

## Analytical Study of Adverse Drug Reactions Reported at Adverse Drug Reaction Monitoring Centre in a Tertiary Care Teaching Hospital in Andhra-Pradesh, India

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**Abstract:** In a health care system, adverse drug reactions are important as they account for hospitalization, disability, mortality, congenital anomaly economic burden. A small study was conducted by collecting data from Suspected ADR forms reported at AMC Guntur, to know the commonly occurring ADRs, severity of ADRs, suspected drugs causing ADRs and to improve public and patient safety. The data obtained from Suspected ADR reporting forms were analyzed for demographic distribution, causality assessment, the common organ system involved, the common causative drug, by using WHO-ADR terminology, WHO-ART classification. Of the total of 120 reactions reported the most commonly implicated organ system were skin and appendages (38.33%) blood (27.5%) and gastro-intestinal (17.5%). The major causative drug classes were anti-retroviral (37.5%), anti-cancer agents (19.66%), antimicrobials (10.83%). More than half of reactions were classified as probable/likely (52.5%), only few as Certain (1.66%), and some of the reactions are preventable. In this study a total of 65 (54.16%) patients were recovered, 49 (40.83%) patients were recovering at the time of last assessment. Many studies suggest that rational selection of drugs as per indications will improve patient safety.

**Keywords:** Adverse drug reaction, Suspected drug, ADR monitoring unit, Causality, Serious reaction.

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### I. Introduction

The World Health Organization, defined an Adverse Drug Reaction as, "any noxious, unintended and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis or therapy"[1]. In a healthcare system, Adverse drug reactions (ADRs) are important as they account for hospitalization, disability, mortality, congenital anomaly and also economic burden. Important risk factors for ADRs are multiple medications, elderly age group, new drugs, alcohol intake, conditions of reduced hepatic / renal functions, pregnancy and breast feeding [2]. The patterns of ADRs vary due to different prescribing habits, use of newer drugs and referral bias [3]. Many of these ADRs are preventable. Identification of them helps in achieving a substantial reduction in health care cost [4].

To safe guard the health of 1.27 billion people of India, the Central drugs Standard Control Organisation(CDSCO), New Delhi has initiated a nation-wide, Pharmacovigilance programme of India (PvPI) which is coordinated by the Indian Pharmacopoeia Commission (IPC) located at Ghaziabad. As a part of PvPI, Adverse drug reaction Monitoring Centre (AMC) was established at Guntur Medical College/Government General Hospital Guntur, Andhra-Pradesh, India in the year 2013. In view of public health safety and improving patient safety a small study was conducted by analysing the adverse drug reactions reported at AMC, Guntur Medical College/Government general Hospital, Guntur.

### II. Aim & Objectives

To study the patterns of adverse drug reactions reported at Adverse drug reaction Monitoring Centre at Guntur Medical College/Government General Hospital Guntur, Andhra-Pradesh, India, to know the commonly occurring ADRs, severity of ADRs, suspected drugs causing ADRs and to improve public and patient safety.

### III. Materials & Methods

After prior approval from authentic research authorities of the institution, study was carried by maintaining a strict confidentiality about patient details. At the Adverse drug reaction Monitoring Centre, at Guntur Medical College/Government general Hospital, Guntur, 120 Adverse Drug Reactions were reported in Suspected Adverse Drug Reaction Reporting Forms (SADRRFs) by various departments of the hospital, over a period of four months. The data from these 120 SADRRFs were evaluated in the study.

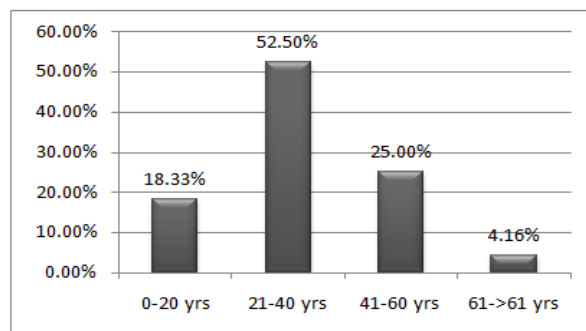
From each SADRRF data was collected about age, sex, weight, adverse drug reaction, severity of the event, causative drugs with dosage, route, frequency, duration of administration, dechallenge (withdrawal of the

suspected drugs after the reaction) and it's outcome, rechallenge (reintroduction of the suspected drugs after the recovery from the reactions) and it's outcome, concomitant medications, relevant investigations. The organ system involvement for ADR was labelled per WHO-ADR terminology [5]. The seriousness of reactions was evaluated according to WHO criteria[1]. ADRs were analysed for causality by WHO-UMC method, preventability by modified Schumock and Thornton's criteria. The collected data were recorded in Excel sheet using a structured format containing age group, gender, description of ADR, organ system involved, drugs, duration of reactions, outcome, causality, seriousness of ADRs. Finally, the data was analysed statistically.

#### IV. Results

##### 4.1: Age & Gender distribution :

A total of 120 adverse drug reactions were included for the analysis.



" Figure"- 1 : Age group Distribution.

The age group distribution for 0-20yrs, 21-40yrs, 41-60yrs, 61- > 61 years was 22 (18.33%), 63 (52.5%), 30 (25%), 5 (4.16%) respectively. The youngest patient was a 3months old female infant and the eldest was 80-year-old female. ("Fig."- 1). The females (80= 66.66%) experienced higher reactions than males (40=33.34%). The males : females ratio was 1 : 2.

##### 4.2 : Organ System Involvement and types of observed ADRs :

"Table "- 1 : Organ system involvement and types of observed ADRs.

Organ System Involvement (System-Organ Classification, SOC)	Types of Observed ADRs (WHO-ART Classification)	n (%)
Skin and appendages disorders	Maculo-papular rash (18), Alopecia (8), Skin rashes (5), Hyperpigmentation of Palms & soles (4), Urticaria (3) Steven Johnson Syndrome (2), Mycosis fungoides (1) Skin necrosis (1), Exfoliative dermatitis (1), Bullous eruption (1), Hirsutism (1), Pruritis (1)	46 (38.33%)
Blood disorders	Anaemia (32), thrombocytopenia & leucocytoclastic vasculitis (1)	33 (27.5%)
Gastro-intestinal system disorders	Vomiting (10), gingival hypertrophy (2), Diarrhoea (2), Siallorhoea (2), Abdominal pain (1), Constipation (1) Xerostomia (1), Candidiasis (1), gastroenteritis (1)	21 (17.5%)
Body as a whole -General disorders	Rigors (3), Pyrexia (2), Application side edema (1)	6 (5%)
Central nervous system disorders	Extrapyramidal disorders (2), Insomnia (1), Ataxia (1)	4 (3.3%)
Cardiovascular disorders	Tachycardia(1), Hypertension(1), Orth.Hypertension (1)	3 (2.5%)
Psychiatric disorders	Depression (1), Acute psychosis (1)	2 (1.66%)
Musculo - skeletal disorders	Muscle Twitching (1), Arthralgia (1)	2 (1.66%)
Respiratory system disorders	Cough	1 (0.83%)
Liver	Hepatitis	1 (0.83%)
Ophthalmic	Diplopia	1 (0.83%)

A total of 39 different types of ADRs from 11 organ systems were reported. The commonly involved organ systems were Skin and Appendages 46 (38.33%) followed by Blood disorders 33 (27.5%) and Gastro-intestinal system 21 (17.5%) . The commonly reported ADRs were Anaemia (32), Maculo-papular rash (18), Vomiting (10), Alopecia (8). (shown in Table-1)

##### 4.3 : Causative drugs for suspected ADRs. :

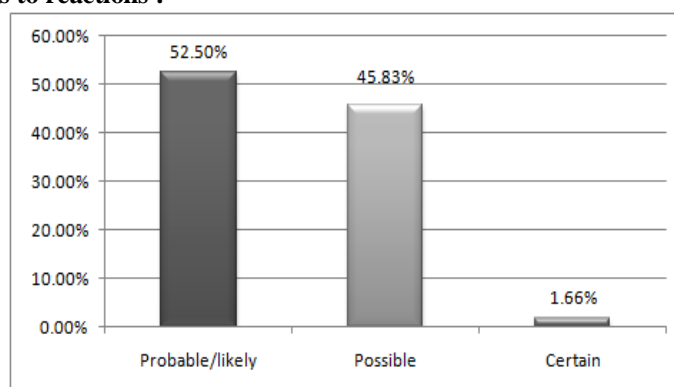
"Table"- 2 : Causative drugs for suspected ADRs.

Group & Drugs	n (%)	Group & Drugs	n (%)
<b>Anti Retroviral (Total)</b>	<b>45 (37.5%)</b>	Rifampin, Ethambutol	1 (0.83%)
Zidovudine, Nevirapine, Lamivudine	40 (33.33%)	Pyrazinamide, Ethambutol	1 (0.83%)
Efaverinz	1 (0.83%)	<b>Anti-psychotics</b>	<b>6 (5%)</b>
Nevirapine	4 (3.33%)	Clozapine	1 (0.83%)

<b>Anti-cancer (Total)</b>	<b>23 (19.66%)</b>	Olanzapine	1 (0.83%)
Cisplatin	5 (4.16%)	Olanzapine, Risperidone	1 (0.83%)
Cyclophosphamide	4 (3.33%)	Risperidone	1 (0.83%)
Adriamycin,5-flourouracil,Cyclophosphamide	4 (3.33%)	Topiramate	1 (0.83%)
Paclitaxel	3 (2.5%)	Haloperidol	1 (0.83%)
5 flourouracil	2 (1.66%)	<b>Analgesics</b>	<b>5 (4.16%)</b>
Paclitaxel, Adriamycin	1 (0.83%)	Paracetamol	3 (2.5%)
Oxaliplatin	1 (0.83%)	Diclofenac	1 (0.83%)
Paclitaxel, cyclophosphamide	1 (0.83%)	Tramadol	1 (0.83%)
Bleomycin, Cisplatin, Etoposide	1 (0.83%)	<b>Steroids</b>	<b>3 (2.5%)</b>
Ifosfamide, Etoposide, Adriamycin	1 (0.83%)	Prednisolone	2 (1.66%)
<b>Antimicrobials</b>	<b>13 (10.83%)</b>	Dexamethasone	1 (0.83%)
Metronidazole	5 (4.16%)	<b>Others</b>	<b>10 (8.33%)</b>
Amoxicillin, Clavulanic acid	2 (1.66%)	Ondansetron	1 (0.83%)
Ampicillic, Cloxacillin	1 (0.83%)	Lidocaine	1 (0.83%)
Ampicillin	1 (0.83%)	Levodopa	1 (0.83%)
Ceftriaxone	1 (0.83%)	Glibenclamide, Metformin	1 (0.83%)
Ciprofloxacin	1 (0.83%)	Pyridostigmine	1 (0.83%)
Cotrimazole	1 (0.83%)	Furosemide	1 (0.83%)
Arteether	1 (0.83%)	Deriphylline	1 (0.83%)
<b>Phenytoin</b>	<b>8 ((6.66%)</b>	Acenocoumarol	1 (0.83%)
<b>Anti-tubercular agents (Total)</b>	<b>7 (5.83%)</b>	Cetrimide,Chlorhexidine	1 (0.83%)
Rifampin,Isoniazid,Pyrazinamide,Ethambutol	4 (3.33%)	Enalapril	1 (0.83%)
Rifampin, Isoniazid, Pyrazinamide,	1 (0.83%)	<b>Total</b>	<b>120 (100%)</b>

Major suspected drug group were Anti-Retroviral (37.5%), Anti-cancer drugs (19.66%), Anti-microbials (10.83%). The commonly implicated drugs were Phenytoin (8), Cisplatin (5)- ("Table"-2).

#### 4.4 : Causality of drugs to reactions :



" Figure" - 2 : Causality of drugs to reactions.

The causality distributions of " Probable/Likely ", "Possible", "Certain" categories were 63 (52.5%), 55 (45.83%), 2 (1.66%) respectively ("Fig."-2). Among 120 reported cases, 28 (20.25%)cases belonged to serious category. The reasons for the seriousness were- Hospitalization (22), Life threatening (4), permanent damage(1), and Fatal (1). The skin and appendages was the commonly involved system in serious ADRs. Anti-retroviral, Anti-microbials were the common offenders for serious reactions.

In most of the patients, 114 (95%) reactions abated after stopping the drug. All the cases were improved after dechallenge. The Rechallenge of the drug was not performed in any patient.

#### 4.5 Outcome of reactions :

"Table"- 3 : Outcome of Reactions.

Outcome	n (%)
Recovered	65 (54.16%)
Recovering	49 (40.83%)
Unknown	3 (2.5%)
Not recovered	2 (1.66%)
Fatal	1 (0.83%)

A total of 65 (54.16%) patients were recovered, 49 (40.83%) patients were recovering, in 3 (2.5%) patients recovery was unknown, 2 (1.66%) patients not recovered, at the time of the last assessment. One fatal (0.83%) outcome was observed in the study ("Table"- 3).

## V. Discussion

In this study demographic data showed a moderately high incidence of ADRs in females. female gender is considered important risk factor for ADRs. [6, 2]. The adults showed high frequency of reactions, which is in concurrent with the studies by venkatesan et al., [7], Rajkannan et al.[8].

Most commonly involved system was Skin in the present study and a similar trend was reported in other studies[9,10] also. Cutaneous reactions most commonly accounted for hospitalization. The fatal reaction in the study was thrombocytopenia, bleeding, leucocytoclastic vasculitis leading to death of the patient. The major causative drug group was Anti-retrovirals. This finding is concurrent with many studies. The most commonly identified ADRs were Anaemia [11], maculo-papular rash more common with Nevirapine[12] . Among antimicrobials Metronidazole was the most commonly implicated drug. Phenytoin also accounted for gingival hyperplasia and similar observation was noted in another study [10]. Among antipsychotic drugs, Olanzapine, risperidone were the commonly identified drugs. They were most commonly involved in extrapyramidal symptoms that are in line with the previous study [13]. In this study among anti-cancer drug group, Cisplatin, cyclophosphamide, paclitaxel were the most commonly implicated drugs.

The causality assessment of suspected drugs to reactions shown more than half of reactions belonged to Probable/Likely category and only a few percentage reactions belonged to Certain category. Almost one third patients, were on multiple medications which is an important risk factor for ADRs. [14]. The withdrawal of suspected drugs was required in many reactions, and majority of them showed improvement at the time of the last assessment. In remaining cases Dechallenge was not done due to therapeutic reasons. Rechallenge was not done in any case, for ethical reasons.

## VI. Conclusion

Adults and females experienced more ADRs. Organ systems most commonly involved in ADRs were skin & appendages, blood, gastro-intestinal system. Cutaneous reactions were more serious reactions and required hospitalization/intervention. The commonly implicated drugs were anti- retroviral agents, anti-cancer agents, antimicrobials. Irrational use of antimicrobials is the common reason for the preventable ADRs. Many studies suggest that the rational selection of drugs as per the indications, monitoring the adverse drug reactions will improve the patient safety.

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