To study the prevalence of adverse drug reactions (ADRs) in various departments of tertiary care hospital

Brijesh Kumar Duvey[1], Rajendra Kumar Chouksay[1]

[1]Research Scholar, Sun Rise Unversity, Alwar, Rajasthan, India
[1]Professor, Sun Rise Unversity, Alwar, Rajasthan, India

**Correspondence*
Brijesh Kumar Duvey
Research Scholar, Sun Rise Unversity, Alwar, Rajasthan, India
E-Mail: brijesh.duveu@gmail.com

Abstract

Introduction : An ADR is defined by the World Health Organization (WHO) 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 for the modification of physiological function'.1 Each year, millions of patients experience ADRs, especially with the increased use of medicinal drugs. ADRs take the place as the fourth to sixth major cause of death, eclipsing pulmonary disease, diabetes, acquired immunodeficiency syndrome and pneumonia. According to the Centers for Disease Control and Prevention, ADRs are responsible for almost 1,300,000 emergency department visits annually.**Method:** A spontaneous reporting technique was followed. Patients were selected in the medical ward. We attended ward rounds and encouraged the doctors to report suspected (ADEs) as well as nurses, pharmacist, patient and their care taker. All the in-patients who assessed for ADR's during the study period are check their past medication history. Patient was selected from general medicine department according to the inclusion and exclusion criteria of WHO. **Result And Discussion:** During the study period total 6930 patients case sheets were reviewed among them 540 (07.79%) patients have experienced at least one adverse drug reaction (ADR). Out of 540 patients are divided into two groups 212 (39.25%) experienced 265 ADRs and admitted in hospital. In the age group 31-40 maximum ADRs was found. It also have seen male patient of all age group have more ADRs, and most ADRs. Study also soonest1 ADRs, **Conclusion:** The study show that ADRs Are the main cause of increase of medication cost which may be reduced by establishing of proper ADRs monitor center and establishing ADRs information center and their collaboration with other agencies.

Key words: ADRs, WHO scale, hospitalizations.

Introduction

An ADR is defined by the World Health Organization (WHO) 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 for the modification of physiological function'[1]. Each year, millions of patients experience ADRs, especially with the increased use of medicinal drugs[2]. From 2009 to 2012, approximately 47% of people in the United States reported using no less than one prescription medication in the past month and approximately 11% reported using no less than five prescription medications concomitantly[3].As a result, the amount spent on prescription drugs was estimated to be US$270 billion in 2013 according to the National Center for Health Statistics report in 2014[3,1]. Lazarou and his colleagues estimated, in a landmark meta-analysis in 1998, that ADRs were associated with over 2,216,000 hospitalization cases annually in USA (admitted because of ADR or suffered ADR while in hospital), leading to more than 106,000 deaths each year. Therefore, ADRs take the place as the fourth to sixth major cause of death, eclipsing pulmonary disease, diabetes, acquired immunodeficiency syndrome and pneumonia[4].According to the Centers for Disease Control and Prevention, ADRs are responsible for almost 1,300,000 emergency department visits annually[5].In 1995, the burden of ADRs in financial terms was estimated to be up to US$136 billion dollars annually[6]. More recently, Poudel et al. estimated the cost of ADR related hospitalizations in 2011 to be US$38.9 billion dollars[7]. Article selection and search criteria A literature search was conducted by searching Medline/PubMed, as well as Google Scholar, using relevant keywords (post marketing surveillance, pharmacovigilance, spontaneous reporting, adverse drug reactions, VigiBase, drug safety). Articles older than 20 years were filtered out, unless they were still highly relevant, no updated information can be removed, or for historical perspective. Non-relevant results were excluded as well. After initiating the review, and in order to get more details on a specific point or topic, a Google search was conducted and the reference fulfilling the sought information was included.

Three of the main limitations of pharmacovigilance are: under-reporting, difficulty in identifying low risks, and the difficulty or impracticality of quantifying risks. Moreover, ADR reporting is determined by numerous factors, for example how serious or severe an ADR is, how long the drug has been on the market, the experience of the health care professional, and the qualifications of the reporting physician (specialists report more often than general practitioners do)[8].

Future prospects of pharmacovigilance Pharmacovigilance has clear, well-established goals: to detect ADRs associated with the use of drugs as early as possible, and to avoid risks that may outweigh the benefits of the medication[9]. The evolution of pharmacovigilance has been a slow and steady one. From individual doctors noticing unusual effects in patients and sharing their findings with colleagues to the methods used today to monitor a drug after its release into the market, including spontaneous reports, risk management plans, prospective safety studies, and registries[10]. The main focus of pharmacovigilance has been to detect rare ADRs while giving less attention to the common ones.

Receantly, however, there has been a climate of change and efforts are now being made to focus on patient-centered pharmacovigilance rather than population-based and regulation-based Pharmacovigilance[11]. A study was conducted to evaluate the different aspects of pharmacovigilance currently, and in the future. The study claimed that there are developments within the field of pharmacovigilance, including the setting of rules and regulations, as well as the scientific-related issues. Specifically, the study mentioned details regarding those two aspects by stating that: 'On a regulatory level, these include conditional approval and risk management plans; on a scientific level, transparency and enhanced patient involvement are two important elements'. Overall, these new developments will guarantee continuous progress in pharmacovigilance[12]. There are three aspects to consider when evaluating ADRs: causality, severity and preventability. There are systems for assessing each of the three categories, which set scales that are then scored to quantify and hence evaluate them. For instance, there are two systems to assess causality: the first is the WHO–UMC causality assessment system and the second is Naranjo's ADR probability scale[13]. To assess severity, there is the Hartwig and Siegel ADR severity assessment scale, and finally, in order to assess the preventability of an ADR, the Schumock and Thornton ADR preventability assessment scale is used[14]. ADRs impact profoundly our healthcare system, contributing significantly to patient morbidity, mortality, hospital admissions, and healthcare costs. In an attempt to closely monitor and help reduce the incidence of ADRs in the country, the National Department of Health has employed a Pharmaceutical and Therapeutic Pharmacovigilance team to advise on issues relating to ADRs. The objectives of this committee are to promote the safety of the patient, endorse the rational and cost-effective use of drugs, inform healthcare institutions of policy and guideline changes, promote awareness of ADRs and the need to report all suspected ADRs[15-16] .

Adverse drug reactions classification

ADRs classification on cause and severity

1) Type A (Augmented) Reaction: These are pharmacology reactions whose response is distinct and quantitative. They are dependent on dose, widespread, and expected. They lead to toxic side effects. Ex: bleeding due to heparin
2) Type B (Bizarre) Reactions are dependent on patient features that are not related to drug dosage. Reactions also have a relation with genetic and environmental factors. The best example is a penicillin-induced anaphylactic reaction.
3) Type C (Chronic) Reactions occur when medications are used for a longer period. These reactions can be identified and foreseen. Some examples are benzodiazepine and analgesic nephropathy.
4) Type D (Delayed) Reactions are due to carcinogenesis or teratogenesis.
5) Type E (Ending of Use) Reactions occur because of sudden ceasing in the chronic therapy[16].

Common risk factors for ADRs in India

- Drug-drug interactions
- Over-use of medication
- Overdose of drugs
- Wrong Administration
- Drug use without indication
- OTC (Over Counter) medications used[21]

Pharmacists have a key role in reducing ADRs by educating patients with the required information as well as the physician about important ADRs. Different types of technologies have been developed by the various healthcare systems (including Drug interaction screening software, Computerized medical records)[17]

Methodology

Selection of department

The general medicine department of Prakash Hospital and Trauma Center, Mau UP, was selected for the study. The reasons for selecting the department were a combination of disorders, which compels the physician to prescribe more categories of drug that leads to possibility of adverse drug reactions. Our department has associated with entire department of the medical team. It is the one of the reason for selection of the department for study.

Study Type – It was a Prospective, Observational and non-interventional over a period of Two year four month (July 2020 To Oct. 2022) at Prakash Hospital and Trauma Center.

A spontaneous reporting technique was followed. Patients were selected in the medical ward. We attended ward rounds with the doctors as a part of the regular clinical pharmacy services. During the ward rounds, we encouraged the doctors to report suspected adverse drug events (ADEs). Nurses also filled in the reporting forms. All the in-patients were assessed for ADR's during the study period. In the suspected cases, past medical/medication history of patients were collected. Patients were interviewed, monitored daily throughout their hospital stay and their medical records were reviewed.

Patients Selection

Patient was selected from general medicine department according to the inclusion and exclusion criteria.

Inclusion Criteria

- All patients admitted in Prakash Hospital.
- All suspected ADR's that conforms to WHO's definition.
- Patients of either sex receiving treatment.
- Any patient who developed ADR's during the treatment period.
- Patients willing to Participate.
- Medication errors cases

Exclusion Criteria

- Patients unable to respond to verbal questions.
- Patients who are not willing to participate
- Out Patient Dept.(OPD) patients
- Day Care surgery patient
- Emergency Patients.

Source of Data

All the relevant and necessary data was collected from:

- Patients' case observations
- Treatment charts.
- Laboratory and analytical reports.
- Interviewing patients / patients care takers (whenever necessary).

DESIGNING OF DATA COLLECTION FORM (DCF)

A suitable data collection form was designed to collect, document and analyses the data. Patient consent form was also

incorporated in the DCF. There were no personal question are mentioned in DCF. The patient consent form is prepared in both English and Hindi Language for better understanding of study purpose.

Procedure

- In-patients treated with drugs in the various departments of hospital will be reviewed on daily basis.
- Patients who meet the study criteria will be enrolled into the study by taking their consent.
- All relevant patient data will be collected in a suitably designed patient data collection form.
- Patient or patient's care takers will be interviewed for confirmation of any suspected ADR's.
- Doctor notes and laboratory reports will be reviewed for presence of any documented ADR's.
- All suspected ADR's will be suitably assessed for causality, severity, preventability and predictability to the respective department of spontaneous ADR's reporting.
- Collection of the incidence of ADR's was also done by voluntary reporting through phone calls and verbally from doctors, nurses and pharmacists.
- From the ADRs form which was distributed to the respective department for reporting and documentation of the suspected ADR's[18-20].

Result and Discussion

During the study period total 6930 patients case sheets were reviewed among them 540 (07.79%) patients have experienced at least one adverse drug reaction (ADR). The 540 patients are divided into two groups.

Group -1 Patients Visited or admitted in Hospital due to ADRs and

Group -2 ADRs experienced or observed during the Hospital stay.

Table 1: Patients were distribution according to type of ADRs

Sr. No.	Groups	No. of patients	Percentage (%)	Ratio
1	Group-1	212	39.25	1:1.54
2	Group-2	328	60.74	
Total		540	99.99	

Among the 540 cases documented 212 (39.25%) patients were admitted or visited to hospital due to ADRs and 383(60.74%) ADRs were observed during the Hospital stay.

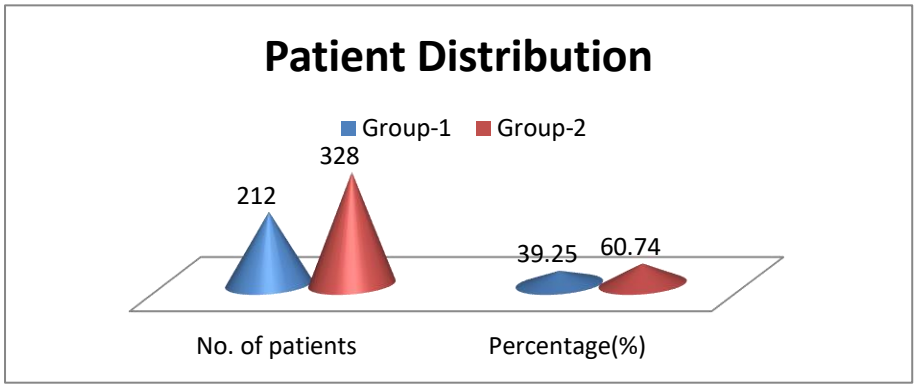

Fig. 1: Distribution of Patients as per ADR type

Group-1 Patients Visited or admitted in Hospital due to ADRs

Among the 212 cases, 265 ADRS were identified, which shows the probability of multiple ADRs in a single patient. In the following table, 212 patients were distributed according to the age considering 10as class interval.

Table 2: Age wise distribution of patients

Sr. No.	Age (years)	No. of patients	Percentage (%)
1	1-10	37	17.45
2	11-20	17	08.01

3	21-30	19	08.96
4	31-40	44	20.75
5	41-50	43	20.28
6	51-60	21	09.90
7	61-70	20	09.43
8	71-80	07	03.30
9	81-90	04	01.88
Total		212	100

Among 212 patients the higher prevalence of adverse drug reactions was observed inpatients of age 31 to 40 yrs (20.75%) followed by 41-50yrs (20.28%), 05 – 10yrs (17.45%), 51 - 60yrs (09.90%), 61- 70yrs (09.43 %), 21-30yrs (08.96), 11-20yrs (08.01%), 71- 80 yrs (03.30%), 81-90 yrs (01.88).

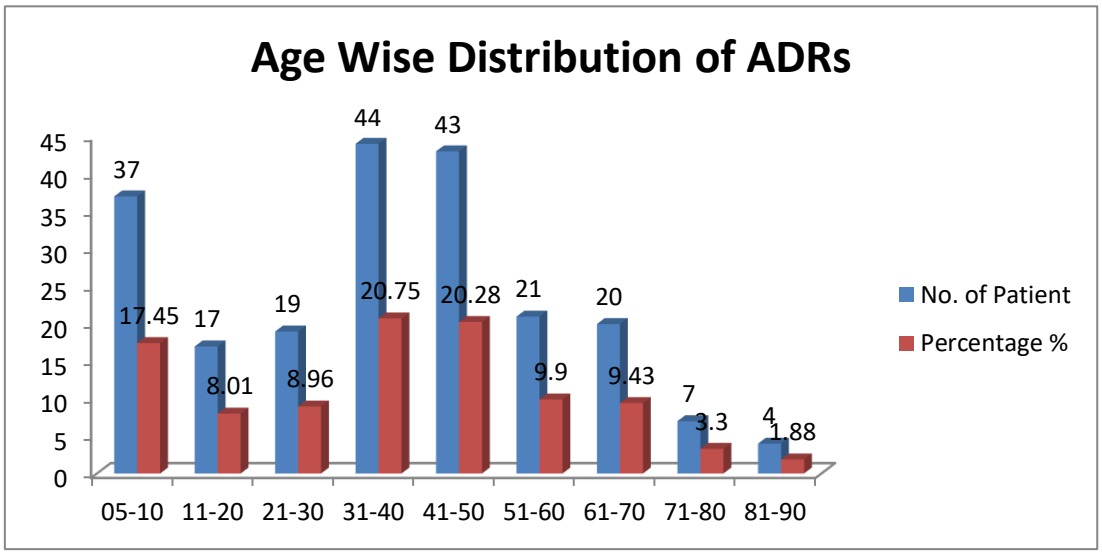

Fig. 2: Age wise Distribution

In the following table 212 patients were distributed according to their class of age and gender.

Table 3: Prevalence of ADR according to Age group & gender

Sr. No.	Age group	FrequencyN (%)	Gender		Ratio
			Female	Male	
1.	Children	60 (28.30%)	23	34	1.47
2.	Adults	114 (53.77%)	39	76	1.95
3.	Geriatrics	38 (17.92%)	19	21	1.10

The table shown that among 212 adults 114 (53.77%) were predominant over children 60 (28.30%) andgeriatric 39 (17.92%) in terms of prevalence, while males have higher risk to develop ADRs among all age group compare to female.

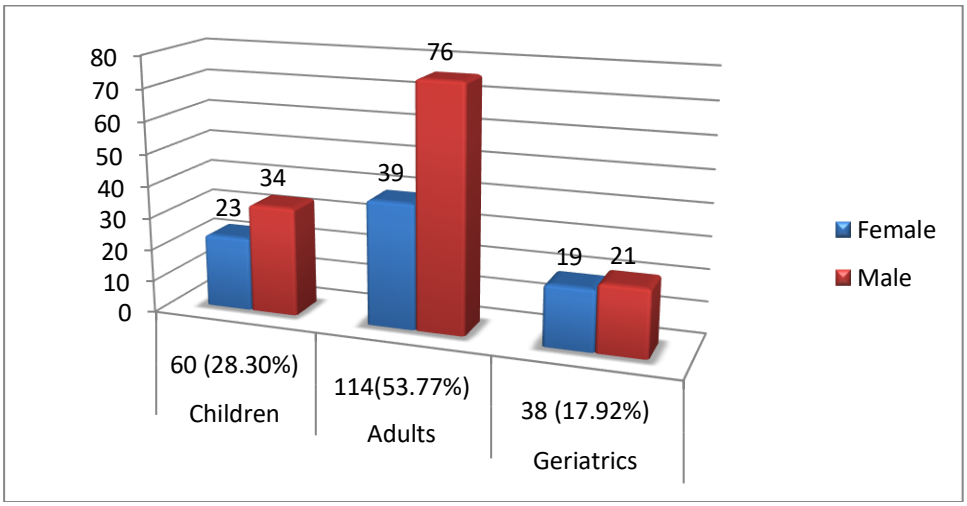

Fig. 3: Distribution according to Age group

In the following table 212 patients were distributed according to their sex.

Table 4: Sex wise distribution

Sr. No.	Sex	No. of patients	Percentage (%)	Ratio
1	Male	131	61.80	
2	Female	81	38.20	
Total		212	100	1.61

Total 212 cases documented out of which 131(61.80%) were male and 81 (38.20%) are female it also indicate male is showing 1.61 times higher risk to develop ADRs as compared to female.

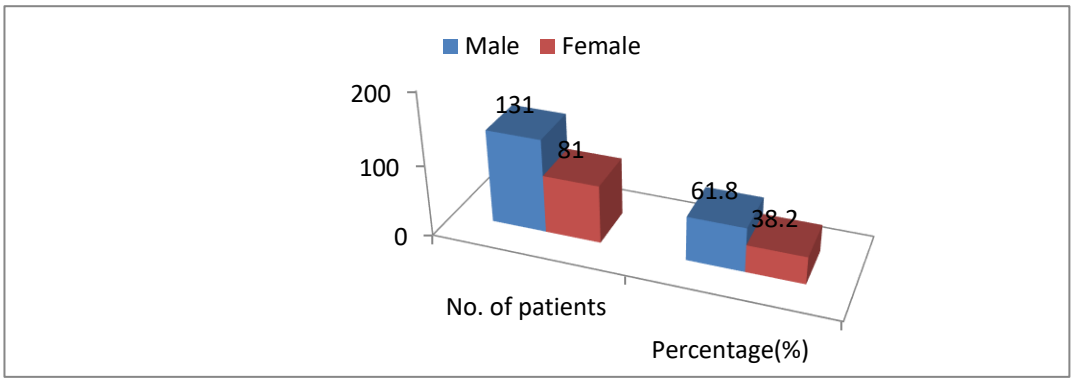

Fig. 4: sex wise distribution of group 1 ADRs

Distribution of the 240 cases documented according to the past medical history is depicted in the following table.

Table 5: Distribution according to past medical history

Sr. No.	Past medical history	Frequency	Percentage (%)
1	Cardiac Disorder (CHF, MI, Angina etc.)	51	24.05
2	CNS Disorder	48	22.64
3	Metabolic Disorder (diabetes)	37	17.45
4	Skin Disorder	26	12.26
5	Renal Disorder	15	07.07

6	Respiratory Disorder	07	03.30
7	GI Disorder	06	02.83
8	Others	21	09.91
	Total	212	100

Among 212 cases the higher prevalence of adverse drug reactions was observed in patients having past medical history of Cardiac disorder 51 (24.05%) followed by CNS disorder 48 (22.64%), Metabolic disorder 37 (17.45%), Skin disorder 26 (12.26%) Renal disorder 15 (07.07%), respiratory disorder 07 (03.30%) GI disorder 06 (02.83%), and Others 21 (05.19%).

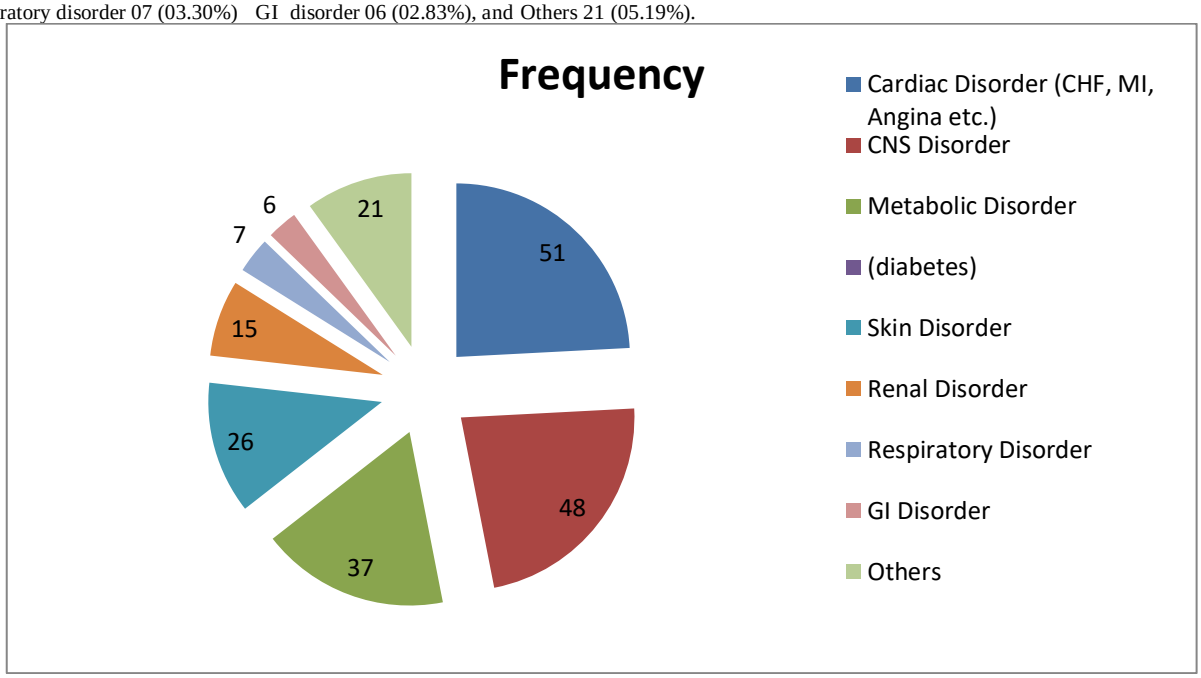

Fig. 6: Distribution according to Past Medical History

The 265 ADRs were distributed according to the WHO ART system codes in table 6.

Table 7: List of ADRs according to the WHO ART system codes

Sr. No	System	ART Codes	No. of ADRs	Percent (%)
1	Dermatology	100	65	24.53
2	Muscular skeletal	200	10	03.77
3	Central nervous	410	27	10.19
4	Ophthalmic	420	14	05.28
5	Otic system	431	10	3.77
6	Gastrointestinal	600	56	21.13
7	Hepatic system	700	23	08.68
8	Endocrine	900	27	10.19
9	CVS	1000	12	4.53
10	General Disorders	1810	21	7.29
Total			265	100

It includes different systems and number of ADR'S found in each system: most of ADRs were experienced by dermatology 65 (24.53%) followed by Gastrointestinal 56 (21.13%) and it may be to allergic reaction of drug.

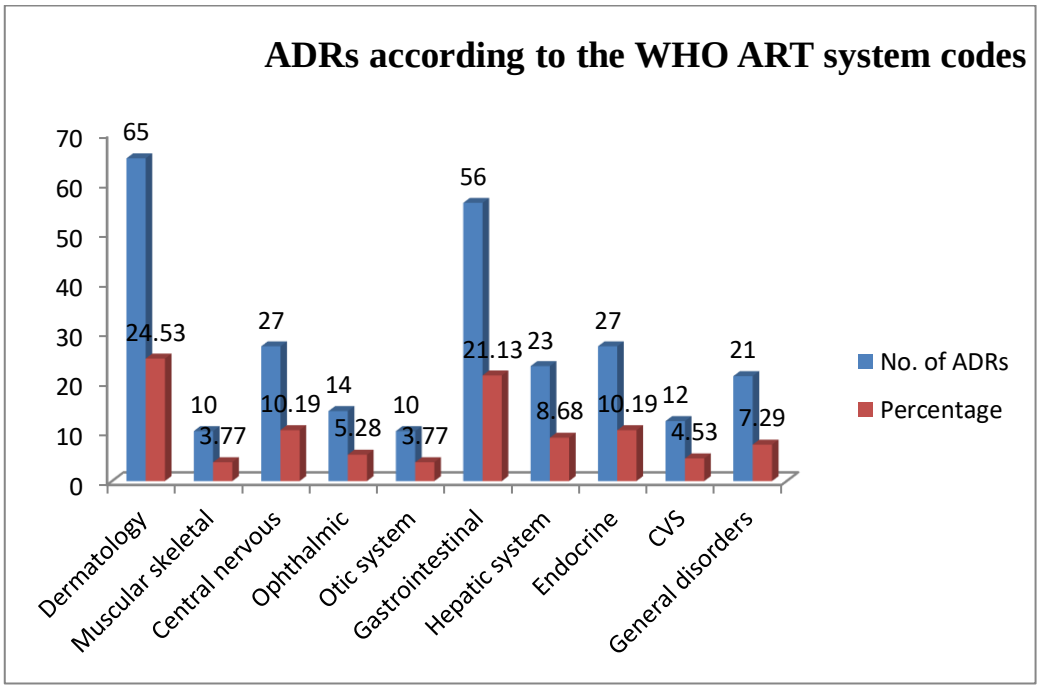

Fig. 7: ADRs were distributed according to the WHO ART system codes

Conclusion

The present study shown that, during the study period total 6930 patients case sheets were reviewed among them 540 (07.79%) patients have experienced at least one adverse drug reaction (ADR). Out of 540 only 212 patients were experienced ADRs and they admitted in hospitals. It was also find that dermatology department (24.53%) has highest degree of ADRs according to WHO ART system after that gastrology department and it may be due to multiple drug therapy and long term therapy while frequency of ADRs is highest in cardiac disorder related 51 (24.05%) medication. It is also found that adults 114 (53.77%) are more prone towards ADRs and it may be due to self medication or use of some OTC drug**.**

Though this study provide better understanding about distribution of ADRs their frequency and highest rate of prevalence among the adult age group of patient and sex but further study is required to understanding the cause of ADRs and correlates it with clinical presentation and which will reduce the cost of treatment.

References

1. World Health Organization. Safety of medicines: a guide to detecting and reporting adverse drug reactions: why health professionals need to take action. Geneva: World Health Organization, 2002.
2. Schutte T, Tichelaar J, Reumerman MO, et al. Feasibility and educational value of a student-run pharmacovigilance programme: a prospective cohort study. Drug Saf 2017; 40: 409–418.
3. Cai R, Liu M, Hu Y, et al. Identification of adverse drug-drug interactions through causal association rule discovery from spontaneous adverse event reports. Artif Intell Med 2017; 76: 7–15.
4. Lazarou J, Pomeranz BH and Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 1998; 279: 1200–1205.
5. Centers for Disease Control and Prevention. Adverse drug events in adults, www.cdc.gov/ medicationsafety/adult_adversedrugevents.html (2017, accessed 12 May 2020).
6. Johnson JA and Bootman JL. Drug-related morbidity and mortality: a cost-of-illness model. Arch Intern Med 1995; 155: 1949–1956.
7. Poudel DR, Acharya P, Ghimire S, et al. Burden of hospitalizations related to adverse drug events in the USA: a retrospective analysis from large inpatient database. Pharmacoepidemiol Drug Saf 2017; 26: 635–641.
8. Faillie JL, Montastruc F, Montastruc JL, et al. Pharmacoepidemiology and its input to pharmacovigilance. Therapie 2016; 71: 211–216.
9. Meyboom RH, Leufkens HG and van Puijenbroek EP. Thoughts on pharmacovigilance in the future: there are more Weber-effects. In: Edwards R and Lindquist M (eds) Pharmacovigilance: critique and ways forward. 1st ed. Cham: Springer, 2017, pp.115–120.
10. Van Puijenbroek EP and Harmark L. Broadening the scope of pharmacovigilance. In: Edwards R and Lindquist M (eds) Pharmacovigilance: critique and ways forward. 1st ed. Cham: Springer, 2017, pp.131–144.
11. Härmark L and Van Grootheest AC. Pharmacovigilance: methods, recent developments and future perspectives. Eur J Clin Pharmacol 2008; 64: 743–752.
12. Bellare PS, Ashwin K, Prakash PU, et al. A retrospective evaluation of adverse drug reactions due to cancer chemotherapy in a tertiary care hospital in South India. J Young Pharm 2016; 8: 251–254.
13. Mr. Shivkumar, Kashinath Shete, Dr. K. Sattanathan, Analysis of patient admissions in hospital due to adverse drug reaction, Journal of Drug Delivery & Therapeutics. 2018; 8(5):5-9.
14. Pharmacovigilance Programme of India (NCC-PvPI) Indian Pharmacopoeia Commission (IPC) (a WHO-CC for

Pharmacovigilance), Ministry of Health & Family Welfare, Government of India VOL 8, ISSUE 25 l 2019 https://www.ipc.gov.in/PvPI/et.html
15. Upasala monitoring center, WHO Drug news letter December 2022 https://who-umc.org/pv-products/#
16. Upasala monitoring center, WHO Drug Newsletter, **September 2022** https://who-umc.org/pv-products/#
17. Pharmacovigilance Programme of India (NCC-PvPI) Indian Pharmacopoeia Commission (IPC) (a WHO-CC for Pharmacovigilance), Ministry of Health & Family Welfare, Government of India VOL 9 l ISSUE 27 l 2019 https://www.ipc.gov.in/PvPI/et.html
18. Bushra R, Baloch SA, Jabeen A, Bano N, Aslam N. Adverse drug reactions: factors and role of pharmacist in their prevention.J Ayub Med Coll Abbottabad.2015 Jul-Sep[cited 2017 Dec 21];27(3):70-26.
19. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA* 1998; 279(15):1200-1205.
20. Mehta U, Durrheim DN, Blockman M, et al. Adverse drug reactions in adult medical inpatients in a South African hospital serving a community with a high HIV/AIDS prevalence: prospective observational study. *Br J Clin Pharmacol* 2008;65(3):396-406.
21. Tripathi KD, essentials of medical pharmacology, 8th editions, Jaypee Publication, New Delhi, pg no. 92-101

Source of Support: Nil
Conflict of Interest: Nil