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A NEW DISCERNMENT FOR ADVANCING THE ADVERSE DRUG REACTION MONITORING AND REPORTING IN A TERTIARY CARE TEACHING HOSPITAL: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Adverse drug reactions are posing a major challenge to the health care system as they compromise the safety on drug therapy. Adverse drug reactions are not only the cause of mortality and morbidity but also significant increase in the health care cost.

KEYWORDS: Adverse drug reactions, prospective observational study, Pharmacovigilance, causality and side effects.

INTRODUCTION

WHO defines adverse drug reactions as "A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or modification of physiological function".[1] Adverse drug reactions are posing major challenge to the health care system as they compromise the safety of drug therapy. Adverse drug reactions are not only the cause of mortality and morbidity but also significant increase in the health care cost.[2] Several contributing factors for adverse drug reactions include age, sex, polypharmacy, concurrent diseases, race and genetic polymorphism.[3] The other predisposing factors that would increase the risk of developing adverse drug reactions include drug related factors, patient related factors, disease related factors, patient related factors, disease related factors and social factors.[4]

WHO defines Pharmacovigilance as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems".[5] Pharmacovigilance plays a key role in ensuring that patients receive safe drugs. It is the process of being alert to the possible unwanted or harmful effects of therapeutic medications so that they could be detected early and remedial measures instituted.[6-7] Benefits of adverse drug reaction reporting includes:

- Provide information regarding risk profile of the drug.
- Harmonizes the risk-management activities and efforts to minimize the drug related problems.
- Assess the safety profile of drugs, especially recently approved drugs.
- Quantify the adverse drug reactions incidence rate.
- Awareness development in health care professional and patients about potential drug related problems
- Assessment of economic impact due to adverse drug reactions and strategies to minimize the same by assessing severity and preventability.[4]

The classification of adverse drug reaction

Table 1: I. Rawlins-Thompson classification of adverse drug reactions.

Type of	Characteristics	Examples	Management
Type A (augmente deffects)	Dose-related Common (overall proportion of adversedrug reactions - 80%) Suggestive timerelationship	Drug toxicity Respiratorydepression caused by opioids. Bleeding manifestationscaused	Reduce dose or withholdConsider e ffects of concomitant therapy

	Related to a pharmacological actionof the drug Predictable from knownpharma cology Variable severity, butusually mild High morbidityLow mortality R eproducible	by warfarin Side effects: Constipation caused by chronic opioid use Anticholinergiceffect s of tricyclic antidepressants Secondary effects: Development of super infection after suppress ionof bacterial floraby Antibiotics	
Type B(bizarree ffects)	Not dose–relatedUncommon Not related to a pharmacological actionof the drug Not predictable from known pharmacology Variable severity, proportionate ly moresevere than type A High morbidity High mortality Not reproducible	Intolerance Tinnitus caused by small doses ofaspirin Allergy (hypersensitivity or im munological) Result of an immune responseto a drug: Penicillin- induced urticaria Pseudo allergic(non - immunological) Immediate, gen eralised reaction involving mast- cell mediator release: respiratory sy ndromes caused by NSAIDs	Withhold and avoid in thefuture
Type C (chronic effects)	Uncommon Related to cumulativedose Long term exposurerequired	Osteonecrosis ofjaw caused by chronic use of bisphosphonates	Reduce dose or withhold; withdrawal may have to b eprolonged
Type D (delayed effects)	Uncommon Usually dose-related Seen on prolonged exposure to a drug orexposure at a critical time	Teratogenesis Carcinogenesis Tardive dyskinesia causedby antipsychotic medication	Often intractable
Type E (endof treatment effects)	Uncommon Occurs soon after withdrawal of a drug	Withdrawal seizures upon terminating anti-convulsant therapy	Reintroduce and withdrawslowly
Type F (failure of therapy to produce thedesire effect)	Common May be dose-related Often caused by drug interactions	Ineffectiveness Resistance of a microorganism ortumour to the drug action Tolerance Tachyphylaxis	Increase dosage or changethe therapeutic agent; Consider effects of concomitant therapy

Table 2: WILLS and BROWN Classification.

Classification of ADR	Features	Examples
Type A (Augmented)	i. Relatively common ii. Pharmacologically predictable iii. Dose related iv. Improves ifmedicine is withdrawn	i. Hypoglycaemia with oralhypoglycaemics ii. Bradycardia with b-blockers, etc.
Type B (Bizarre)	i. Involves interaction with a microorganism ii. Pharmacologically predictable iii. Improves if medicine iswithdrawn	i. Dental caries with sugarcoated tablets ii. resistance due to overuseof any one antibiotic, etc.
Type C (Chemical)	i. Related to drug concentration ii. An irritant reaction	i. Extravasation reactions ii. Angioedema etc.
Type D (Delivery)	i. Caused by method of administration or nature offormulation ii. Improves if medicine is withdrawn or method of deliverychanged	i. Inflammation or infectionaround implant particles ii. Infection at site ofinjection, etc.
Type E (Exit/End of treatment)	i. Pharmacologicallypredictable ii. Begins only when the medicine	i. Withdrawal reactions due to opioids, benzodiazepines,clonidine, b- blockers, etc.

	is stopped or dose is reduced iii. Improves if medicine isreintroduced	
Type F (Familial)	Occurs only in the geneticallypredisposed	i. Haemolytic anaemia with Primaquin in G6PD deficientindividuals, etc.
Type G (Genotoxicity)	Causes irreversible geneticdamage	i. Teratogenic agents like thalidomide causing geneticdamage in the foetus, etc.
Type H (Hypersensitivity)	i. Requires activation of immunesystem ii. Improves if medicine iswithdrawn	i. Anaphylaxis with penicillin ii. Allergic skin reactions with antimicrobial agents,etc.
Type U (Unclassified)	Mechanism not understood	i. Taste disturbances withsimvastatin ii. Nausea and vomiting withgaseous anaesthetic, etc.

II. Classification based on the severity of reaction

Karch and Lasanga classified adverse drug reactions, based on severity into minor, moderate, severe and lethal as defined below:

i. Minor: no antidote, therapy or prolongation of hospitalization required.
ii. Moderate: requires a change in drug therapy, specific treatment or anincrease in hospitalization by at least 1 day.
iii. Severe: potentially life threatening, causing permanent damage or requiring intensive medical care.
iv. Lethal: directly or indirectly contributes to the death of the patient.[5]

III.Classification based on frequency

The following standard categories of frequency are recommended:[6]

Table 3: Based on frequency.

Classifications	Frequency
Very common	>1/10 (> 10%)
Common (frequent)	>1/100 and < 1/10 (> 1% and < 10%)
Uncommon (infrequent)	>1/1,000 and < 1/100 (> 0.1% and < 1%)
Rare	> 1/10,000 and < 1,000 (> 0.01% and <0.1%)
Very Rare	< 1/10,000 (< 0.01)

MATERIALS AND METHODS

A prospective observational study was conducted in Government General Hospital, Guntur, which is a 1400 bedded tertiary care teaching hospital to which patients come from 4 districts. The study was conducted in a period of 6 months i.e. from November 2020 to April 2021 in patients who developed an adverse drug reaction in both inpatients and outpatients in specified departments.

Study Site: Government General Hospital, Guntur.

Study period: 6 months i.e., from October 2020 to March 2021

Study Design: Prospective observational study

Study Population: Patients who developed an adverse drug reaction in specified departments in both IP and OP

Materials used

1. Adverse drug reaction reporting forms
2. Naranjo ADR probability assessment scale
3. WHO causality assessment scale
4. Hartwig's severity assessment scale
5. Alert cards

Inclusion Criteria

1. Patients of all ages and both genders who have suspected adverse drug reaction after the drug treatment from selective departments [general medicine, neurology, cardiology, oncology, psychiatry, anti-retroviralcentre, gynecology].
2. Patients receiving allopathic medications from the selective departments included in the study.

Exclusion criteria

ADRs due to Drug-drug interactions, over dosing or excess consumption, medication errors, Drug-food interactions.

STUDY PROCEDURE

The study was approved by the Institutional Human Ethics Committee of Guntur Medical College and Government General Hospital, Guntur, Andhra Pradesh, filed under number GMC/IEC/390/2020 and was conducted in accordance with the ethical guidelines of the Declaration of Helenski (created in 1964 and revised in 2002). Informed consent form was taken from all the subjects prior to the study which was mentioned in the local language (Telugu).

ANNEXURES
DATA COLLECTION FORM

Version-1.3

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by Healthcare Professionals

INDIAN PHARMACOPOEIA COMMISSION
(National Coordination Centre-Pharmacovigilance Programme of India)
Ministry of Health & Family Welfare, Government of India
Sector-23, Raj Nagar, Ghaziabad-201002

Report Type □ Initial □ Follow up

FOR AMC/NCC USE ONLY

AMC Report No. :
Reg. No. /IPD No. /OPD No./CR no. :
Worldwide Unique No. :

A. PATIENT INFORMATION

1. Patient Initials _____
2. Age at time of Event or Date of Birth _____
3. M □ F □ Other □
4. Weight _____ Kgs

12. Relevant tests/ laboratory data with dates

B. SUSPECTED ADVERSE REACTION

5. Date of reaction started (dd/mm/yyyy)
6. Date of recovery (dd/mm/yyyy)
7. Describe reaction or problem

13. Relevant medical/ medication history (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction etc.)

14. Seriousness of the reaction: No □ if Yes □ (please tick anyone)
□ Death (dd/mm/yyyy) □ Congenital-anomaly
□ Life threatening □ Required intervention to Prevent permanent impairment/damage
□ Hospitalization/Prolonged
□ Disability □ Other (specify)

15. Outcomes
□ Recovered □ Recovering □ Not recovered
□ Fatal □ Recovered with sequelae □ Unknown

C. SUSPECTED MEDICATION(S)

S.No	8. Name (Brand/Generic)	Manufacturer (if known)	Batch No. / Lot No.	Exp. Date (if known)	Dose used	Route used	Frequency (OD, BD etc.)	Therapy dates		Indication	Causality Assessment
								Date started	Date stopped		
i											
ii											
iii											
iv											

S.No as per C	9. Action Taken (please tick)						10. Reaction reappeared after reintroduction (please tick)			
	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	Yes	No	Effect unknown	Dose (if reintroduced)
i										
ii										
iii										
iv										

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S.No	Name (Brand/Generic)	Dose used	Route used	Frequency (OD, BD, etc.)	Therapy dates		Indication
					Date started	Date stopped	
i							
ii							
iii							

Additional Information:

D. REPORTER DETAILS

16. Name and Professional Address: _____
_____
Pin: _____ E-mail _____
Tel. No. (with STD code) _____
Occupation: _____ Signature: _____

17. Date of this report (dd/mm/yyyy):

Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Programme staff is not expected to and will not disclose the reporter's identity in response to a request from the public. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction.

INFORM CONSENT FORM

ADVICE ABOUT REPORTING

- Report adverse experiences with medications
- Report serious adverse reactions. A reaction is serious when the patient outcome is:
  - death
  - life-threatening (real risk of dying)
  - hospitalization (initial or prolonged)
  - disability (significant, persistent or permanent
  - congenital anomaly
  - required intervention to prevent permanent impairment or damage
- Report even if:
  - You're not certain the product caused adverse reaction
  - You don't have all the details, however, point nos. **1, 5, 7, 8, 11, 15, 16 & 18** (see reverse) are essentially required.
- Who can report:
  - Any health care professional (Doctors including Dentists, Nurses and Pharmacists)
- Where to report:
  - Please return the completed form to the nearest **Adverse drug reaction Monitoring Centre (AMC)** or to **National Coordinating Centre**
  - A list of nationwide AMCs is available at: http://ipc.nic.in and also at http://cdsco.nic.in/pharmacovigilance.htm
- What happens to the submitted information:
  - Information provided in this form is handled in strict confidence. The causality assessment is carried out at Adverse Drug Reaction Monitoring Centres (AMCs) by using WHO-UMC scale. The analyzed forms are forwarded to the National Coordinating Centre through the ADR database. Finally the data is analyzed and forwarded to the Global Pharmacovigilance Database managed by WHO Uppsala Monitoring Center in Sweden.
  - The reports are periodically reviewed by the National Coordinating Centre (PvPI). The information generated on the basis of these reports helps in continuous assessment of the benefit-risk ratio of medicines.
  - The information is submitted to the Steering Committee of PvPI constituted by the Ministry of Health and Family Welfare. The Committee is entrusted with the responsibility to review the data and suggest any interventions that may be required.

Suspected Adverse Drug Reaction Reporting Form

For VOLUNTARY reporting of suspected adverse drug reactions by health care professionals

सत्यमेव जयते

IPC

National Coordinating Centre
Pharmacovigilance Programme of India
India Pharmacopoeia Commission
Ministry of Health & Family Welfare
Government of India
Sector-23, Raj Nagar, Ghaziabad-201002
Tel.:0120-2783400, 2783401, 2783392,
FAX: 0120-2783311
www.ipc.nic.in

Pharmacovigilance Programme of India for Assuring Drug Safety

Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Programme staff is not ex-pected to and will not disclose the reporter's identity in response to a request from the public. **Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction.**

ASSESSMENT SCALES FOR ADVERSE DRUG REACTION OF ANY DRUG
WHO CAUSALITY ASSESSMENT SCALES:

Causality term	Assessment criteria (all points should be reasonably complied)
Certain to drug intake	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (ie, an objective and specific medical disorder or a recognized pharmacologic phenomenon) • Rechallenge satisfactory, if necessary
Probable/likely	• Event or laboratory test abnormality, with reasonable timerelationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable

	• Rechallenge not required
Causality term	**Assessment criteria (all points should be reasonably complied)**
Possible	• Event or laboratory test abnormality, with reasonable timerelationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanation
Conditional/unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable/unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient orcontradictory • Data cannot be supplemented or verified

Naranjo ADR probability assessment scale

Question	Yes	No	Don'tknow
Are there previous conclusion reports on this reaction?	+1	0	0
Did the adverse event appear after the suspect drug was administered?	+2	–1	0
Did the AR improve when the drug was discontinued or a specificantagonist was administered?	+1	0	0
Did the AR reappear when drug was re-administered?	+2	–1	0
Are there alternate causes [other than the drug] that could solely havecaused the reaction?	–1	+2	0
Did the reaction reappear when a placebo was given?	–1	+1	0
Was the drug detected in the blood [or other fluids] in a concentrationknown to be toxic?	+1	0	0
Was the reaction more severe when the dose was increased or less severewhen the dose was decreased?	+1	0	0
Did the patient have a similar reaction to the same or similar drugs in anyprevious exposure?	+1	0	0
Was the adverse event confirmed by objective evidence?	+1	0	0

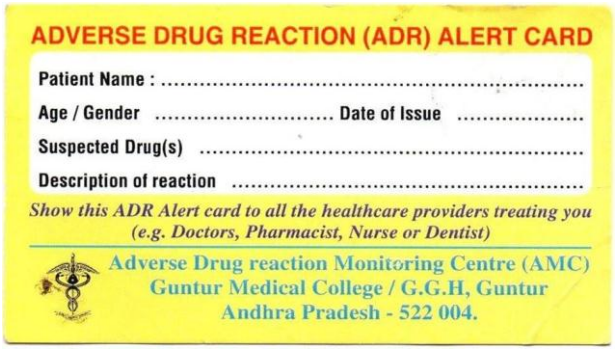
Scoring for Naranjo algorithm: >9 = definite ADR; 5–8 = probable ADR; 1–4 =possible ADR; 0 = doubtful ADR.

Hartwig's severity assessment scale

Level 1	An ADR occurred but required no change in treatment with the suspected drug
Level 2	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS)
Level 3	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. AND/OR An Antidote or other treatment was required. No increase in LOS
Level 4	Any Level 3 ADR which increases length of stay by at least 1 day. OR The ADR was the reason for the admission
Level 5	Any Level 4 ADR which requires intensive medical care
Level 6	The adverse reaction caused permanent harm to the patient
Level 7	The adverse reaction either directly or indirectly led to the death of the patient

Mild = Levels 1 and 2; **moderate** = Levels 3 and 4; **severe** = Levels 5, 6 and 7.

Alert Card



RESULTS

- A total of 167 adverse drug reactions were identified among patients in a study period of 6 months i.e. from November 2020 to April 2021.
- These collected ADRs were categorized according to departments, patient's demographics, organ systems involved, category of drugs, seriousness of reactions, outcomes and causality assessment was done using WHO-UMC causality scale and Naranjo's probability assessment scale and severity was assessed using Hartwig's severity assessment scale.

Table 4: number of adrs from different departments.

S.no	Departments	No of ADRs	Percentage (%)
1.	Oncology	76	46%
2.	General medicine	34	20%
3.	Neurology	7	4%
4.	Psychiatry	9	5%
5.	Cardiology	6	4%
6.	Anti – retroviral therapy	23	14%
7.	Gynecology	12	7%
	Total	167	100%

Table-4: depicts that out of 159 ADRs majority of ADRs reported from oncology (46%) and followed by general medicine (20%), anti–retroviral therapy (14%), psychiatry (5%), neurology (4%), cardiology (4%) and gynaecology (7%).

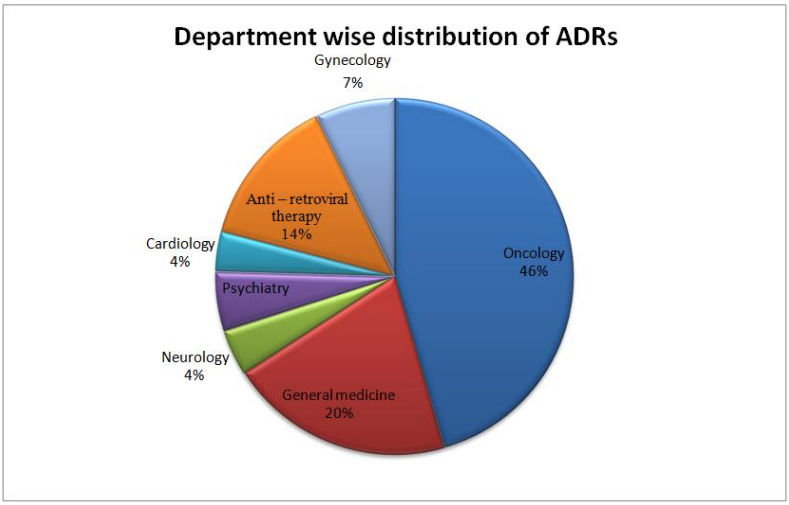
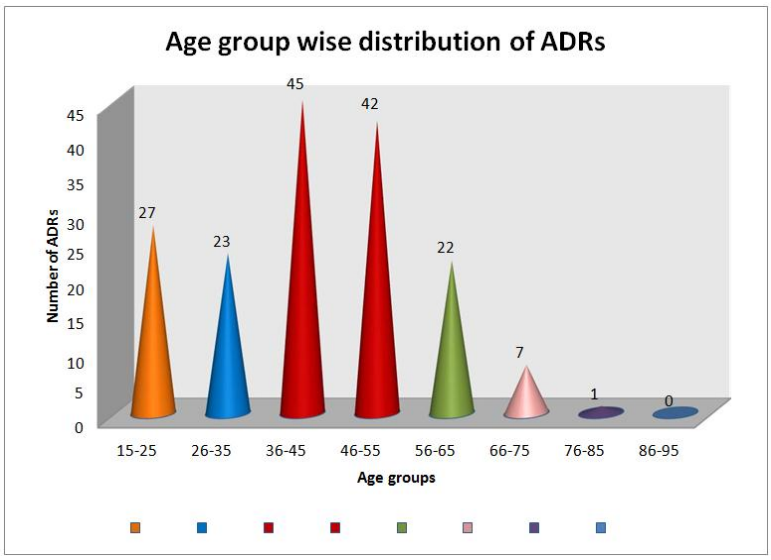


Fig. 1: Number of ADRs reported from different departments.

Table 5: Prevalence of adrs among various age groups.

S.no	Age groups	Number of ADRs	Percentage (%)
1.	15-25	27	16.16%
2.	26-35	23	13.77%
3.	36-45	45	26.94%
4.	46-55	42	25.14%
5.	56-65	22	13.17%
6.	66-75	7	4.19%
7.	76-85	1	0.63%
8.	86-95	0	0
	Total	167	100%

Table-5: The prevalence of ADRs mostly occurred in the age groups of 36- 45(26.94%) and 46-55(25.14%).

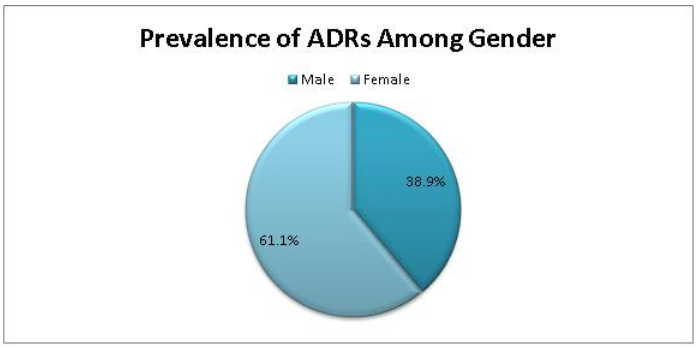


"Fig.2": Prevalence of ADRs among various age groups.

Table 6: Prevalence of adrs among gender.

s.no	Gender	Number of ADRs	Percentage (%)
1.	Male	65	38.9%
2.	Female	102	61.1%
	Total	167	100%

Table-6: The prevalence of ADRs mostly occurred in female patients 102(61.1%) compared to male patients 65(38.9%). The male to female ratio was 0.637.

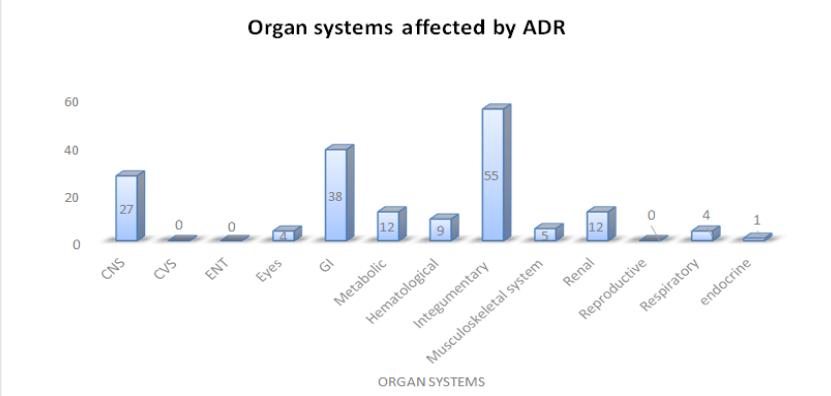


"Fig.3": Prevalence of ADRs among gender.

Table 7: Organ systems affected by adverse drug reactions.

S.no	Organ system involved	No of ADRs	Percentage(%)
1.	CNS	27	16.2%
2.	CVS	0	0
3.	ENT	0	0
4.	Ocular	4	2.4%
5.	GI	38	22.7%
6.	Metabolic	12	7.2%
7.	Hematological	9	5.38%
8.	Integumentary	55	32.93%
9.	Musculoskeletal system	5	2.99%
10.	Renal	12	7.2%
11.	Reproductive	0	0
12.	Respiratory	4	2.4%
13.	Endocrine	1	0.6%
	Total	167	100%

Table-7: It reveals that integumentary (32.93%) was found to be most affected organ system then followed by gastrointestinal system (22.7%), central nervous system (16.2%) and least affected were respiratory (2.4%) and eyes (2.4%) and endocrine (0.6%).



"Fig.4": Organ systems affected by ADRs.

Table-8: WHO Causality assessment scales
Table-8: WHO Causality of ADRs.

S.no	Causality parameters	No. of ADRs	Percentage ADRs
1.	Certain	0	0%
2.	Probable / Likely	17	10.2%
3.	Possible	150	89.8%
4.	Unlikely	0	0%
5.	Unclassified / Conditional	0	0%
6.	Un assessable / Unclassifiable	0	0%
	Total	167	100%

Table-8: Out of 167 ADRs, 150 (89.8%) were considered as possible and 17 (10.2%) were probable and none of the reaction was categorized into certain as rechallenging of the drugs was not attempted in any patient as it may worsen the patient's condition.

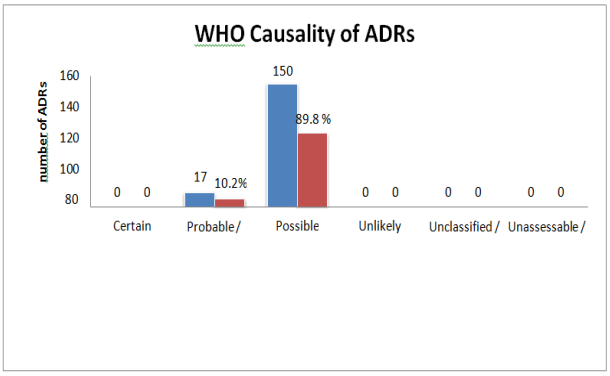


Fig. 5: WHO causality of ADRs.

Table 9: Naranjo probability assessment scale.

S.no	Preventability parameter	Number of ADRs	Percentage of ADRs
1.	Definite	0	0%
2.	Probable	47	28.14%
3.	possible	120	71.86%
4.	unlikely	0	0%
	Total	167	100%

Table 9: It states that 120 (71.86%) were assessed to be possible, 47 (28.14%)were probable.

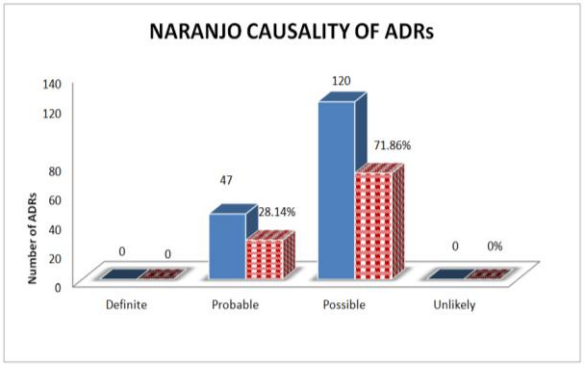
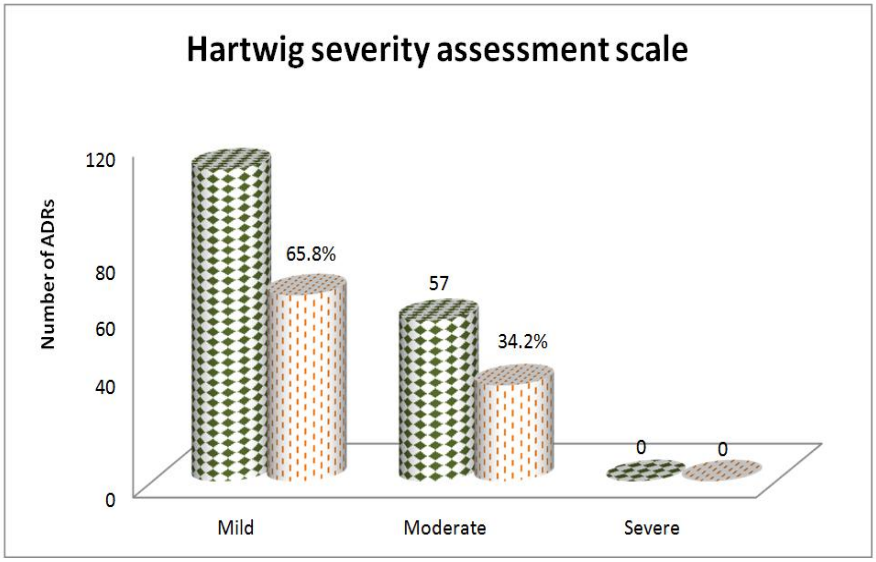


Fig.6: Naranjo causality of ADRs.

Table 10: Hartwig severity assessment scale.

S.no	Level of severity	Number of ADRs	Percentage of ADRs
1.	Mild	110	65.8%
2.	Moderate	57	34.2%
3.	Severe	0	0
	Total	167	100%

Table-10: Severity assessment of ADRs showed that the majority of ADRs aremild 110(65.8%) followed by moderate 57(34.2%).

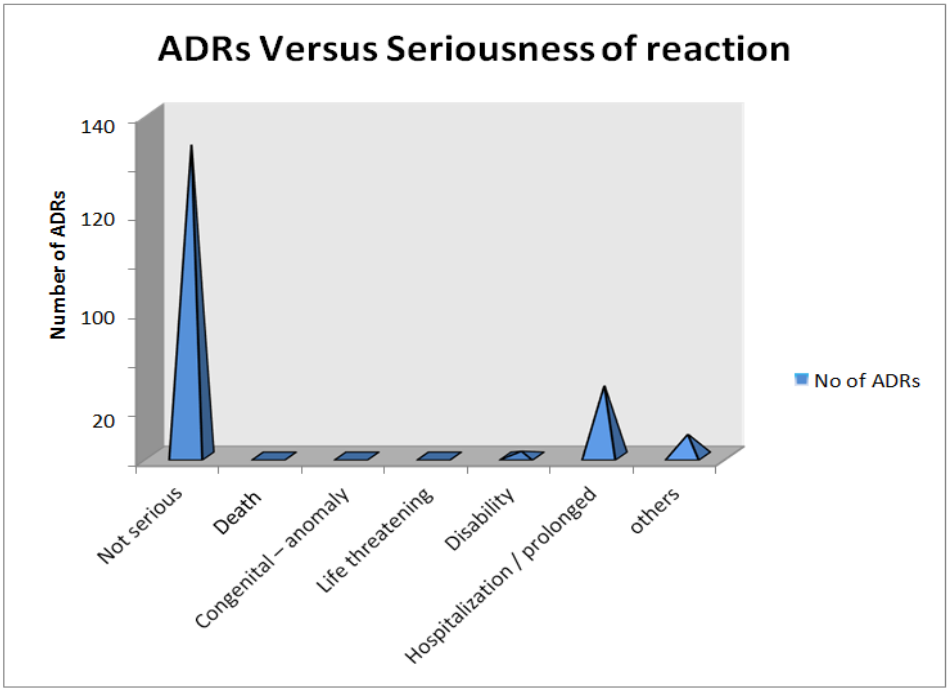


"Fig.7": Hartwig's severity assessment scale.

Table 11: seriousness of the adverse drug reactions.

S.no	Seriousness	Number of ADRs	Percentage of ADRs (%)
1.	Not serious	127	76%
2.	Death	0	0
3.	Congenital – anomaly	0	0
4.	Life threatening	0	0
5.	Disability	2	1.2%
6.	Hospitalization / prolonged	29	17.4%
7.	Others	9	5.4%
8.	Totally	167	100%

Table-11: Regarding seriousness of reaction and majority of ADRs are not serious 127(76%) followed by ADRs led to hospitalization/prolongation 29(17.4%), others 9(5.4%) and disability 2(1.2%)

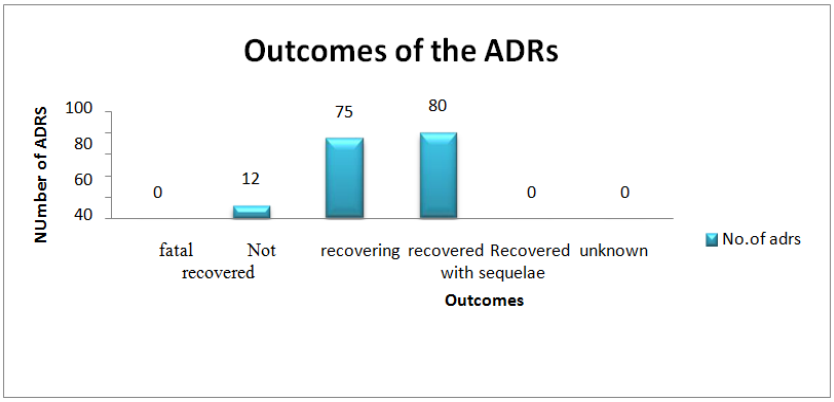


"Fig.8": Seriousness of the adverse drug reactions.

Table 12: outcomes of the ADRs.

S.no	Category	Number of ADRs	Percentage (%)
1.	Fatal	0	0
2.	Not recovered	12	7.2%
3.	Recovering	75	44.9%
4.	Recovered	80	47.9%
5.	Recovered with sequelae	0	0
6.	Unknown	0	0
	Total	167	100%

Table 12: The outcomes of suspected ADRs which were evaluated to understand the Condition of patient the majority of ADRs 47.9% were recovered, 44.9% were found to be recovering and 7.2% of the ADRs were not recovered. There were no Fatal Adverse drug reactions reported.

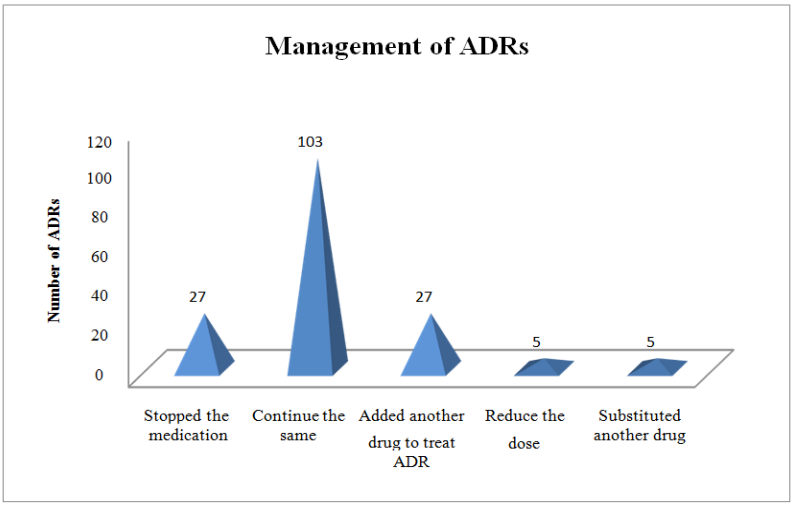


"Fig.9": Outcomes of the ADRs.

Table 13: Management of adrs.

S.no	Treatment	Number of ADRs	Percentage of ADRs (%)
1.	Stopped the medication	27	16.16%
2.	Continue the same	103	61.68%
3.	Added another drug to treat ADR	27	16.16%
4.	Reduce the dose	5	3%
5.	Substituted another drug	5	3%
	Total	167	100%

TABLE-13: The majority of ADRs were managed by continue of same drugs (61.68%) and followed by, stopped the medication (16.16%), added another drug (16.16%), reduce the dose (3%) and substituted by another drug was (3%).

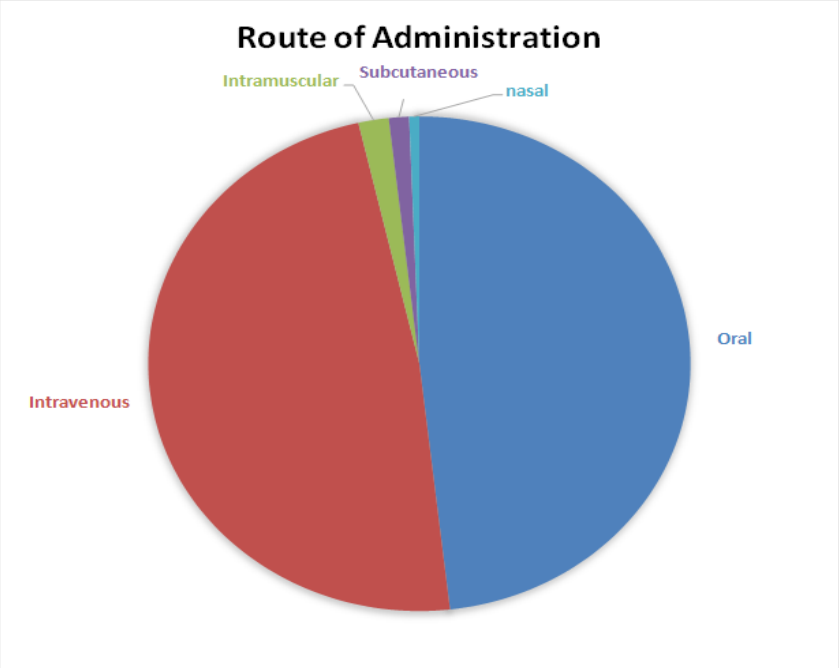


"Fig.10": Management of ADRs.

Table 14: Route of administration.

S.No	Route of Administration	Number of ADRs	Percentage
1.	Oral	81	48.5%
2.	Intravenous	81	48.5%
3.	Intramuscular	2	1.2%
4.	Subcutaneous	2	1.2%
5.	Nasal	1	0.6%
	Total	167	100%

Table-14: Based on Route of Administration of drugs majority of the routes used 81(48.5%), intravenous 81(48.5%), Intramuscular 2(1.2%), subcutaneous 2(1.2%) followed by nasal 1(0.6%)

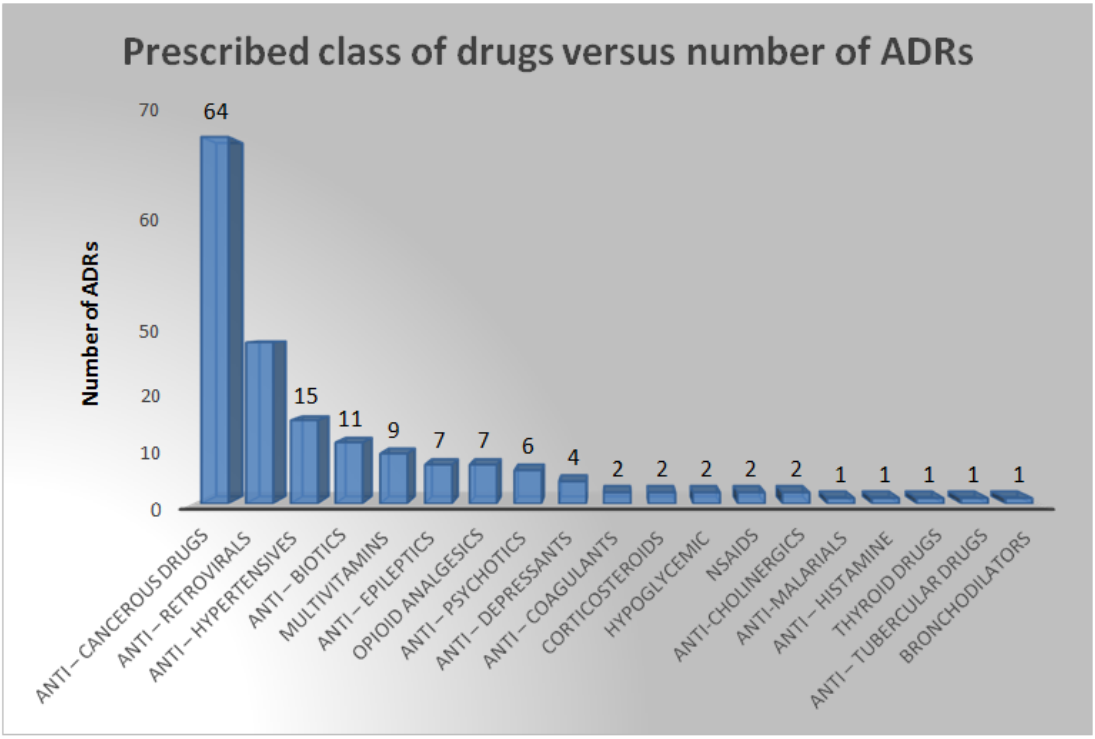


"Fig.11": Route of administration.

Table 15: category of drugs.

S. No	Drugs Category	Number of ADRs	Percentage of ADRs
1.	Anti – cancerous drugs	64	38.32
2.	Anti – retrovirals	29	17.36
3.	Anti – hypertensives	15	8.98
4.	Anti – biotics	11	6.59
5.	Multivitamins	9	5.4
6.	Anti – epileptics	7	4.2
7.	Opioid analgesics	7	4.2
8.	Anti – psychotics	6	3.6
9.	Anti – depressants	4	2.4
10.	Anti – coagulants	2	1.2
11.	Corticosteroids	2	1.2
12	Hypoglycemic	2	1.2
13.	NSAIDs	2	1.2
14.	Anti-cholinergics	2	1.2
15.	Anti-malarials	1	0.6
16.	Anti – histamine	1	0.6
17.	Thyroid drugs	1	0.6
18.	Anti – tubercular drugs	1	0.6
19.	Bronchodilators	1	0.6
	Total	167	100%

Table-15: It describes that those anti-cancer agents accounts for majority of ADRs i.e., 64 (38.32%) which was followed by anti-retroviral agents 29 (17.36%), anti-hypertensives 15(8.98%).



"Fig.12": Prescribed class of drugs versus number of ADRs.

DISCUSSION

A prospective observational study was conducted in a period of 6 months on to detect, document, assess and report the suspected adverse drug reactions, adverse events in a tertiary care teaching hospital. The collected information includes patient's initial, age, gender, reporting department of the hospital, description of the ADR, name of the suspected drug causing ADR, outcomes and management for the specific ADR. The study revealed the pattern of ADRs in General Medicine, Oncology, neurology, psychiatry, cardiology, gynaecology and it was depicted in table-4.

Out of 167 ADRs reported and assessed, 26.94% of ADRs were in the age groups of 36-45 years and 25.7% of ADRs were found in the age group of 46-55 years which was consistent with the Lobo et al.,[19] The reasons that might be due to the patients at this age group suffer with many co-morbidities such as diabetes, hypertension for which they require more number of medications which increases the risk of adverse drug reactions.

Female predominance was noted over males in case of ADRs. From the total number of patients with ADRs, 65(38.9%) were men and 102(61.1%) were women. The male to female ratio was 0.637. This finding is consistent with the study carried out by Patidar et al.,[1] and Ratan J Lihite et al.,[22] but it differs from Harsha Ramakrishna et al.,[20] This might be due to hormonal influences on physiological functions. These differences can affect the way the body deals with drugs by altering the pharmacokinetics and pharmacodynamics, of the drugs including drug absorption, distribution, metabolism and elimination.

The most common organ system associated with ADRs in our study was integumentary system (32.93%) which was consistent studies conducted by Lobo et al.,[19] Patidar et al.,[1] Integumentary system followed by gastrointestinal (22.7%) and CNS (16.2%).

To strengthen and further emphasize the validity of the finding of the study, causality assessment was done by using the WHO-UMC causality assessment scale. Out of the 167 ADRs reported 89.8% ADRs were possible and 10.2% ADRs were probable. None of the reactions was categorized into certain as rechallenging of the drugs was not attempted in any patient as it may worsen the patient's condition.

According to Naranjo probability scale maximum ADRs were possible (71.86%) followed by probable (28.14%) which was consistent with the study conducted by Ratan J.Lihite et al.,[22]

The severity assessment was done by using the Hartwig's severity assessment scale. According to this ADR severity assessment scale, the level of severity of ADR is classified on a scale ranging from 1 to 7. Level 1 and 2 indicates mild, level 3, 4(a) and 4(b) are moderate and level 5, 6 and 7 are severe. On evaluation of the severity of ADRs by the Hartwig's severity assessment

scale, it was evident that most of the ADRs reported in the study were of mild severity (65.8%). Similar findings were reported in Patidar et.al, (1). Mild reactions are followed by moderate (34.2%). Regarding seriousness of reaction and majority of ADRs are not serious 127(76%) followed by ADRs led to hospitalization/prolongation 29(17.4%), others 9(5.4%) and disability 2(1.2%).

Regarding outcomes of the reaction recovered reactions were more i.e., 80(47.9%) followed by recovering reactions 75(44.9%) and this was due to patients with mild reactions were still recovering at the time of discharge. Outcomes of about 12(7.2%) reactions were not recovered.

Based on routes of administration, majority of the ADRs were associated with oral therapy 81(48.5%) and intravenous 81(48.5%) followed by intramuscular 2(1.2%) and subcutaneous 2(1.2%) followed by intranasal 1(0.6%).

In 103(61.68%) cases, the suspected drug was continued without any change as they are self-limiting and very mild while suspected drug was withdrawn in 27(16.16%) cases and in 27(16.16%) cases, symptomatic treatment such as oral anti-histamines and anti-emetics was required. Dose of suspected drug was reduced in 5(3%) cases and the suspected drug was substituted with another drug in 5(3%).The drug class most commonly implicated with ADRs was anti-cancer agents 66(38.32%) followed by anti-retroviral agents 29(17.36%), anti- hypertensives 15(8.98%), anti-biotics 11(6.59%) and multivitamins 9(5.4%). The drug classes least affected were bronchodilators 1(0.6%), anti-tubercular drugs 1(0.6%), thyroid drugs 1(0.6%), anti-histamines 1(0.6%) and anti-malarials 1(0.6%).

CONCLUSION

Under reporting is a major limitation of spontaneous reporting system in Pharmacovigilance and should take care while analysing the data. Since only one hospital data was taken into consideration and the results may not be applicable to the general population. But definitely, healthcare providers should be enlightened with the present data.

By observing the results of this study, it indicates the baseline information on incidence and pattern of ADRs and their distribution among the various age groups, gender, organ systems affected and therapeutic class of drugs. This study suggests that there is a need of spontaneous ADR reporting from all the departments for monitoring and assessment of ADRs. As ADRs are an important cause of morbidity and mortality which imparts a negative impact on the treatment and exerts a greater economic burden on the patients when in results in hospitalization or other comorbidities.

We conclude that monitoring of ADRs is an ongoing, ceaseless and continuing process. By imparting knowledge and awareness on ADRs reporting among health care professionals will improve the reporting rates of reactions. Careful consideration involved in planning and monitoring of drug therapy will improve drug safety and rational use of drugs there by it will lead to prevention of ADRs.

ETHICAL MATTERS

The study was approved by the Institutional Human Ethics Committee of Guntur Medical College and Government General Hospital, Guntur, Andhra Pradesh, filed under number GMC/IEC/390/2020 and was conducted in accordance with the ethical guidelines of the Declaration of Helenski (created in 1964 and revised in 2002).Informed consent form was taken from all the subjects prior to the study which was mentioned in the local language (Telugu).

ACKNOWLEDGEMENT

Reported ADRs (six months i.e. Nov-2020 to April-2021) Received ADRs are communicated to NCC-PvPI. Reported ADRs Unique Numbers:-

IN-IPC-300517378- Loose motions: Imatinib
IN-IPC-300517424- Headache: Zoledron
IN-IPC-300517425- Swelling of face: Imatinib
IN-IPC-300517426- Alopecia: Epirubicin
IN-IPC-300517427- Alopecia: Adriamycin
IN-IPC-300517428- Alopecia: Adriamycin
IN-IPC-300517428- Rashes: Gefitinib
IN-IPC-300517430- Blurred Vision: Chloroquine
IN-IPC-300517431- Rashes: Gefitinib
IN-IPC-300517432- Vertigo: Tramadol
IN-IPC-300517433- Dyspnea: Aspirin
IN-IPC-300517434- Skin Hyperpigmentation: Adriamycin
IN-IPC-300517435- Vertigo: Tramadol
IN-IPC-300517436- Skin hyperpigmentation: Cyclophosphamide
IN-IPC-300517437- Dry mouth: Amitriptyline
IN-IPC-300517667- Shortness of breath: Tramadol
IN-IPC-300517677- Renal Calculi: Calcium
IN-IPC-300517680- Polyuria: Cyclophosphamide
IN-IPC-300517686- Dyspnea: Aspirin
IN-IPC-300517689-Rashes: Buscopan
IN-IPC-300517694- Vomiting: Paclitaxel
IN-IPC-300517700- Constipation: Gemcitabine
IN-IPC-300517705- Alopecia: Gemcitabine
IN-IPC-300517730- Abdominal pain: Adriamycin
IN-IPC-300517742- Skin hyperpigmentation: Wysolone
IN-IPC-300517748- Back pain: Trastuzumab
IN-IPC-300517758- Vertigo: Adriamycin
IN-IPC-300517763- Urticaria: Prednisolone
IN-IPC-300517767- Hematuria: Heparin
IN-IPC-300517779- Peripheral Neuropathy: Zidovudine + Nevirapine +Lamivudine
IN-IPC-300518063-Erythematous rash: Efavirenz + Lamivudine + Tenofovir
IN-IPC-300515342-Constipation: Calcium carbonate + Vit-D3
IN-IPC-300515353-Vertigo: Calcium carbonate + Vit-

D3
IN-IPC-300515357-Headache: Calcium carbonate + Vit-D3
IN-IPC-300515363- Headache: Calcium carbonate + Vit-D3
IN-IPC-300515373- Headache: Calcium carbonate + Vit-D3
IN-IPC-300515434-Vertigo: Calcium carbonate + Vit-D3
IN-IPC-300515436- Vertigo: Calcium carbonate + Vit-D3
IN-IPC-300515437- Vertigo: Calcium carbonate + Vit-D3
IN-IPC-300515438- Headache: Calcium carbonate + Vit-D3
IN-IPC-300515440- Gynecomastia: Lasilactone
IN-IPC-300515442- Tremors: Asthalin
IN-IPC-300515444- Vomiting: Gemcitabine
IN-IPC-300515446- Alopecia: Paclitaxel
IN-IPC-300515450- Alopecia: Gemcitabine
IN-IPC-300515452- Ataxia: Phenytoin
IN-IPC-300515454- Tremors: Sodium Valproate
IN-IPC-300515455- Hyperpigmentation: Adriamycin
IN-IPC-300515456- Constipation: CPM
IN-IPC-300515457- Abdominal pain: Azithromycin
IN-IPC-300515458- Vaginal irritation: Metronidazole
IN-IPC-300515459- Constipation: Loperamide
IN-IPC-300515460- Hypoglycemia: Actrapid
IN-IPC-300515461- Urticaria: Amoxicillin
IN-IPC-300515463- Dry Cough: Enalapril
IN-IPC-300515440- Gynecomastia: Lasilactone
IN-IPC-300515464- Vomiting: Ciprofloxacin
IN-IPC-300515465- Anaemia: Losartan
IN-IPC-300515466- Mucositis: 5-Flu
IN-IPC-300515467- Diarrhoea: 5-Flu
IN-IPC-300515468- Alopecia: Paclitaxel
IN-IPC-300506523-Itching: Norfloxacin
IN-IPC-300506526-Pedal edema: Amlodipine
IN-IPC-300506533-Hypoglycemia: Metformin
IN-IPC-300506550-Nausea: Tramadol
IN-IPC-300506552-Pedal edema: Amlodipine
IN-IPC-300506553-Pedal edema: Amlodipine
IN-IPC-300506554-Delusions: Olanzapine
IN-IPC-300506555-Melanoncychia: Adriamycin
IN-IPC-300506601-Hypersenstivity reaction: Paclitaxel
IN-IPC-300506616-Hematuria: Heparin
IN-IPC-300506634-Alopecia: Paclitaxel
IN-IPC-300506648-Shortness of breath: Etopside
IN-IPC-300506664-Diarrhoea: Paclitaxel
IN-IPC-300506854-Vomiting: Etopside
IN-IPC-300506857-Alopecia: Ifosphamide
IN-IPC-300506858-Alopecia: Adriamycin
IN-IPC-300506977-Alopecia: Ifosamide
IN-IPC-300506988-Rashes: Paclitaxel
IN-IPC-300507021-Alopecia: Paclitaxel
IN-IPC-300507150-Melanonychia: Adriamycin
IN-IPC-300507170-Hypoglycemia: Actrapid
IN-IPC-300507178-Dry Cough: Enalapril
IN-IPC-300507196-Pale skin: Pemetrexed
IN-IPC-300507205-Vomiting: Tramadol
IN-IPC-300507215-Pancytopenia: ZLN
IN-IPC-300498914-Tremors: Sodium valproate
IN-IPC-300498932-pedal edema: Amlodipine
IN-IPC-300498934-Urticaria: Ibuprofen
IN-IPC-300498935-Vomiting: Paclitaxel
IN-IPC-300498936-Tremors: Sodium valproate
IN-IPC-300498943-Blurred vision: THP
IN-IPC-300498944-Abdominal pain: Levothyroxine
IN-IPC-300498945-Vomiting: Chloroquine
IN-IPC-300498946-Diarrhoea: Amikacin
IN-IPC-300498947-Pedal edema: Amlodipine
IN-IPC-300499451-Diarrhoea: Piptaz
IN-IPC-300499457-Erythematous rash: Acyclovir
IN-IPC-300499461-Erythematous rash: Acyclovir
IN-IPC-300499465-Erythematous rash: Acyclovir
IN-IPC-300499470-Dystonia: Haloperidol
IN-IPC-300499508-Hypersentivity reaction: Paclitaxel
IN-IPC-300499509-Blurred vision: Phenytoin
IN-IPC-300499512-Urinary retention: Amitriptyline
IN-IPC-300499513-Skin allergy: Carbamazepine
IN-IPC-300493067-Alopecia: 5-Flu
IN-IPC-300493068-Alopecia: 5-Flu
IN-IPC-300493069-Alopecia: Adriamycin
IN-IPC-300493071-Vomiting: Paclitaxel
IN-IPC-300493338-Alopecia: Adriamycin
IN-IPC-300493341-Alopecia: Gemcitabine
IN-IPC-300493342-rashes: Adriamycin
IN-IPC-300493347-excessive urination: Vincristine
IN-IPC-300494602-Peripheral neuropathy: Vincristine
IN-IPC-300494618- Alopecia: 5-Flu
IN-IPC-300494635- Vomiting: Paclitaxel
IN-IPC-300494640- Alopecia: Paclitaxel
IN-IPC-300494717- Leucopenia: Paclitaxel
IN-IPC-300494807- Mucositis: 5-Flu
IN-IPC-300494810- Hyperpigmentation: Adriamycin
IN-IPC-300494812-Skin pigmentation: 5-Flu
IN-IPC-300494813- Mucositis: 5-Flu
IN-IPC-300494814- Joint pain: Paclitaxel
IN-IPC-300494817- Mucositis: 5-Flu
IN-IPC-300494818- Neuropathy: Paclitaxel
IN-IPC-300495307- Diarrhoea: 5-Flu
IN-IPC-300495308- Seizures: OPV
IN-IPC-300495310- Constipation: CPM
IN-IPC-300495312- Constipation: OPV
IN-IPC-300495315- Hypokalemia: Lasix
IN-IPC-300495319- rash: Amoxyclav
IN-IPC-300495320- Diarrhoea: Amoxicillin
IN-IPC-300495323- Hepatitis: ZLE
IN-IPC-300495325- Skin pigmentation: ZLN
IN-IPC-300495327- Anaemia: ZLN
IN-IPC-300495618- Loose of appetite: TLE
IN-IPC-300495625- Burning sensation: ZLN
IN-IPC-300495632- Hyperpigmentation: ZLN
IN-IPC-300495639- Vomiting: ZLN
IN-IPC-300495644- Anemia: TLE
IN-IPC-300495656- Anaemia: ZLN
IN-IPC-300495662- Diarrhoea: Isoniazid
IN-IPC-300495671- Nausea: Tramadol
IN-IPC-300495678- pitting edema: Amlodipine
IN-IPC-300495687- Chills: Tramadol

IN-IPC-300489457- Peripheral edema: Metoprolol
IN-IPC-300489459- Itching: Carbamazepine
IN-IPC-300489465- Tremors: Sodium valproate
IN-IPC-300489468- Vomiting: Sodium valproate
IN-IPC-300489478- Diarrhoea: Calcium
IN-IPC-300489483- Vomiting: Ifosamide
IN-IPC-300489486- Alopecia: Vincristine
IN-IPC-300489520- Pigmentation: Carboplatin
IN-IPC-300489525- Alopecia: Adriamycin
IN-IPC-300489532- Alopecia: Cisplatin
IN-IPC-300489786- Rigidity of limbs: Haloperidol
IN-IPC-300489788- Alopecia: Paclitaxel
IN-IPC-300489791- Alopecia: Paclitaxel
IN-IPC-300489793- Vomiting: Gemcitabine
IN-IPC-300489795- Itching: Pemetrexed
IN-IPC-300489797- Alopecia: Adriamycin
IN-IPC-300489799- Alopecia: Docetaxel
IN-IPC-300489801- Vomiting: Cisplatin
IN-IPC-300489804- Vomiting: Etopside
IN-IPC-300489810- Vertigo: Paclitaxel
IN-IPC-300489824- Vertigo: Paclitaxel
IN-IPC-300489829- weight gain: Olanzapine

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