patterns of CADRs, the major presentations were exfoliative dermatitis (n= 17; 18.89%), Fixed drug eruption (n= 17;78%) and 15.56% of them were urticarial rashes. Both bullous drug eruption and mucositis were 11.11%. Other CADRs were hypersensitivity, steroid induced striae and acne which comprised 10% of CADRs. Various pattern of rashes like macular (6.67%), maculopapular (4.44%), and papular (3.33%) were also observed.

Drugs suspected to cause CADR in the study population were broadly classified in 10 groups. Among them 26.67% of CADR were caused by various NSAIDs. This was followed by Flouroquinolone and nitroimidazole fixed dose combination (21.11%), β - lactam antibiotics (14.4%), antiretroviral therapy (11.11%) and only Flouroquinolone (8.89%). Antiepileptic comprising of phenytoin and valproate showed 5.56% of CADRS. Lower incidence of CADR were observed with some steroid (3.33%), nitroimidazole only (4.44%), sulfa drugs (2.22%), azithromycin (2.22%).

Table-2 CUTANEOUS ADVERSE DRUG REACTION DUE TO NON STEROIDAL ANTIINFLAMATORY DRUGS (NSAIDS)

drugs	urticaria n=5	FIXED DRUG ERUPTION n=2	BULLOUS DRUG ERUPTION n=3	EXFOLIATIVE DERMATITIS n=6	MUCOSITIS n=2	MACULAR RASH n=3	MACULOPAPULAR RASH n=1	OTHER n=2
nsaids (n=24)	diclofenac (2) paracetamol(2) naproxen (1)	paracetamol (1) aceclofenac (1)	aspirin (1) diclofe nac (1) paracetamol(1)	diclofenac (2) ibuprofen (2) nimesulide (1) aceclofenac (1)	nimesulide (1) diclofenac (1)	diclofenac (1) paracetamol (1) aceclofenac (1)	diclofenac (1)	diclofenac (2)

This table data emanated that the overall cutaneous ADRs shown by NSAIDS were 26.67%. Among these Diclofenac sodium caused urticaria (n=2), bullous drug eruption (n=1), exfoliative dermatitis (n=2), mucositis (n=1), macular rash (n=1), maculopapular rash (n=1) and other unspecified dermatological reactions (n=2). Another congener of diclofenac, aceclofenac caused fixed drug eruption (n=1), macular rash (n=1) and exfoliative dermatitis (n=1). In only one case Aspirin produced bullous drug eruption. Fixed drug eruption (n=1), Urticaria (n=2), Bullous drug eruption (n=1),Macular rash (n=1) was also seen with Paracetamol. Exfoliative dermatitis was the most common reaction followed by urticaria

Table-3 CUTANEOUS ADVERSE DRUG REACTION TO FLOROQUINOLONES, NITROIMIDAZOLE AND THEIR FIXED DOSE COMBINATION

drugs	fixed drug eruption n=12	bullous drug eruption n=6	exfoliative dermatitis n=2	mucositis n=4	maculopapular rash n=2	sjs n=1	other n=4
floroquinolones and nitroimidazole fdc (n=19)	norfloxacin+ tinidazole (3) ciprofloxacin + tinidazole (3) ofloxacin+ ornidazole	norfloxacin+ tinidazole (1) ciprofloxacin + tinidazole (1) ofloxacin+ ornidazole	norfloxacin+ tinidazole (1)	ciprofloxacin + tinidazole (1) ofloxacin+ ornidazole (1)	ciprofloxacin + tinidazole (1)	_	norfloxacin+ tinidazole (1) ciproflox acin+ tinidazole (2)

	(3)	(1)					
FLOROQUINOLONES ONLY (n=8)	OFLOXACIN (1)	OFLOXACIN (2) CIPROFLOXACIN (1)	OFLOXACIN (1)	CIPROFLOXACIN (1)	CIPROFLOXACIN (1)	_	OFLOXACIN (1)
NITROIMIDAZOLE (N=4)	METRONIDAZOLE (2)	-s	_	TINIDAZOLE (1)	_	TINDAZOLE(1)	

Different pattern of cutaneous ADR shown by fluroquinolones, nitroimidazoles and their fixed dose combination are shown in this table. In this study population ,the maximum number of reactions were fixed drug eruption (n=12) followed by bullous drug eruption (n=6).Among all the fixed drug eruption cases norfloxacin + tinidazole, ciprofloxacin + tinidazole, ofloxacin+ ornidazole showed equal proportion of occurrence. Only few fixed drug eruption was observed with metronidazole (n=2), ofloxacin (n=1). Different FDC of flouroquinolone and nitroimidazole showed maximum cutaneous reaction (n=19) followed by flouroquinolones only (n=8), nitroimidazole only (n=4). Bullous drug eruption to different fluroquinolone and nitroimidazole was also a common presentation of cutaneous ADR. The other minor reaction like mucositis, exfoliative dermatitis, maculopapular rash was also observed. In one case of Tinidazole user SJS was observed.

TABLE-4 CAUSALITY ASSESSMENT AND SEVERITY SCALE OF CUTANEOUS ADRs

CUTANEOUS ADR	SEVERITY SCALE	CAUSALITY ASSESSMENT
URTICARIA	Severe(6) Moderate(8)	Certain(6) Probable(8)
EXFOLIATIVE DERATITIS	Severe(17)	Possible(17)
BULLOUS DRUG ERUPTION	Severe(10)	Possible(10)
FIXED DRUG ERUPTION	Moderate(16)	Probable(16)
MUCOSITIS	Moderate(10)	Probable(10)
MACULAR/MACULOPAPULAR/ PAPULAR RASH	Moderate(13)	Probable(13)

The severity scale and causality assessment of different CADRs are depicted in this table. 37.5% of CADRs were of severe type and 62.5% were of moderate degree. As per WHO-UMC scale 6.67% of ADRs were under certain category. 53.3% and 40% of ADRs were of Probable and possible cause respectively

Figure-3

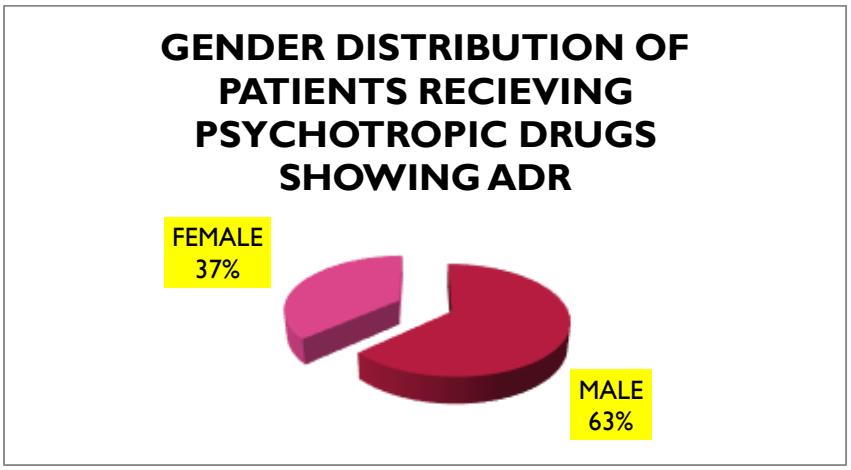

Table-5 ADR RELATED WITH DRUGS USED FOR DIFFERENT PSYCHIATRY ILLNESS

DRUGS	NO OF CASE (%)	EPS (%)	ANTICHOLINERGIC (%)	WEIGHT GAIN(%)	PEDAL EDEMA (%)	SEDATION (%)	LEUKOPENIA (%)
HALOPERIDOL	25 (20.83)	25 (100)	0	0	0	0	0
TCA	20 (16.67)	0	12 (60)	0	0	8 (40)	0
OLANZAPINE	17 (14.17)	0	0	12 (70.59)	5 (29.41)	0	0
SSRI	17 (14.17)	0	8 (47.06)	7 (40.18)	0	2	0
RISPERIDONE	16 (13.33)	16 (100)	0	0	0	0	0
CLOZAPINE	15 (12.5)	0	0	9 (60)	4 (26.67)	0	2 (13.33)
VALPROATE	10 (8.33)	0	0	7 (70)	0	3	0
TOTAL CASE	120	41 (34.17)	20 (16.17)	35 (29.17)	9 (7.5)	13 (10.83)	2 (1.67)

In this study, a total of 9900 patients were screened for ADR. Out of which 60 patients were suspected at least one ADR (0.61%). Among them, 38 were male patients and 22 females. The median age of subjects showing ADRs was 42 years. Seven major different kinds of drugs were used for different kind of psychiatry illness. Extrapyramidal side effects was the commonest ADR (n=41; 34.17%) reported followed by weight gain (n=35; 29.17%). Anticholinergic side effects and sedation were observed in 16.17% and 10.83% of cases respectively. The most common drug causing extrapyramidal side effect was haloperidol (n=25; 20.83%) and all risperidone users showed extrapyramidal side effects. Olanzapine (n=12) was commonest to cause weight gain and tricyclic antidepressant (n=12) were the major cause of anticholinergic side effects.

Table-6 CAUSALITY ASSESSMENT AND SEVERITY SCALE OF ADRs WITH PSYCHOTROPIC DRUGS

ADVERSE DRUG REACTION	SEVERITY SCALE	CAUSALITY ASSESSMENT
EXTRAPYRAMIDAL SIDE EFFECTS(41)	Severe	Probable
ANTI CHOLINERGIC EFFECTS (20)	Moderate	Possible
WEIGHT GAIN (35)	Moderate	Possible

Pedal edema (9)	Moderate	Probable
Sedation(13)	Severe	Probable
Leukopenia(2)	Moderate	Probable

Severity scale and causality assessment of ADRs to psychotropic drugs are depicted in this table. 45% of ADRs were severe in nature and 55% were in moderate degree. As per WHO-UMC scale of causality assessment 55% and 45% of ADRs were probable and possible cause respectively

Figure-4

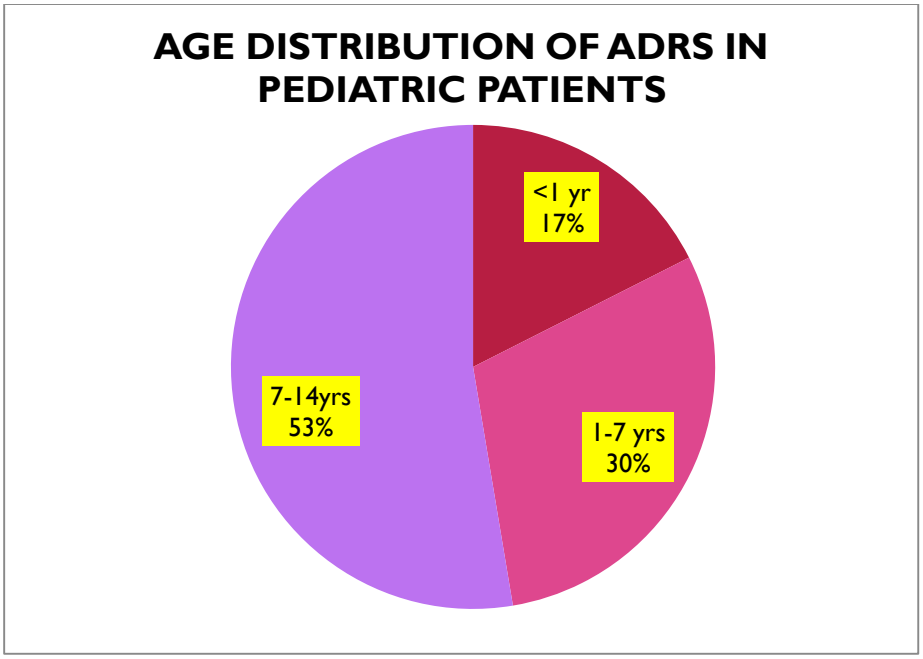

Table-7 DISTRIBUTION OF ADRs IN DIFFERENT PAEDIATRIC AGE GROUPS

AGE IN YEARS	COMMON ADRs REPORTED
< 1 YEAR (n=10)	Rash, Urticaria, Fixed drug eruption
1—7 YEAR (n=17)	Steven Jhonson's syndrome, Urticaria, Macular eruption, Papular eruption, Anaphylactic shock
7---14 YEAR (n=30)	Fever, Redman syndrome,Urticaria,Gastritis, Anaphylactic reaction, Hypersensitivity

Table-8 ADR RELATED TO DRUGS USED FOR DIFERRENT PAEDIATRIC ILLNESS

DRUGS	NO.OF CASES(%)	URTICARIA & RASH(%)	VOMITING (%)	ANAPHYLATIC SHOCK(%)	FEVER (%)	DIARRHOEA (%)
OFLOXACIN	15 (26.28)	10(66.67)	5(33.33)	0	0	0
CEFTRIAXONE	7 (12.28)	2(28.57)	3(42.86)	1(14.29)	1(14.29)	0
METRONIDAZOLE	7 (12.28)	5(71.43)	2(28.57)	0	0	0
CEFIXIME	4(7.02)	4(100)	0	0	0	0
AZITHROMYCIN	5(8.77)	4(80)	0	0	0	1(20)

VANCOMYCIN	1(1.75)	1(100)	0	0	0	0
CEFOTAXIME	1(1.75)	1(100)	0	0	0	0
PIPERACILLIN+ TAZOBACTAM	1(1.75)	0	0	1(100)	0	0
DICLOFENAC	8 (14.04)	3(37.50)	5(62.50)	0	0	0
PARACETAMOL	2(3.51)	2(100)	0	0	0	0
OFLOXACIN +PARACETAMOL	2(3.51)	2(100)	0	0	0	0
DOXYCYCLINE	1(1.76)	1(100)	0	0	0	0
AZITHROMYCIN+ OFLOXACIN+ PARACETAMOL	3(5.27)	1(33.33)	2(66.67)	0	0	0

The commonest drug to develop ADR was ofloxacin (26.28%) followed by diclofenac (14.04%). Only 12.28% of ADR were with Ceftriaxone and metronidazole. The commonest reaction to different drug was urticaria (63.16%) followed by vomiting (29.82%.) Only minor reactions like fever and diarrohea were 1.76% in each category

Table-9 CAUSALITY ASSESSMENT AND SEVERITY SCALE OF PAEDIATRIC ADRs

ADVERSE DRUG REACTION	SEVERITY SCALE	CAUSALITY ASSESSMENT
URTICARIA(36)	Severe(2) Moderate(34)	Probable(2) Possible(34)
VOMITING(17)	Moderate	Probable
ANAPHYLATIC SHOCK(2)	Severe(2)	Certain
FEVER(1)	Moderate	Probable
DIARRHOEA	Moderate	Probable

In this table, severity and causality assessment of drug reactions seen in pediatric age group are depicted. Out of all only 7% reactions were severe grade and 93% were of moderate degree. WHO- UMC scale of causality analysis of the reactions revealed that, 3.5%, 36.4% and 59.6 % of them were in certain, probable and possible category respectively.

Table-10 CANCER CHEMOTHERAPEUTIC DRUGS SHOWING HEMATOLOGICAL ADRS

DRUGS	ANEMIA	THROMBOCYTOPENIA	NEUTROPENIA
PACLITAXALE+CARBOPLATIN (n=1)	1	-	-
PACLITAXALE (n=1)	1	-	-
ADIRAMCIN+CYCLOPHOSPHAMDE(n=2)	1	1	-
CARBOPLATIN+CYCLOPHOSPHAMIDE (n=3)	1	1	1
CARBOPLATIN+5-Florouracil (n=1)	1	-	-
OXALIPLATIN (n=1)	1	-	-
PEMITRAXATE+CARBOPLATIN (n=1)	1	-	-
BLEOMYCIN+ETOPOSIDE (n=1)	-	-	1
VINCRISTINE (n=1)	-	-	1

During this study period a total 326 patients received different cancer chemotherapeutic agents among which 30 patients (9.22%) developed various ADRs. The most common ADR was nausea and vomiting (53.33%), hematological ADR (40%), hepatotoxicity skin rash and diarrohea were least to occur. Anemia was most common ADR to all cancer chemotherapeutic agents.

TABLE-11 CANCER CHEMOTHERAPEUTIC DRUG SHOWING GASTROINTESTINAL AND CUTANEOUS ADRS

DRUGS	Nausea, vomiting	Hepatotoxicity	Rash	Diarrhoea
PACLITAXALE+CARBOPLATIN (n=3)	2	-	-	1
PACLITAXALE (n=3)	-	1	2	-
ADIRAMCIN+CYCLOPHOSPHAMDE (n=2)	2	-	-	-
ADIRAMYCIN+CYCLOPHOSPHAMIDE+ 5-FU (n=2)	1	1	-	-
CYCLOPHOSPHAMIDE+DOXORUBICIN+ 5-FU (n=2)	2	-	-	_
CHOP (n=1)	-	1	-	_
CARBOPLATIN+5-FU (n=2)	2	-	-	-
CARBOPLATIN+IFOSAMIDE (n=1)	1	-	-	-
5-FU (n=1)	1	-	-	-
DOCETAXALE+DOXORUBICIN (n=1)	1	-	-	-
BLEOMYCIN+ETOPOSIDE N=1	1	-	-	-
BLEOMYCIN+ETOPOSIDE+ CARBOPLATIN (n=1)	1	-	-	-
IFOSAMIDE+DOXORUBICIN (n=1)	1	-	-	-
5-FU+CISPLATIN+ DOCETAXALE (n=1)	_	-	_	1
CYCLOPHOSPHAMIDE+DOCETAXALE n=1	1	-	-	-

In this study sample, the commonest ADR, Nausea and vomiting was observed with all the chemotherapeutic combinations. Hepatotoxicity was observed with paclitaxale and adiramycin. Cutaneous reractions were seen only with paclitaxal. Patients receiving 5-FU+Docetaxale+cisplatin, and paclitaxale + carboplatin had severe diarrohoea.

Table-12 CAUSALITY ASSESSMENT AND SEVERITY SCALE OF ADR DUE TO CANCER CHEMOTHERAPY

ADVERSE DRUG REACTION	SEVERITY SCALE	CAUSALITY ASSESSMENT
NAUSEA,VOMITING(16)	Moderate	Probable
ANEMIA(7)	Moderate	Possible
NEUTROPENIA(3)	Moderate	Possible
THROMBOCYTOPOENIA(2)	Moderate	Possible
RASH(2)	Moderate	Probable
HEPATOTOXICITY(3)	Severe	Possible
DIARRHOEA(2)	Moderate	Probable

In this study, it was observed that only hepatoxiciy cases were of severe grade. Rest all patterns of reactions were of moderate degree in severity. Only 57.14% reactions had probable causality, all other ADRs had possible causal association with different anti - neoplastc drugs.

No case of death due to ADR was observed during the study period.

4. DISCUSSION:

In the present investigation a total number of 1,02,436 patients were enrolled both in and out patient department during the study period. Among them 258 had various adverse drug reactions. As per inclusion criteria only 237 patients were enrolled for further analysis. Relative incidence of CADR among the patients attending dermatology OPD was found to be 4.02 per 1000 in our study. This is lower than the observation reported in earlier Indian studies, such as those by Chatterjee, *et al.2006.*

[9] (26 per 1000) and Ghosh, *et al 2006.* [10] (285 per 1000). One possible explanation for this low incidence rate is that the study is conducted in a tertiary center, so that minor rashes may not have come to the dermatology OPD or patients could have been treated by physicians in other disciplines.

Analysis of CADRs collected from dermatology OPD

In this study exfoliative dermatitis was the commonest reaction (18.89%) which was mostly caused by NSAIDs (6/17) and to a lesser extent by β lactam antibiotics (4/17) and few cases were due to antiretroviral drug combiation (3/17), flouroquinolone and nitroimidazole fixed dose combination (2/17).[Table-1,2,3]. But R.M.Patel reported that NSAIDs are responsible to cause fixed drug eruption to most extent (22.8%) which differs from our observation. [11]. The next common reaction, fixed drug eruption (17.78%) which was due to flouroquinolone and nitroimidazole fixed dose combination (9/16) , followed NSAIDs and nitroimidazole only to equal proportion i.e 2/16. [table-1,2,3]. Norfloxacin+tinidazole, Ciprofloxacin+tinidazole and ofloxacin+ornidazole combination caused such reaction in equal proportion. We received one report from each category use of ofloxacin only ,predinisolne, telmisartan . But study done by Patel RM, Marfatia Y S shows co-trimoxazole as the commonest offending agent in causing FDE . In this study the period of development of FDE was within 2-12 days with a mean of 3.69±0.63 days , which differs from Patel R.M et al 2008(01-45 days). [11]. Urticarial rashes (15.56%) were the next common reaction observed in our study. It was produced by drugs like Piperacillin+tazobactam combination (6/14), NSAIDS (5/14), antiretroviral drugs (3/14) like nevirapin and zidovudine. Among NSAIDs diclofenac (2/5),paracetamol (2/5) ,naproxen (2/5) were the causative agents of such reaction. This observation differs from Abanti et al 2012 in which few urticaria cases were reported. In an earlier north indian study the incidence of urticaria was reported to be 14% which simulates with our observation**.(12)**

A high percentage of urticarial reaction (32.2%) was reported in the study of Inbaraj SD et al 2012. Other CADRs were hypersensitivity, steroid induced striae and acne comprised 10% of CADRs. Various pattern of rashes like macular rash (6.67%), maculopapular rash (4.44%),papular rash (3.33%) were also observed.

Pharmacovigilance of ADRs to drugs used in psychiatry illness

During this study period a total of 9900 patients attended psychiatry OPD. Among them 60 patients developed ADR due to different psychotropic drugs. Hence the incidence of ADR was 0.61%. A similar result was psychotropic drugs in the study of Dimitrova Z et al 2002. Among 60 patients they had one or more adverse drug reaction that accounted for total of 120 reactions. Hence total number of ADRs outnumbered total patients. In our study we found antipsychotic drugs were most commonly responsible for ADRs. Among which haloperidol (25), olanzapine (17), risperidone (16), clozapine (15) were the commonly prescribed drugs.The most common adverse drug reaction observed in the study was caused by haloperidol (100%),risperidone (100%). Weight gain was another commonest adverse effects with olanzapine (12), clozapine (9). In few cases of olanzapine and clozapine users pedal edema were also observed. Only in two cases leukopenia was also observed with clozapine.

In another Indian study done by Sengupta et al 2011 olanzapine was the most frequent incriminating drug to cause 31.82% of ADR followed by haloperidol (19.03%), which differs from our observations.[3] This discrimancy is possibly because olanzapine was frequently prescribed drug and the study was on the free of cost dispensed drug from their hospital pharmacy. In our observation, among the antidepressants amitryptyline was the most common incriminated drug to cause ADR followed by fluoxetine, clomipramine and paroxetine which caused equal frequency of ADRs. Among different pattern of ADR anticholinergic side effects were commonest reaction to be caused by amitryptyline (8). Clomipramine paroxetine,fluoxetine also produced anticholinergic side effects with equal frequency (4). Sedation was another minor unpleasant reaction which was observed with all the antidepressants except fluoxetine. Both fluoxetine and paroxetine caused abnormal weight gain in 5 and 2 number of patients respectively. Valproate ,an antiepileptic another psychotropic drug is being most frequent prescribed drug in our hospital setup. Apart from weight gain (70%), sedation (30%) no other side effects observed. Regarding severity score all the extrapyramidal symptoms and sedations were of severe grade and the rest ADRs were of moderate degree. On causality assessment only anticholinergic and weight gain were of possible type and the rest all were of probable type. In our study we had no case of causality of certain category, since rechallenge was not attempted with the offending drug. This finding corroborates with Sengupta et al 2011.[3]

Analysis of ADR patterns in paediatric patients

Most common drug implicated in our study was ofloxacin which caused urticaria to most extent then by vomiting. The next common incriminated drug was diclofenac (14.04%) which cause vomiting in majority of cases (62.5%) and urticaria with rash in few cases (37.5%). Both ceftriaxone and metronidazole were the next common drugs each of which accounted for 12.8% of total ADR reports. Ceftriaxone induced vomiting to most extent followed by urticaria and fever. Only one case of anaphylatic shock was observed with i.v. ceftriaxone.

Metronidazole was the next category of drug to produce urticaria. 80% of azithromycin induced ADRs were urticarial rash. Only one case of diarrhea was seen with this drug. Two cases of vomiting were reported with combination therapy of

azithromycin, ofloxacin ,paracetamol. Only one case of anaphylatic shock was observed with i.v. piperacillin and tazobactam combination. A significant finding of this study was no case of death due to ADR was reported. Our findings corroborate with Priyadarshini et al 2011. [5] The majority of urticarial reactions observed in this study were of moderate degree (34/36) and 94.4% of ADRs were possible causality. Severe reactions included ofloxacin induced steven-jhonson syndrome and vancomycin induced redman syndrome.

Among all reported ADRs in our study (57) only 4 reactions were of severe type, rest all were of moderate grade (93%). 36.8% of all ADR were of probable causality and to lesser extent were of possible category as per WHO-UMC scale. A similar observation was reported by Priyadarshini et al 2011 and Smyth et al 2012. [5,13]. As this study was able to recognize the ADRs within a short period and was limited to a solitary institute, still it highlights the impact of intensive prospective collection of ADRs to improve early detection of ADR and paediatric drug safety.

Pharmacovigilance of ADRs to drugs used in cancer chemotherapy

In the present investigation a total of 326 patients had taken cancer chemotherapy drugs out of them 30 patients developed various ADRs a having the incidence of 9.22%. Different pattern of ADR found to be more common in male population. Patients of median age 35.5 year encountered major ADR. Among them 6 number of patients more than 50 years of age. Most common cancer in our study was stomach cancer followed by breast cancer. Nausea, vomiting were found to be commonest ADR (53.3%), followed by hematological reactions (40%). Very few cases of hepatotoxicity, minor skin reactions, diarrhea were also observed. The commonest insulting drug causing major ADRs were paclitaxale and paclitaxale and carboplatin combination. Nausea ,vomiting was observed with all the cancer chemotherapeutic combination. Hepatotoxicity was observed with paclitaxale,adiramycin,cyclophosphamide. A similar observation was reported by Prashad et al 2013 in which cisplatin was highlighted the most offending drug. Probably the more frequent prescriptions of paclitaxale and paclitaxale carboplatin combination, we have received more ADR with these drugs. Out of total patients only 7 cases of anemia were observed. Except hepatotoxicity all other ADRs were of severe category. With regards to causality assessment nausea, vomiting, cutaneous rash and diarrhea were of probable scale and all other ADRs were under possible category. On WHO-UMC scale out of 35 total reactions 57.1% were probable category and 42.9% were possible category. Within this study period as few cases are encountered the analysis of ADR reports provide a baseline data. A longer study and active surveillance will detect ADRs earlier.

5. CONCLUSION:

The patterns of the adverse drug reactions and the drugs which caused them, varied in our study according to the different pattern of the drug intake, the associated illness and the susceptibility of the patients. This study was able to recognize the ADRs within a short period and was limited to a solitary institute. Yet, the results convincingly prepare for the edifice to lead us to further long term active surveillance in early detection of ADRs and drug safety. Further study in collecting ADRS with drugs used in special situations, population and drug interactions is an immense need.

A sound knowledge of the adverse drugs reactions, a careful history taking and a cautious approach during the prescription of new drugs can prevent most of the adverse drug reactions. As newer drugs are entering our market at a rapid pace, Pharmacovigilance, with special attention to monitoring and reporting of adverse drug reactions must be encouraged. We should provide the necessary information to regulators who can amend the recommendations on the use of the medicines. Improving communication between the health professionals and the public; and educating the health professionals to understand the effectiveness and risk of medicines they prescribe is the need of this era. Thus the harm can be minimized by ensuring the quality, safety, efficacy and the rational use of drugs

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[1] Dr.RohanC.Hire, Dr.ParagJkinage, Dr.Nilesh N.Gaikwad. Causality assessment in pharmacovigilance: a step towards quality care. Scholars Journal of Applied Medical Sciences2013;1(5):386-392

[2] Saha Abanti, Das Nilay Kanti, Hazra Avijit, Gharami Ramesh Chandra, Chowdhury Satyendra Nath,Datta Pijush Kanti.Cutaneous adverse drug profile in a tertiary care outpatient setting in eastern india.indian j pharmacol 2012;44(6):792-7

[3] Gairik Sengupta, Subhrojyoti Bhowmick, Avijit hazra,Ananya Datta,Musfikur Rahaman. ADR monitoring of psychotropoic drugs in an Indian hospital.indian journal of pharmacology 2011;43:36-39.

[4] Ravi Philip Raj kumar,George melvin.Pharmacovigilance to psychiatry: an introduction.indian j psychiatry 2014.56;(2):176-181.

[5] R. Priyadharsini, A. Surendiran, C. Adithan, S. Sreenivasan1, Firoj Kumar Sahoo.. Adverse drug reactions in paediatric population. Journal of Pharmacology and Pharmacotherapeutics 2011;2(4):277-80

[6] Anju Prasad, Pratyay Pratim Datta1, Jibak Bhattacharya, Chaitali Pattanayak, Ashok Singh Chauhan1 and Parbaty Panda. Journal of Pharmacovigilance 2013; 1(2).1000107.

[7] www.who-umc.org

[8] Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm 1992;49:2229-32

[9] Chatterjee S, Ghosh AP, Barbhuiya J, Dey SK. Adverse cutaneous drug reactions: A one year survey at a dermatology outpatient clinic of a tertiary care hospital. Indian J Pharmacol 2006;38:429-31

[10] Ghosh S, Acharya LD, Rao PG. Study and evaluation of various cutaneous adverse drug reaction in Kasturaba Hospital, Manipal. Indian J Pharm Sci 2006;68: 212-5

[11] Patel RM, Marfatia Y S. Clinical study of cutaneous drug eruptions in 200 patients. Indian J Dermatol Venereol Leprol 2008;74:430

[12] Sharma VK, Sethuraman G, Kumar B. Cutaneous adverse drug reactions:Clinical pattern and causative agents - a 6 year series from Chandigarh, India.J Postgrad Med 2001;47:95-

[13] Smyth, R.M., Gargon, E., Kirkham, J., Cresswell, L., Golder, S., Smyth, R., Williamson, P. Adverse drug reactions in children-a systematic review. PLoS ONE 3 2012, e24061

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