www.jmscr.igmpublication.org
Impact Factor 5.244

Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i8.76

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Evaluation of Adverse Drug Reactions in teaching hospital in Kumoun Region

Authors
Gaur S[1], Paramjeet S[2], Srivastava B[3], Bhardwaj R[4], Ahuja S[5], Gunjita B.[6]
[1,4] Associate Professor, Department of Pharmacology GMC Haldwani
[2] Associate Professor Department of Medicine GMC Haldwani
[3]Professor, Department of Pharmacology GMC Haldwani
[5]Assistant Professor, Department of Pharmacology GMC Haldwani
[6]Technical Associate Department of Pharmacology GMC Haldwani
Corresponding Author
Dr Sanjay Gaur
Associate Professor, Dept of Pharmacology, Government Medical College Haldwani. Nainital Uttarakhand
Email: *gaursanjay75@gmail.com*

Abstract
Objective: *The main aim of the study was to assess the occurrence and pattern of ADR_S , assess causality and documentation of Suspected ADR_S, inteaching hospital in Kumoun Region.*
Methods: *It is a retrospective study about the occurence, nature, pattern and outcome of ADR monitoring from Aug 2015 to July 2016. The ADR_S were assessed for casualty using world health organization (WHO) casualty assessment Scale and Naranjo's algorithm.*
Result: *466 ADR_S were recorded from 251 ADRs form, Male: Female ratio was 1:1.6. Antibiotics / Antimicrobial (32.06%) followed by Anti-viral (23.76%), Anti-tubercular (19.50%) and NSAIDS (6.05%). The common drugs causing ADR were Albendazole 15.24%, Duloutine 8.52%, Pyrizenamide 6.95%, and Metronidazole 4.48%. The most common system involved were gastro intestinal tract 31.16% of ADR, followed by central and peripheral nervous system 27.35%, skin and appendages 22.42% and hormonal system 8.07%. Out of the total ADRs, 62% were possible, 30% were probable 2% were certain and 6% were uncertain. 60.08% of the ADRs were moderate intensity 34.97% were mild and 4.93% of ADRs were severe*
Conclusion: *ADRs are one of the commonest and important cause of mortality and mortality. There is need for greater awareness among doctors health care workers so that it can be minimized and managed.*
Keywords: *Adverse drug Reactions, causality Naranjo's scale.*

Introduction

Adverse drug Reaction (ADRs) cause a sizeable part of overall morbidity and mortality with increase in medical expenses. ADRs have been defined by the World health organization (WHO) as "any response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function .[1] Considering the importance of monitoring ADRs for improving public health, Pharmacovigilance programme of India (PvPI)

was started in 2010.[2] Under this programme, ADR monitoring centres have been started in many medical institution and hospital all over the country. These ADRs result in diminished quality of life, increased physician visits, hospitalization and even death. Polypharmacy, multiple chronic medical problem and frequent acute illness. Debilitating cachexic carcinoma puts patients at increased risk for ADRs.

In order to prevent ADRs, methods should be developed to identify, report, analyse and issue warnings for safer use of medicine. ADR incidence in Indian population ranges between 1.8% and 25% with 8% resulting in hospitalization. 50% of the approved drugs are associated with some type of adverse effect that are only seen after approval of the drug[3,4]. Identification of these helps in achieving a substantial reduction in health care cost[5]. ADRs also makes the patients loose confidence in the prescription and the treating physician.

Pharmacovigilance has evolved as an excellent system of monitoring with the objective of understanding the various characteristics of ADRs like severity, expectedness, risk factors, seriousness, association and their frequency. Monitoring of ADRs can be undertaken by several method. Passive surveillance by voluntary reporting, stimulated reporting by physician, active surveillance by prescription event monitoring, patient registries, epidemiological studies, cohort and case control study are some of the important methodologies used globally. Most of the countries have adopted spontaneous or voluntary reporting system which has led to the withdrawal of useful drugs like Rofecoxils, Terfeandine and cerivastatin.

The present study was carried out with the purpose of analyzing the ADRs so as to identify the suspected drugs causing ADRs and gain insight into the pattern of their reactions so that feedback to the national co-ordinating centre and the prescribers can be given.

Material and Methods

Study Area: The Study was conducted at the tertiary care centre at Government Medical College & Dr. Sushila Tiwari Hospital Haldwani Nainital. Approval of the Institutional Ethical Committee was Obtained for the study.

Study Period and Study Population: The data was obtained from suspected ADRs reporting forms, between February 2016 to July 2016, from the Dr. Sushila Tiwari Hospital Haldwani to the ADRs monitoring centre attached to department of Pharmacology under the Pharmacovigilance programme of India (PvPi)

Study Design: It was a retrospective study conducted from ADR reporting form, reported from Dr. Sushila Tiwari Hospital Haldwani.

The demographic details of the patients were recorded. Details of medication given were also noted. Chief Complaint, past history, drug history were also recorded. Details about the occurrence and nature of ADRs, severity, de challenge and rechallenge were recorded. Concomitant medications administered were also obtained. Relevant laboratory investigations were also recorded.

Inclusion criteria- Patients of both sexes and all ages, developing at least one ADR during or after the treatment period were included in the study.

Exclusion criteria: Patients who developed ADRs due to fresh blood or blood products infusion or due to intentional or accidental poisioning or history of drug abuse were excluded from the study [6].

Study tool: ADR reporting form, designed by centre for Drug standard Control organization (CDSCO) was used to collect data. The reported ADRs were assessed for causality using both WHO causality assessment scale and Naranjo's algorithm [7].

The severity was assessed using Hartwig and Siegel scale [8].

The WHO causality assessment scale determines the causal relationship of a suspected drug to the ADR in question and categorize into "Certain", "probable", "possible", "unlikely", "conditional",

/ "unclassified" and "unasseseable" / "unclassifiable".

Naranjo's algorithm has 10 objective questions with three option for answer – yes, no and do not know. Scores are given accordingly and the causality is assessed as "definite", "probable", "possible", and "unlikely".

The modified Hartwig and Siegel scale classifies severity as "mild", "moderate", and "severe". The data collected, was analyzed using Microsoft excel and frequency and percentage were determined for each variable.

Result

265 ADRs form were received from Dr. Sushila Tiwari Memorial Hospital, Haldwani, Nainital Uttarakhand from February 2016 to July 2016 a period of 6 months to the ADR monitoring centre department of Pharmacology. Fourteen(14) were rejected as it was incomplete in may ways and finally 251 ADR forms was analysed of which 96 were males 155 female. The most common age group at which ADRs occurred was been 18-39 yrs. (45.41%) followed by 40-59yrs. (27.88%). (Table- 1)

Table- 1. Demographic profile

Males	96	
Females	155	
Less than 18	43	17.13%
18-39 yrs	114	45.14%
40-59 yrs	70	27.88%
60 and above	17	6.77%

The most common therapeutic class of drug causing ADR was Antibiotics/Antimicrobial (32.06%) followed by Anti-viral(23.76%),Anti-tubercular (19.50%) and NSAIDS (6.05%).(Table-2)

Table- 2. Therapeutic class of Drugs causing ADRs

Class of drug causing ADR	No of ADRs (n)	Percentage
NSAIDs	27	6.05%
Antibiotics and antimicrobials	143	32.06%
Antituberculars	87	19.50%
Anticonvulsants	7	1.56%
Opiates	2	0.45%
Antivirals	106	23.76%
Antipsychotics	21	4.70%
Antidepressants	11	2.46%
Steroids	6	1.34%
Antihistamnics	7	1.56%
Antiemetics	5	1.12%
Coauglants and anticoauglants	6	1.34%
Hormones	3	0.68%
DMARDs	10	2.25%
Antihypertensives	2	0.45%
Bronchodilators	3	0.68%
Total	446	

The common drug in the group causing ADR were Albendazole 15.24%, Duloutine 8.52%, Pyrizenamide 6.95%, and Metronidazole 4.48%.(Table- 3).

Table- 3. Commonly involved drugs causing ADRs

Drug	No of ADRs	Percentage	ADRs
Diclofenac	16	3.59%	Fixed drug eruptions (2), Rashes(2),Gastritis(8),Anaphylaxis(1), Diarrhea(3)
Metronidazole	20	4.48%	Chills & Rigors (10), Metallic taste (2), Nusea(2),Vomitting(2), Headache(1),Itching (1),Pain Abdomen (1), Rashes (1)
Albendazole	68	15.24%	Abdominal pain(21),Unconciousness(12),Headache (13), Nausea (6), Vomitting(6), Fever (04),Anxiety(04), Convulsions(02)
Pyrazinamide	31	6.95%	Hepatitis(14), Vomitting(6), Pain Abdomen (3),Anorexia (3), Hyperuricemia (2), Nausea(1) , Itching(1) , Rash(1)
Leveriracetam	10	2.24%	SJS(1), Rashes(2), Nasopharyngitis (4), Diarrhea(3)
Duloxitine	36	8.56%	Drowsiness(12) , Diziness (8) , Nausea (1) , Headache(10) , Unconciousness (1), Restlessness (2), musculoskeletal pain (2)
Olanzapine	19	4.26%	Sedation (4), Headache (3), Tremors (1), Increased apetitite (1), Constipaton(1), Drowsiness (1).Altered Behaviour(8)
Hydroxyhloroquine	11	2.47%	Hyperpigmentation (4), Gastritis (3)Neuropathy (4)

Types of ADRs occurring with organ system involvement were observed. The most common system involved were gastro intestinal tract 31.16% of ADR, followed by central and peripheral nervous system 27.35%, skin and appendages 22.42% and hormonal system 8.07%.(Table- 4)

Table- 4 Organ System involvement

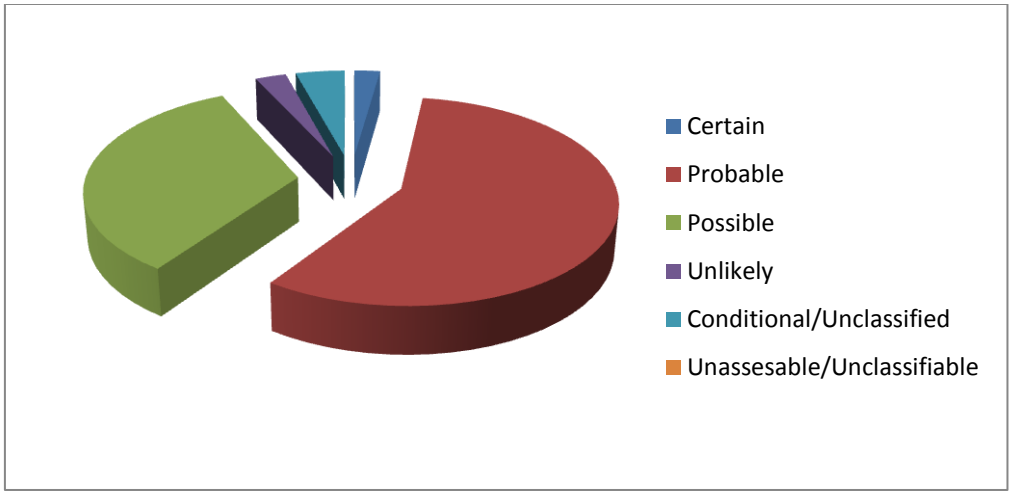
Organ System involvement	Types of Observed ADR	Number	Percentage %
Gastric intestinal disorders	Nausea & Vomiting (37), Diarrhea (32), Gastritis(29), Constipation(9), Anorexia(14), Dry Mouth(4), Oral Ulcer(14)	139	31.16
Skin and appendages disorder	Rashes(43), Urticaria(31), Angioqedema(9), Fixed drug eruption(5), SJS(3), TEN(1), Thinning of skin(2), Dermatitis(1), Hyperpigmentation (5)	100	22.42
Central and Peripheral Nervous System	Dizziness(12), Sedation(24), Neuropathy(11), Headache(28), Verligo(10), Insomnia(2), Weakness(2), Bodyache(4), Extraphramidal Syndrome(2), Restlessness(1), Treanor(3), Altered taste(10), Loss of couscioneness(12), Conational(1)	122	27.35
Hormonal System	Acne(16), Herusulesin(1), hyperpeolactaemia(5), Hot fusils(5), Hyperthyroidism(2)	36	8.07
Respiratory System	Cough(5)	5	1.12
Psychiatric Disorder	Night terror(1), Alterid behavior(16)	17	3.81
Urinary System Disorder	Discoloration of urine(4)	4	0.89
Vision Disorder	Astrid vision(6)	6	1.34
Liver & Biliary System	Hepatitis(10)	10	2.24
Syltion CVS, Heart Rate	Ventricular tachycardia(2), Facial Oedema(5)	7	1.56
Total		446	

The collected data was analysed using WHO causality assessment scale. 57% of the ADRs were “Probable”, 33.40% was “possible” and 2.24% was “certain”. 4.26% of the ADRs were “unclassified”.(Table- 5)(Figure 1)

Table- 5 WHO causality assessment

Type of Reaction	No of ADRs	Percentage
Certain	10	2.24%
Probable	256	57%
Possible	149	33.40%
Unlikely	12	2.69%
Conditional/Unclassified	19	4.26%
Unassesable/Unclassifiable	0	0
Total	446	

Figure 1. WHO causality assessment

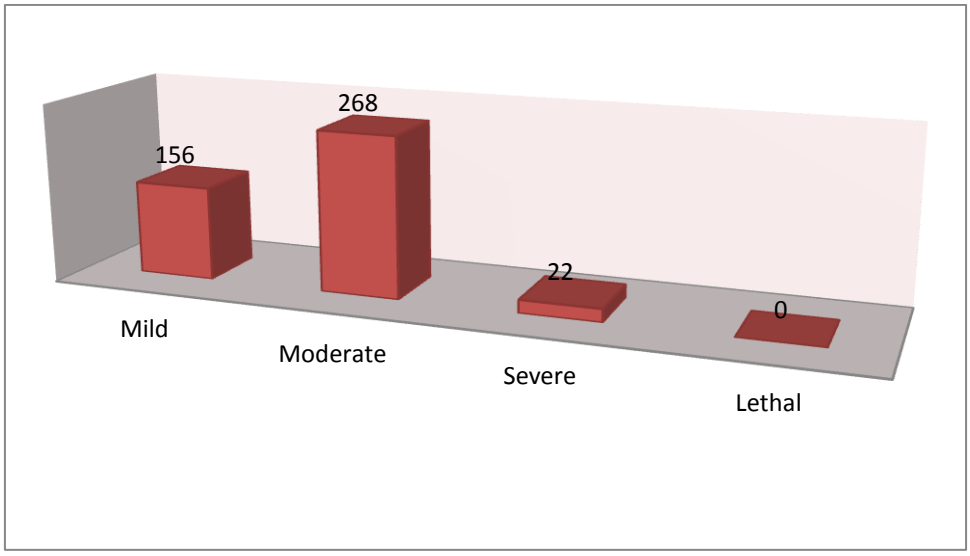


Severity assessment done by Hartwig & Seigel scale showed that 60.08% of the ADRs were moderate intensity 34.97% were mild and 4.93% of ADRs were severe. No lethal ADRs were reported. (Table- 6)

Table- 6. Severity assessment (Hertwig and Seigel scale)

Grade	No of ADRs	Percent
Mild	156	34.97%
Moderate	268	60.08%
Severe	22	4.93%
Lethal	0	

(Figure 2). Severity assessment



Discussion

The present study evaluates the pattern of ADRs, its association with organ system, common ADRs, its causality and severity.

Of the 251 ADR forms evaluated, 96 were males and 155 females.

In our study ADRs commonly occurred in women, when compared to men, this finding is similar with other studies. [8][9][10][11].

Females are more likely than men to interpret the discomport that is caused due to drugs. Most common age group was 18-39 years (45.45%) followed by 40-59 years (27-88%). This finding partially agrees with other studies which elaborated the increased uses of medicine, increase the incidence of disease , such as diabetes & hypertension [14]

Female gender is considered important risk factor for ADRs. [12][13]

Scheneiderjk etal in his study reported higher incidence of ADR in elderly population.

The most common therapeutic class of Drugs causing ADR was antibioitics & antimicrobial (32.06%). Many previous studies have revealed that antimicrobials are the culprit in the majority of ADRs incidences since they are the most prescribed drugs.[14]. Major antimicrobials drugs causing ADR was albendazole (15.24%), pyrzinamide (6.95%) Metronidazole (4.48%)

Due to presence of overwhelming infection in the society and irrational prescribing of antimicrobials , incidence of ADR has increase with these drugs. Development of resistance has forced health care professionals to injudiciously use antimicrobial for treatment of even mild injection. Ceftriaxone hare caused skin rashes, urticaria & itching floroquindones hase caused hypersentivity reaction which is observed in literature.

Most common organ system involved was gastrointestinal tract (31.16%) followed by central & peripheral hervous system (27.35%) skin & appendages (22.42%). Similar trend was reported in previous study[15][16][17]

The most common adverse effect in GIT was nausea and vomiting, followed by diarrohea gastritis. Skin and appendages reported third commonest with some serious cutanious reactions like, Stevens Johnson syndrome and Toxic epidermonecrolysis reported in the patients , which was also reported by other research[17]

The reasons for predominant cutaneous reaction reported is the visibility, because of which they are easily diagnosed and reported.

As per the causality assessment done by WHO Scale, there were 57% probable" reaction, possible was 33.40%, and 2.24% were certain."This was in line with the preveous studies[15,18]. 33.40% cases were possible which was due to multiple drug suspect. This may be due to practice of polypharmacy.2.24% certain cases were with Diclofenae, Albendazoled and Metromidazole in which reaction abated after de-challenge and they were the only drug used.

Severity assessment done by Hartwig and Siegel Scale showed that most of the reactions were from "mild to moderate " intensity which could be managed by physician and which resolved after sometime. In 2.24% of certain cases of ADR withdrawal of the drug was done and with treatment the patient recovered.

The study had some limitation. There is underreporting of ADRs from some of the departments with improper documentation , lack of interest for reporting and fear of legal implication , some other restrictions to name a few.

The result of the current study points towards an urgent need for a good Pharmacovigilance monitoring and active participation of all stake holders .There is a need for formulating hospital based guidelines for treatment of various diseases so as to minimise ADRs.

Conclusion

In the present most of the ADR were due to antibiotics, Antiviral and Antitubercular drug. Most organ system effected mainly was gastrointestinal tract followed by CNS skin and appendages.

The causiality assessment showed most of the reaction were mild to moderate severity. Therefore creating awareness by rational drug prescription, close monitoring of the prescribed drug and improvement in reporting will go a long way in decreasing the ADR burden of the society

References

1. The use of the WHO-UMC system for standardised case causality assessment. [Internet] [Cited 2015July 4]. Available from: http://who-umc.org/Graphics/24734.pdf.
2. Pharmacovigilance programme of India. [Internet]. 2013 April [Cited 2015 July 4]. Available from: http://ipc.nic.in/write-readdata/linkimages/April-2013,%20PvPI-IPC%20News%20Letter,%20Volume-3,%20Issue-5-4537494506.pdf.
3. Sriram S, Ghasemi A, Ramasamy R, Devi M, Balasubramanian R, Ravi TK, et al. Prevalence of adverse drug reactions at a private tertiary care hospital in south India. J Res Med Sci. 2011;16(1):16-25.
4. Rabbur RS, Emmerton L. An introduction to adverse drug reporting system in different countries. Int J Pharm Pract. 2005;13(1):91-100.
5. Doshi MS, Patel PP, Shah SP, Dikshit RK. Intensive monitoring of adverse drug reactions in hospitalized patients of two medical units at a tertiary care teaching hospital. J Pharmacol Pharmacother. 2012;3(4):308-13.
6. Santosh RC, TragulpainkitP. Pharma-covigilance :an overview. Mahidol University Journal Of Pharmaceutical Science.2011;38:1-7.
7. Central Drug Standard Control Organization. Directorate General of Health Services, Ministry of health and family welfare , Government of India.
8. Lemmens HJM, Burm AGL, Hennis PJ. Infuence of age on the pharmocokinetic of Alfentanil. Clin Pharmcokinetic. 1990:19(5):416-22.
9. Harris RZ, Benet LZ, Schwartz JB. Gender effects in pharmacokinetics and pharma-codynamics. Drugs. 1995;50(2):222-39.
10. Wilkinson GR. Cytochrome P4503A(CYP3A) Metabolism:predicition of in vivo activity in humans. J Pharmacokin Bio Pharm. 1996;24(5):475-90.
11. Alomar MJ. Factors affecting the development of adverse drug reactions. Saudi Pharm J. 2014;22(2):83-94
12. Wu C, Bell CM, Wodchis WP. Incidence and economic burden of adverse drug reactions among elderly patients in Ontario emergency departments: a retrospective study. Drug Saf. 2012;35(9):769-81.
13. Alomar MJ. Factors affecting the development of adverse drug reactions (review article). Saudi Pharm J. 2014;22(2):83-94.
14. Padmaja U, Adhikari P, Pereira P. A prospective analysis of adverse drug reaction in a south Indian hospital. Online J Health Allied Sci. 2009;8(3):12.
15. Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. Br J Clin Pharmacol. 2008;65(2):210-6.
16. Jose J, Rao PG. Pattern of adverse drug reactions notifed by spontaneous reporting in an Indian tertiary care teaching hospital. Pharmacol Res. 2006;54(3):226-33
17. Uppal R, Jhaj R, Malhotra S. Adverse drug reactions among inpatients in a north Indian referral hospital. Natl Med J India. 2000;13(1):16-8.