International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1236-1245 www.ijprajournal.com ISSN: 2249-7781

Assessment and Pharmacist Intervention in Adverse Drug Reaction Monitoring – A Retrospective Study

M. RangaPriya*, Devi shri. G.S, Dina Davis, Ivy Luke, Kanimozhi. R
Department Of Pharmacy Practice, Swamy Vivekanandha College Of Pharmacy, Tamil Nadu, India.

Date Of Submission: 01-03-2021 Date Of Acceptance: 12-03-2021

ABSTRACT:
OBJECTIVE:

- To assess and study the adverse drug reactions reported from both in-patients and out-patients of various departments.
- To analyze the ADRs using Naranjo algorithm scale and study the outcomes.

METHODOLOGY: A Retrospective study was conducted in both in-patients and out-patients of various departments in Vivekanandha Medical Care Hospital, Elayampalayam for a period of 6 months. The Adverse drug reactions were assessed for their causality using Naranjo scale. The outcomes were studied and data were analysed by descriptive statistics.

RESULTS: Total 67 ADRs were reported during the study period, out of which 39 ADRs were found in females and 28 in males. According to the age group, 40 ADRs were reported in 25-64 years followed by 23 ADRs in > 65 years. Antibiotics were the class of drugs implicated in causing more ADRs (23) especially Amoxicillin+ clavulanic acid (13). Most number of ADRs was from the general medicine department followed by cardiology department. The most common type of ADRs were rashes (17) followed by hypersensitivity reactions (6). According to Naranjo's algorithm scale, most of the ADRs were evaluated as probable (57), 8 ADRs seemed possible and 2 were definite.

CONCLUSION: Clinical pharmacists should interact with health care professionals to develop and implement an ADR reporting strategy to achieve optimal care for patients. The results provide an insight to the health care professionals on the importance of monitoring and reporting of adverse drug reactions.

KEYWORDS: Adverse drug reactions, Naranjo scale, Clinical Pharmacists.

I. INTRODUCTION

Adverse drug reactions are one of the major problems in the health care system. According to the World Health organization (WHO) an adverse drug reaction (ADR) is defined as the response to a drug which is unintended, noxious and occurs at doses normally used in a man for diagnosis, prophylaxis, or therapy of disease or for the modification of physiological function. These serious reactions may occur due to a single dose or prolonged administration of a drug resulting from a combination of two or more drugs[1].

According to Epidemiological studies, ADRs have been estimated to be the fourth to sixth leading cause of death. During their hospital admission, approximately 2.9–5% of all hospital admissions caused by ADR as well as 35% of hospitalized patients leads to an ADR during their hospital stay. Serious ADRs accounted for nearly 6.7% of all hospital admissions. Another study concluded that due to hospital admission, 1.8% of deaths caused an adverse drug reaction[2].

The spontaneous reporting system (SRS) is a passive surveillance system. It plays an important role in pharmacovigilance by ensuring the safety signals of the marketed drug[3]. This voluntary system mainly depends upon the knowledge and skills of the prescriber in reporting of ADR[4].

Adverse drug reactions are a global problem and worldwide surveillance is necessary. Every country with an ADR reporting program has a common goal: to educate and create awareness among health care practitioners and the public, thereby reduce or eliminate ADRs[5]. Sharing of information among all reporting facilities, both nationally and internationally, can promote ADR identification. The WHO, using the Uppsala Monitoring Centre in Sweden, aims to improve global ADR detection through a database called VigiBase.

The causality assessment is the assessment of relationship between drug treatment and occurrence of adverse drug event. It is also used to evaluate and check whether the particular treatment is caused for the observed adverse drug event or not. It is considered to be an important part in ADR reporting. Causality assessment can be done by

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1236-1245 www.ijprajournal.com ISSN: 2249-7781

treating health care professionals as a tool for decision making regarding a drug treatment & by regulators as a help in signal detection and aid in risk-benefit decisions regarding medicines[6].

Preventability usually refers to when the drug treatment plan is unsuitable with current evidence-based practice or is unrealistic when taking known circumstances into account[7]. Epidemiological studies result in to the findings that between a third and a half of ADRs are (at least potentially) preventable although preventability is much easier to diagnose in hindsight. However, interventions that reduces the probability of an ADR occurring can be a mandatory way to reduce the risk of patient harm.

Adverse drug reaction (ADR) as we all know is one of the leading grounds for death in many countries, as stated by the WHO, it accounts for approximately 5% of the hospital admissions which depicts for an important plague on the patient and on the governing Indian pharmacopoeia. Moving down the lane, it is highly recommended that the importance of ADR reporting is well versed for the following reasons. There are numerous benefits that can be obtained in the society if the ADR reporting is done in the most effective manner[8].

Economic and optimal usage of drug can be tracked down for minimized liability on the Indian pharmacopoeia commission. Strict regulatory execution can be carried out on the basis of reports obtained from ADR reports to safeguard patient's health and risks to exposure. On the other hand, various authorization of marketing withdrawal can be improvised based on the report of the drug performance which can also help in the modification of the categorization from over the counter drugs to prescription only medicines[9].

Clinical pharmacy practice was developed in the recent decades and resulted in increased number of pharmacists working worldwide[9]. Pharmacists are the drug experts having the central role in ensuring drug safety by detecting and reporting of ADRs[10]. Pharmacists have the potential of reporting ADRs on their own because of their clinical experience and also have a vital role in medication safety monitoring. Early detection and monitoring of ADR are essential to reduce the harm to the patients[11].

Polypharmacy refers to the concurrent use of multiple drugs prescribing to a person increases the occurrence of Adverse Drug Reactions[10,11].Thus, leads to unnecessary drug expenses and poor quality of life[12].In developed countries most of the ADR are occurred by polypharmacy[11].

Pharmacovigilance (PV) is the branch of pharmacy which deals with the activities of recognition, detection, understanding, assessment, reporting and prevention of the cause of any drugs and its adverse effects with the possible solution for the drug related problems[13].It is very important that the adverse drug reaction (ADR) rate is constantly checked upon as it is the only way to track down the incidence and know the characteristics of different ADR from different drug related perspective. As per a study conducted, it depicts an incidence of ADR to be 2.4-6.5% for the countries in the west, with just 6-10% being reported[14].

Mainly the need of PV in the health care sector is important due to the unavailability of various preclinical safety data , this happens mainly because the animal studies are mostly not a good predictor for human physiological effects. Similarly the evidence of safety from clinical trials is not sufficient due to the limited size, constricted narrow population (age & sex specific), narrow indications (only particular disease) and short duration. Similarly, the fast changing pharmaceutical marketing strategy which includes the direct to consumer advertising which is launched in many countries at the same time, with multiple changing physicians and patient preferences, there is an increased use of newer drugs, adding on to the drastic shift of self supervised drug administration therapy[15] . Thus, the study was aimed to analyze the ADRs using Naranjo algorithm scale and study the outcomes.

II. METHODOLOGY

A Retrospective study was conducted in Vivekanandha Medical Care Hospital for 6 months on 75 cases with the approval of the Institutional Ethical Committee. The study comprises of an inclusion criteria which includes all age groups, both in patients and outpatients and of the exclusion criteria the patients under Ayurveda, homeopathy, Unani treatment, mentally retarded patients , pregnant and lactating woman were excluded from the study.

A Specially designed data entry form was used to collect the details about the patients. It consists of following details such as name, age, sex, past medication history, diagnosis, therapeutic chart and suspected adverse drug reaction.

The study was analysed for its causality by the Naranjo causality assessment scale. Naranjo scale consists of nine questions. According to the

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1236-1245 www.ijprajournal.com ISSN: 2249-7781

score, the adverse drug reaction can be classified as definite, probable, possible and doubtful. The scoring consist of 9 = Definite ADR, 5-8 = Probable ADR, 1-4 = Possible ADR, 0 = Doubtful ADR. The data obtained was analyzed using descriptive statistics.

III. RESULTS

The study was conducted in both in-patients and out-patients in various departments of the tertiary care hospital and 75 adverse drug reactions were identified. After considering the exclusion criteria 67 adverse drug reactions were taken into the study.

AGE WISE DISTRIBUTION AND ADVERSE DRUG REACTIONS

Out of the total 67 adverse drug reactions, majority of the errors were observed in age group of ≥ 60 (59.7%), followed by the age group 25-29 (34.3%) and 15-24 (5.9%).

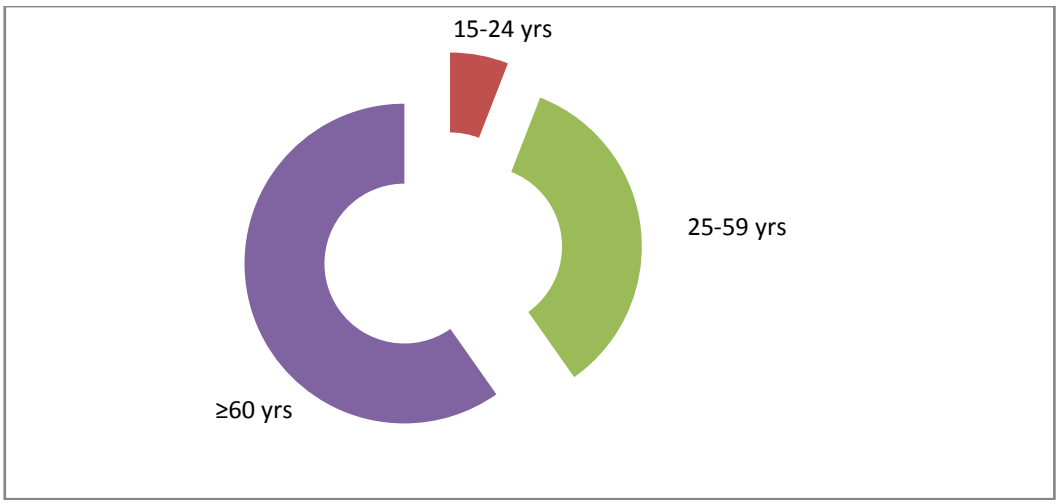

FIGURE- 1: Age Wise Distribution of Adverse Drug Reaction

GENDER WISE DISTRIBUTION OF ADVERSE DRUG REACTION

Out of 67 adverse drug reactions, 58.2 % of the reactions were found in females and 41.7% occurred in males.

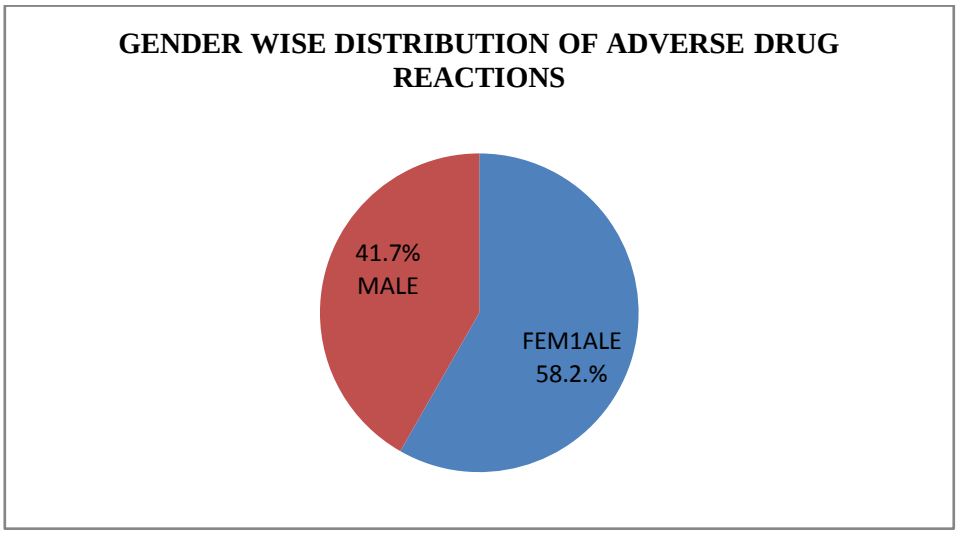

FIGURE - 2: Gender Wise Distribution of Adverse Drug Reactions

DEPARTMENT WISE DISTRIBUTION OF ADVERSE DRUG REACTIONS

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1236-1245 www.ijprajournal.com ISSN: 2249-7781

Out of 67 adverse drug reactions, highest numbers of ADRs were reported from General Medicine department (52.3%), followed by cardiology (11.9%), emergency (7.46) and orthopaedics (28.3%)

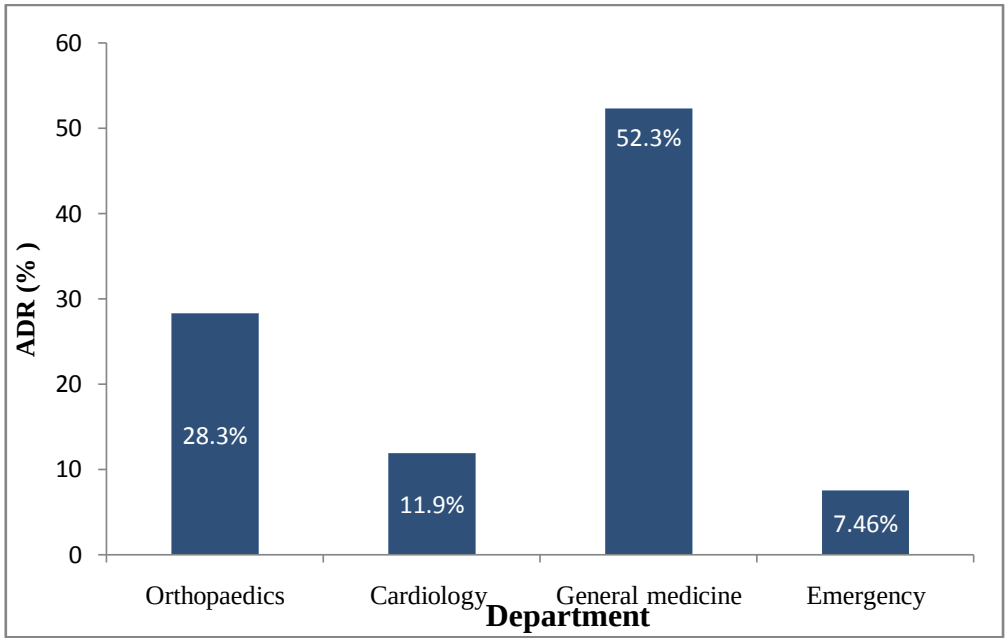

FIGURE - 3: Department Wise Distribution of Adverse Drug Reactions

DRUG CATEGORIES AND ADVERSE DRUG REACTIONS

The categories of drugs reported to cause adverse drug reactions were antibiotics (23), NSAIDS (10), anti-platelet (4), antihypertensive (13) and antiulcer (5).

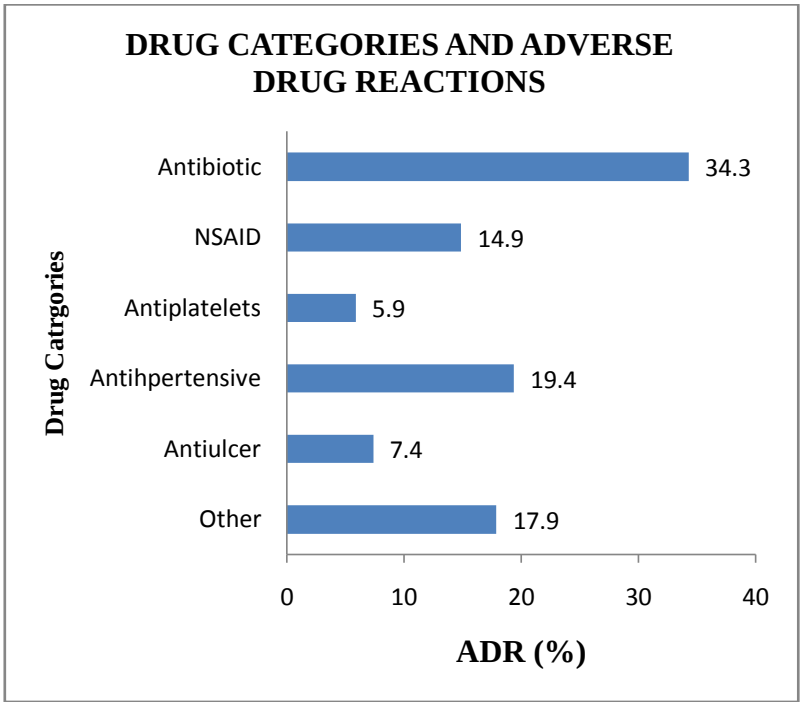

FIGURE - 4: Drug Categories and Adverse Drug Reactions

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1236-1245 www.ijprajournal.com ISSN: 2249-7781

MEDICATIONS RESULTED IN ADVERSE DRUG REACTIONS

Out of the 67 reported ADRs, most of the ADRs were developed by the effect of Amoxicillin + Clavulanic acid (13), followed by Diclofenac sodium(4), Piroxicam (3) ,Tramadol (3) and furosemide (3).

TABLE - 7: MEDICATIONS RESULTED IN ADVERSE DRUG REACTIONS

MEDICATIONS	NUMBER OF ADRs	TYPE OF ADR
Pantoprazole	2	Edema
Olmesartan	2	Hyperkalemia
Piroxicam	3	Edema
Aceclofenac	1	Allergy
Amlodipine	2	Edema
Aspirin	2	Skin allergy
Sulfasalazine	1	Gastric distress
Ceftriaxone	2	Stomach ulcer
Atenolol	1	Lethargy
Clonidine	1	Dry mouth
Amoxillin + Clavulanic acid	13	Diarrhea
Furosemide	3	Hyperkalemia
Tramadol	3	Constipation
Linezolid	1	Diarrhea
Omeprazole	1	Rashes
Moxifloxacin	1	Nausea
Ominipaque	1	Hypotension
Cefuroxime	1	Rashes
Naproxen	2	Constipation
Doxycycline	1	Rashes
Cefoperazone	1	Thrombocytopenia
Gabapentin	1	Dizziness

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1236-1245 www.ijprajournal.com ISSN: 2249-7781

+Methycobalamin		
Levofloxacin	1	Rashes
Etoricoxib	1	Gasterointestinal distress
Azithromycin	1	Hypersensitivity
Diclofenac sodium	4	Vomiting
Heparin	1	Bleeding
Telmisartan+Hydrochlorthiazide	1	Bitter taste in mouth
Flupirtin	1	Drowsiness
Metronidazole	1	Vomiting
Hydroxychloroquine	1	Ocular toxicity
Nitrofurantoin	1	Mouth sores
Fondaparinux sodium	1	Hypotension
Clinidipine	1	Dizziness
Metoprolol	1	Dizziness
Insulin	1	Hypoglycemia
Montelukast fexofenadine	1	Diarrhea
Amitriptyline	1	Hypotension
Ranitidine	1	Constipation
Lidocaine	1	Constipation

COMMONLY REPORTED ADVERSE DRUG REACTIONS

Out of 67 reported adverse drug reactions, the most commonly reported adverse drug reaction were rashes, followed by hypersensitivity reaction, diarrhoea, constipation , edema etc.

TABLE - 8 : COMMONLY REPORTED ADVERSE DRUG REACTIONS

TYPE OF REACTION	NUMBER OF CASES
Hypersensitivity	6
Rashes	17

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1236-1245 www.ijprajournal.com ISSN: 2249-7781

Edema	5
Hyperkalemia	2
Hypotension	4
Diarrhea	5
Constipation	4
Ulcer	2
Dizziness	4
Gastric distress	3
Nausea	3
Hypoglycemia	1
Anemia	1
Dry mouth	1
Vomiting	3
Electrolyte imbalance	1
Ocular toxicity	1
Headache	2
Bleeding	1
Epigastric pain	1

CAUSALITY ASSESSMENT OF ADVERSE DRUG REACTIONS

From the 67 total reported adverse drug reactions 57 cases were classified as probable, 8 were possible and 2 were definite.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1236-1245 www.ijprajournal.com ISSN: 2249-7781

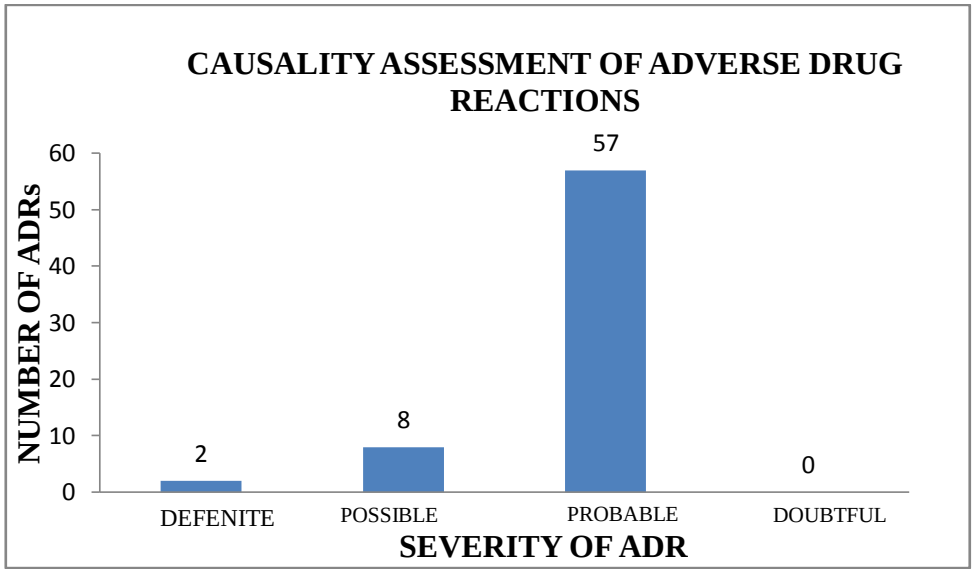

FIGURE - 5: Causality Assessment and Adverse Drug Reactions

IV. DISCUSSION

Adverse drug reactions are uncomfortable or has unwanted effect from medication prescribed for therapy resulting in physical, mental and functional injuries. ADRs are one of the foremost factors adding to illness and also cause overall preventive medicine cost. Reporting of such adverse drug reactions are critical parameter of medication therapy. The present study aims to recognize and illustrate the patterns of ADRs due to frequently used drugs with their possible contributing factors in drug monitoring and ADR management. This study was conducted in Vivekanandha medical care hospital, Elayampalayam for a study period of 6 months.

In this study, majority of the ADRs were observed in age group of above 60 yrs (59.7%), followed by the age group 25- 59 (34.3%) and 15-24 (5.9%). Studies conducted by E.A. Davies et al.(2015)[16] and Shanmugam Srirama et al.(2010)[17] shows that this age group has high prevalence to ADRs as they differ from younger adults in term of co-morbiditiy ,polypharmacy and pharmacokinetics which results in greater prevalence to adverse drug reactions.

A total of 67 cases were observed, among which 39 (58.2%) were female patients and 28 (41.7%) were male patients. Female patients outnumbered male patients by having a 58.2% of ADRs which was in correlation with the study conducted by Jisha M. Lucca et al. (2017)[18] and Sarah Watson et al. (2019) [19] which shows increased adverse drug reactions in women when compared to men . An explanation to this result is that the increase in ADR rates in females maybe due to weight in female, lower body size, change in absorption, protein binding and renal clearance, volume of distribution and metabolism of drugs as well as gender specific hormones that change the physiological function[20].

Department wise categorization of adverse drug reactions revealed that highest rates of ADR reactions were found in General medicine (52.3 %) followed by orthopaedics (28.3%) cardiology (11.9%) and Emergency (7.46%) which was in accordance with a study conducted by Donepudi Pavan Kumar et al.(2019)[24] and Ankitha .L et al.(2020) [21] . This could be due to the fact that there were more inflow of patients in that department and also most patients were having multiple diseases conditions and multiple medications.

In the study, majority of the adverse drug reactions were associated with antibiotics. Among the antibiotics amoxicillin + clavulanic acid was found to have resulted with most of the adverse drug reactions. From the previous studies of In Young Jung et al ,(2017)[22] and Mounika Nirumalla et al .(2019)[23] the mostly reported adverse drug reaction was due to antibiotics. Antibiotics are the class of drugs prescribed widely for any sort of infectious condition, it is also recommended as a prophylactic treatment in order to avoid the risk of infection. This explains the highest rate of antibiotic prescription resulting in increased adverse drug reactions.

Rashes were the most common clinical manifestation that was seen in 17 cases. The most

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1236-1245 www.ijprajournal.com ISSN: 2249-7781

common medication that leads to ADRs was antibiotics which may be the cause for rashes to be most commonly occurring ADR. Previous study reports by Donepudi Pavan Kumar et al. (2019)[24] and Ankitha .L et al.(2020)[21] showed similar results followed by hypersensitivity reactions(6) , edema (5) , diarrhea(5) and dizziness(5).

From the 67 total reported adverse drug reactions 57 were classified as probable, 8 were possible and 2 were definite which was supported by the studies of Shanmugam Sri Ram et al.[17] and Mounika Nirumalla et al .(2019)[23] where most of the ADRs were classified as probable.

A key aspect in the study of adverse drug reactions is the possibility of prevention. More than half of ADRs identified in our study were preventable and avoidable.

V. CONCLUSION

To conclude our study, occurrence of ADRs was found in all age groups and patients more than 60 yrs were found to be more susceptible. Most of the drug reactions are mild and preventable. This study suggests that there is a need of spontaneous ADR reporting and documenting from all the departments of the hospital for monitoring and assessment of ADRs. More awareness regarding drug reactions, poly pharmacy and drug interactions should be reaching early to health care professionals so as to prevent the condition before it becomes serious. Moreover, the patients also need to be counselled regarding the possible side effects and reactions that the drug can cause so that they can seek help before it worsens. Clinical pharmacists should interact with health care professionals to develop and implement an ADR reporting strategy to achieve optimal care for the patients. The results provided an insight to the health care professionals on the importance of monitoring and reporting of adverse drug reactions.

REFERENCE

[1]. Kurma VR, Manchu T, Amancharla MT, Manchu K ,Kandula PK. Pattern of adverse drug reactions in paediatric patients reported to adverse drug reaction monitoring centre in a tertiary care hospital. International Journal of Contemporary Pediatrics. 2019;6(4): 1557-1562 .

[2]. Perez M, Garcia,Figueras A. The lack of knowledge about the voluntary reporting system of adverse drug reactions as a major cause of underreporting: direct survey among health professionals. Pharma coepidemiology and Drug Safety. Official journal of the international society for pharmacoepidemiology. 2011;20(12):1295–1302.

[3]. Ghosh P and Dewanji A. Analysis of spontaneous adverse drug reaction (ADR) reportsusing supplementary information. Statistics in medicine. 2011;30(16): 2040-2055.

[4]. Jovic Z, Djordjevic V, Milena M, Vasic K. Spontaneous reporting of adverse drug reactions at a department of Internal Medicine. Central European Journal of Medicine. 2009;5(3):338-346

[5]. Kumar R, Singh S, Arora S, Bhati S. Adevrse drug reaction: A comprehensive review. Journal of drug delivery and therapeutics.2018;8(1):103-106.

[6]. Meyboom RH, Royer RJ. Causality classification in pharmacovigilance centres in the European community. Pharm acoepidemiology and Drug Safety. 1992;1(2):87–97.

[7]. Ferner RE. Aronson JK. Preventability of drug-related harms - part I: a systematic review. Drug Saftey.2010;33(11):985–994.

[8]. Sharma R & Kellarai A. Pharmacovigilance and adverse drug reaction reporting perspectives among interns and postgraduates of a teaching hospital. Journal of pharmacology and pharmacotherapy. 2014;5(4):248-250.

[9]. DaltonK, Byrne S. Role of the pharmacist in reducing healthcare costs: current insights. Integrated Pharmacy Research and Practice .2017;6:37-46.

[10]. Hadi MA, Neoh CF, Zin RM, Elrggal ME and Cheema E. Pharmacovigilance: pharmacists' perspective on spontaneous adverse drug reaction reporting. Integrated Pharmacy Research and Practice. 2017;6:91-98.

[11]. M. Shamna, C. Dilip, MAjmal, P. Linu Mohan, C. Shinu,C.P. Jafer, And Yahiya Mohammed .A prospective study on adverse drug reactions of antibiotics in a tertiary care hospital. Saudi pharmaceutical journal .2014;22(4):303-308.

[12]. Duerden M, Avery T, Payene R. Polypharmacy and medicines optimization :making it safe and sound .London:The King's Fund;2013:1-56.

[13]. World Health Organization (WHO). The Importance on Pharmacovigilance. Safety

Monitoring on Medicinal Products ,Switzerland:Office of Publications;2002.
[14]. Smith CC, Bennett PM, Pearce HM, Harrison PI, Reynolds DJ et.al.,Adverse drug reactions in a hospital general medical unit meriting notification to committee on safety of medicines. British Journal Of Clinical Pharmacology. 1996;42(4):423–429.
[15]. Talbot JCC, Nilsson BS. Pharmacovigilance in the pharmaceutical industry. British journal of clinical pharmacology. 1998; 45:427-431.
[16]. E.A. Davies, M.S O'Mahony. Adverse drug reactions in special populations – the elderly. British Journal of Clinical Pharmacology . 2015;80(4):796-807.
[17]. Srirama S, Ghasemia A, Ramasamya R, Devia M, Balasubramaniana R, et.al., Prevalence of adverse drug reactions at a private tertiary care hospital in south India. Journal of research in medical sciences. 2011; 16(1): 16-25.
[18]. Lucca JM, Ramesh M, Ram D. Gender differences in the occurrences and pattern of adverse drug reactions in psychiatric patients: A prospective observational study. Tropical Journal Of Medical Research. 2017;20(1):84-90
[19]. Watson S, Caster O, Rochon PA, Ruijter HD. Reported adverse drug reactions in women and men: Aggregated evidence from globally collected individual case reports during half a century. E Clinical Medicine.2019;17(100188):1-10.
[20]. J Kurian, J Mathew, K Sowjanya, K R K Chaitanya, M Ramesh, J Sebastian, D Narayanappa. Adverse Drug Reactions in Hospitalized Pediatric Patients: A Prospective Observational Study. Indian journal of paedeatrics. 2016;83(5): 414-419.
[21]. Ankitha L, Ramesh H . A retrospective study of adverse drug reactions in a tertiary care center. International journal of Basic and Clinical Pharmacology. 2020;9(4):611-615.
[22]. Jung IY, Kim J, Lee SJ, Kim J, Seong Het al., Antibiotic-Related Adverse Drug Reactions at a Tertiary Care Hospital in South Korea. Bio Med Research International. 2017;20(27):1-7.
[23]. Nirumalla M, Sanapala S, Bobbili S V, Unni VKand Prathyusha P. A prospective study of adverse drug reactions in a tertiary care hospital in patients. The Pharma Innovation Journal. 2019; 8(2):277-286.
[24]. Kumar DP. Patterns of Adverse Drug reactions:A study in a tertiary care. International Journal Of Basic and Clinical Pharmacology. 2019; 8(7):1497-1502.