A STUDY ON ADVERSE DRUG REACTION REPORTED IN A SOUTH INDIAN TERTIARY CARE HOSPITAL

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ABSTRACT

This study aims to assess the incidence of adverse drug reactions in a tertiary care hospital in South India. It is an observational study carried out in VMCH, Tamil Nadu for a period from March 2020 to September 2022. A suspected Adverse Drug Reaction Reporting form was used to collect the data to carry out the study. The method of reporting opted for was the Spontaneous reporting method by the pharmacy students during their ward round participation. All the ADRs detected were documented and analyzed by the Adverse monitoring center of our hospital. The causality assessment for each patient reported ADR was done using the Naranjo scale Algorithm as well as by the physicians from the respective department. A total of 67 ADRs were reported in our study. Of these, it indicated that most of the ADRs were encountered by males (61%) when compared to females (39%). Most of the ADRs occurred in the patients of the age group of Middle-Aged Adults and the least was in the age group of Young Adults. While assessing the outcome of the ADRs in patients, it was noticed that most of the patients, nearly 60% recovered from the ADR and the fatality of the patients due to ADR was none. Most of the ADRs occurred in the department of Cardiology (55%) and least in Covid (1%) and oncology (1%) departments in our hospital. The study provides a database of ADRs for clinicians and other healthcare professionals for the safe and optimum use of drugs. A good ADR team consisting of physicians, pharmacists, and pharmacologists must be present for managing and preventing of ADRs. A proper medication review and patient counseling could help in the elimination of adverse drug reactions.

KEYWORDS: *Adverse drug reaction, Pharmacovigilance, SADRRF, Naranjo Scale, Pharmacist.*

INTRODUCTION:

ADRs place a significant burden on healthcare facilities, lengthen hospital stays, and occasionally necessitate additional investigations and drug therapies for the treatment of symptoms and diseases brought on by the patient, according to growing evidence on the increased frequency and severity of ADRs. This increased frequency and severity are associated with a negative impact on the patient's health status. [1]The World Health Organization (WHO) defines an adverse drug reaction (ADR) 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" [2] The quality of life of patients is significantly impacted by ADRs. Understanding typical ADRs and how to reduce their intensity might greatly improve the current health situation. [3] With a frequency ranging from 1.19 to 7.26 per 100 resident months, ADRs are the most common medication-related adverse events in nursing home settings. Therapeutic failures and unfavorable drug withdrawal effects are further examples of adverse medication-related occurrences. [4] In India, the monitoring and reporting of ADRs are still in its development. The lack of well-organized and efficient ADR reporting and monitoring programs is a significant issue in India when it comes to assessing the safety of drugs in Indian populations. Based on data acquired from patients and their own clinical observations, doctors who prescribe and track treatment results are most qualified to identify adverse responses in their patients. However, many unfavorable adverse incidences get unreported because of a lack of interest, clinical acumen, talent, and time. [5] Patients' safety is currently thought of conceptually, and system design, organization, and operation flaws rather than specific practitioners or goods are held primarily accountable for adverse drug reactions. [6]

Pharmacovigilance (PV) is a unique research-based activity that keeps a constant eye on the medicine and any unusual or unusual side effects. According to the WHO, pharmacovigilance is the science and actions concerned with the identification, evaluation, comprehension, and avoidance of side effects or any other drug-related issue. [7] The pharmacovigilance program was established in India in 2010 as PVPI. The PvPI strives to protect the health of the Indian populace by making sure that the advantages of using certain medications outweigh the hazards involved in doing so. With 250 PvPI-established adverse drug monitoring centers across India and the provision of training to healthcare personnel, the culture of reporting ADRs has shown extraordinary progress. Along with the identification of inferior medications and prescriptions, dispensing, and administration problems, the program works hard to foster trust between the doctor and the patient, improving patient safety and public confidence in the nation's healthcare system. [8] Adverse drug reactions are classified into various types and are listed in the given table 1. [9] The most prevalent medicines that cause ADRs, their therapeutic class, demographic information about the patients who experience ADRs, and the concurrent medications used should all be understood since it is crucial to understand the risks of ADRs. Additionally, information unique to ADRs, such as the kind of reaction, the system impacted, and the likely reasons, would be very helpful in reducing ADRs. [10] The present study is done to study the pattern of ADRs occurring in tertiary care hospitals which will be useful in reducing the occurrence of ADRs and also promoting the rational use of safe medications, thus useful for the physicians and patients.

TABLE 1: Types of ADRs

TYPES	REACTIONS
Type A	Augmented
Type B	Bizarre
Type C	Chemical
Type D	Delayed
Type E	Exit/ End of the treatment
Type F	Familial
Type G	Genotoxicity
Type H	Hypersensitivity
Type U	Unclassified

METHOD OF STUDY:

An observational study was conducted in Vivekanandha Medical Care Hospital (VMCH), situated in Tamil Nadu. The population involved in our study was from the in-patient department and there were no specific inclusion/exclusion criteria. The count of the population included was 67 patients. The duration of our study was from March 2020 to September 2022. All the data of ADR reports were obtained during the in-patient department ward rounds by the pharmacy students. Detection of the suspected drug causing ADRs was done through physical appearances, biochemical investigation, subjective markers, and concomitant medications. The form used for reporting the ADRs was SADRRF Version 1.3. The method of reporting opted was the Spontaneous reporting method by the pharmacy students during their ward round participation. All the ADRs detected were documented and analyzed by the Adverse monitoring center of our hospital. The patient's Initial, Gender, Age, Weight, Dates of Adverse drug reaction occurred and recovered, Suspected medication, Its dose, Route of administration, Frequency, Dates of suspected medication started and stopped, Seriousness and non-seriousness of the reaction, the Reason for the use of the suspected drug, Causality assessment and the Department involved were noted. The causality assessment for each patient reported ADR was done by the use of the Naranjo scale Algorithm as well as by the physicians from the respective department.

RESULTS:

During our study, we reported 67 ADRs. Of these, it indicated most of the ADRs were encountered by males (61%) when compared to females (39%) (Fig 1). Most of the ADRs occurred in the patients of the age group of Middle-Aged Adults and the least was in the age group of Young Adults (Fig 2). In weight-wise distribution (Fig 3), the highest number of ADRs was seen in the weight range of 61-70 kg (34%), and the least was seen in >100kg (4%) and 80-90kg (6%). Among the reported ADRs, it was observed that the antibiotic drugs caused the highest percentage (15%) of ADRs in patients (Fig 4). The types of reaction experienced by the patient due to the intake of antibiotics were increased bilirubin level, diarrhea, pancytopenia, hypersensitivity, UTI and thrombocytopenia (Table 1). Among the antibiotics, Beta lactam antibiotics showed the highest ADR (Table 2). In blood (54%), the suspected drug-causing ADR produced reaction the most, and the least was found to be in the skin (2%), CVS

(2%), and CNS (2%) (Fig 5). The route of administration (Fig 6) through which most of the adverse drug reactions observed was in the oral route (70%) followed by the intravenous route (19%), nasal route (6%), and sub-cutaneous route (4%). The data indicates that 61% of the reported ADRs are of a serious reaction and 39% of the ADRs are of non-serious reaction (Fig 7). Among the serious reaction of ADRs (Fig 8), most of the patients underwent hospitalization (78%) and the least was disability (5%). 71% of the ADRs that occurred were of type A reaction (Fig 9), which indicates it is an augmented reaction and predictable type. When the causality assessment (Fig 10) was done for all the reported ADRs by using the Naranjo Scale Assessment, it was noticed that 96% of them were among Probable type scores five (31%), six (25%), seven (28%), eight (12%) and Possible type was of 4%. While assessing the outcome of the ADRs in patients, it was noticed that most of the patients, nearly 60% were recovered from the ADR and the fatality of the patients due to ADR was none (Fig 11). Most of the ADRs occurred in the department of Cardiology (55%) and least in Covid (1%) and oncology (1%) departments in our hospital (Fig 12).

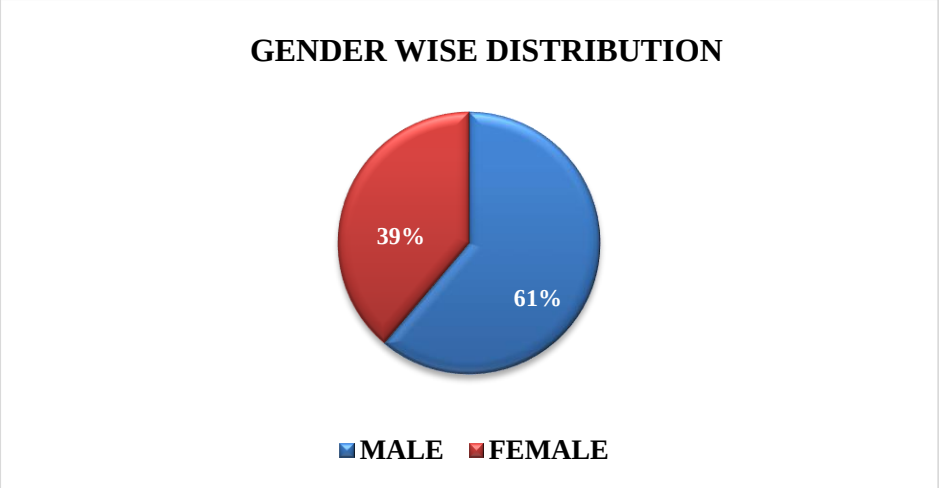

FIG 1: Gender wise distribution

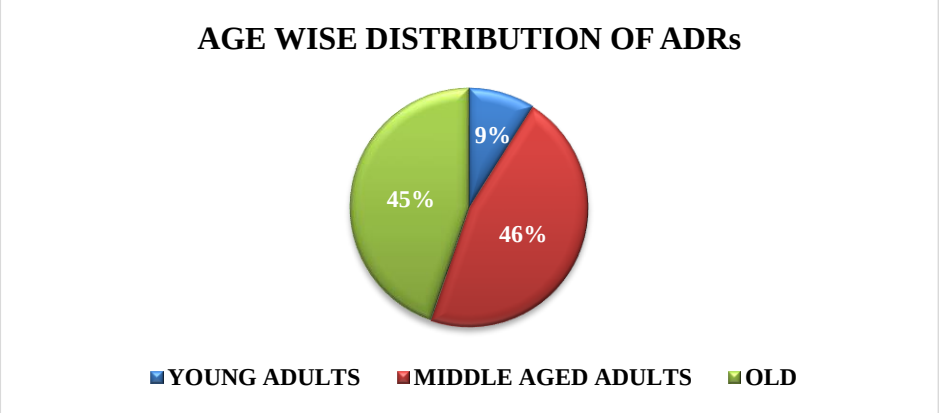

FIG 2: Age wise distribution of ADRs

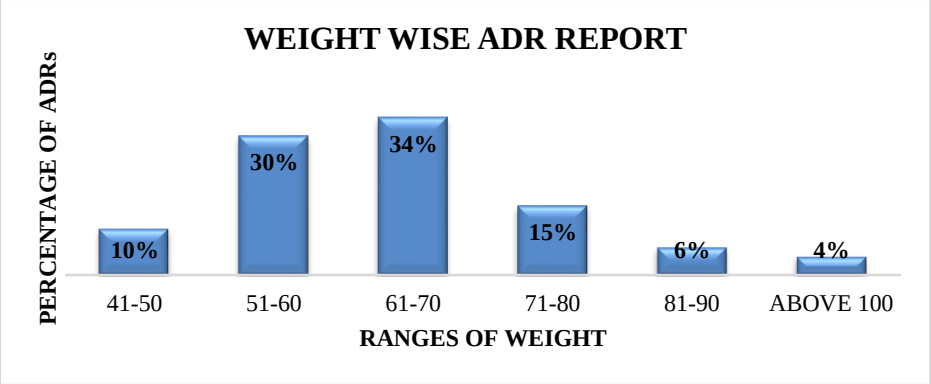

FIG 3: Weight wise distribution of ADRs

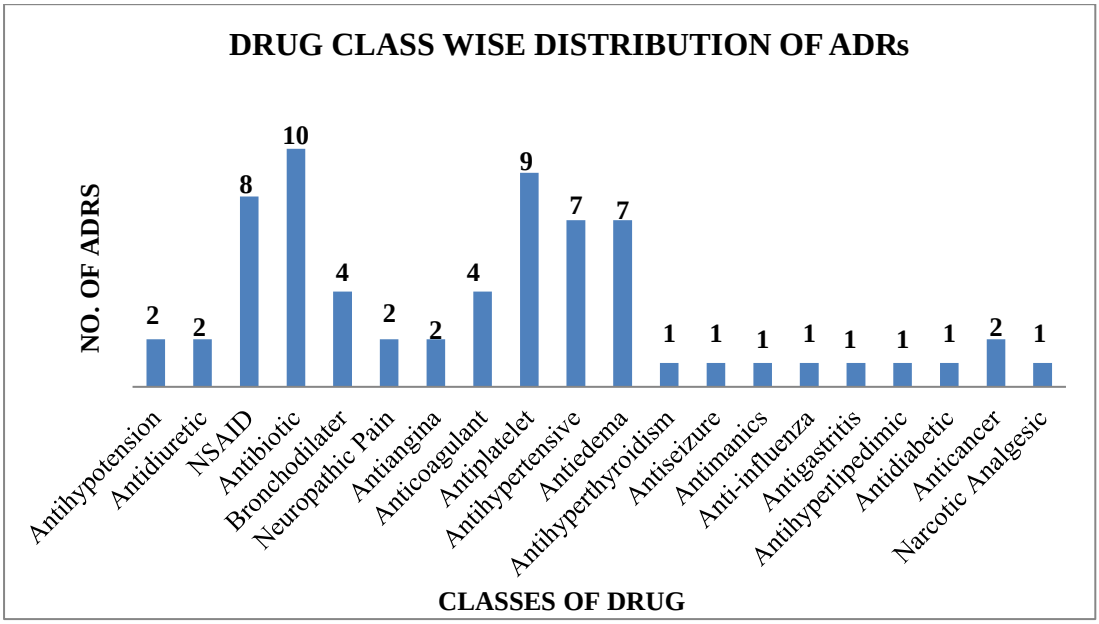

FIG 4: Drug class wise distribution of ADRs

TABLE 2: Types of reaction occurred due to the medications.

DRUG CLASS	DRUG	TYPE OF REACTION
Anti-hypotension	Noradrenaline	Pupil Dilation
Antidiuretic	Vasopressin	Bradycardia
NSAID	Voveron Plus (Paracetamol+Diclofenac) Aspirin Piroxicam	Hives Gastritis, GI bleeding, Hematuria, Malena, Palpitation, Abdominal distension Hypertension
Antibiotic	Cefuroxime Moxifloxacin Cefperazone+Sulbactam Linezolid	Increased Bilirubin Level Diarrhea Hypersensitivity Pancytopenia

	Azithromycin Amoxicillin Ceftriaxone Piptaz (Piperazillin+Tazobactam) Moxikind CV (Amoxycillin+Clavulanic Acid)	Hypersensitivity Diarrhea UTI Thrombocytopenia Diarrhea
Bronchodilator	Salmetrol+Fluticasone Salbutamol Budenoside	Hypokalemia Hyperglycemia Pedal edema
Neuropathic Pain	Nevirin NT (Methyl Cobalamine+ Pregablin+ Nortriptylline)	Constipation
Anti-angina	Nicorandil Nitroglycerin	Headache Headache
Anticoagulant	Fondaparinux Rivaroxaban	Anemia, Burning Micturition, Hematuria Malena
Antiplatelet	Ticagrelor	Dyspnea, Hemoptysis, Dry cough
Antihypertensive	Telmisartan Metosartan Amlodipine Nifedipine/Amlodipine	Hyperkalemia Hypersensitivity Pedal Edema Gingivitis
Antiedema	Lasilactone Lasix	Gynecomastia Hypokalemia, Constipation
Anti-hyperthyroidism	Carbimazole	Agranulocytosis
Antiseizure	Oxcarbezepine	Systemic Lupus Erythematous
Antimanic	Lithium	Altered mental status
Anti-influenza	Oseltamivir	Vomiting
Anti-gastritis	Domperidone+Esomoperazole	Gynecomastia
Antihyperlipidemic	Atorvastatin	Diarrhea
Antidiabetic	Metformin	Hypoglycemia
Anticancer	Methotrexate Cisplatin	Anemia Thrombocytopenia
Narcotic Analgesic	Tramadol	Hypertension

TABLE 3: Therapeutic class of Antibiotics caused ADRs

S.NO	CLASS OF ANTIBIOTIC	NAME OF ANTIBIOTIC	NO. OF ADR
1.	Beta-Lactams	Ceftriaxone Cefperazone+Sulbactam Amoxicillin Piperacillin+Tazobactam Amoxicillin+Clavunic acid Cefuroxime	2 1 1 1 1 1
2.	Macrolides	Azithromycin	1
3.	Quinolones	Moxifloxacin	1
4.	Miscellaneous	Linezolid	1

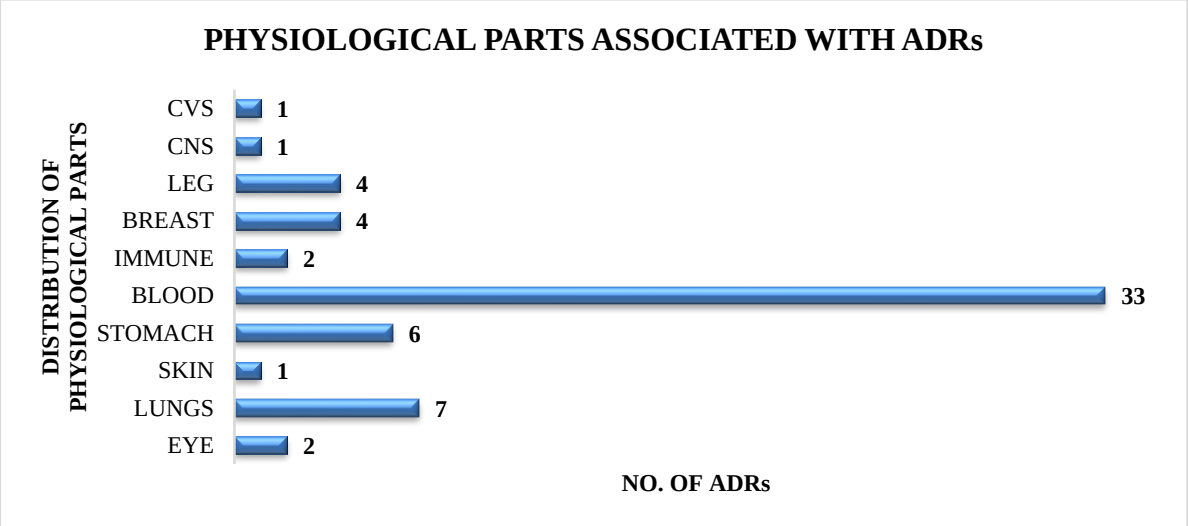

FIG 5: Physiological Parts associated with ADRs

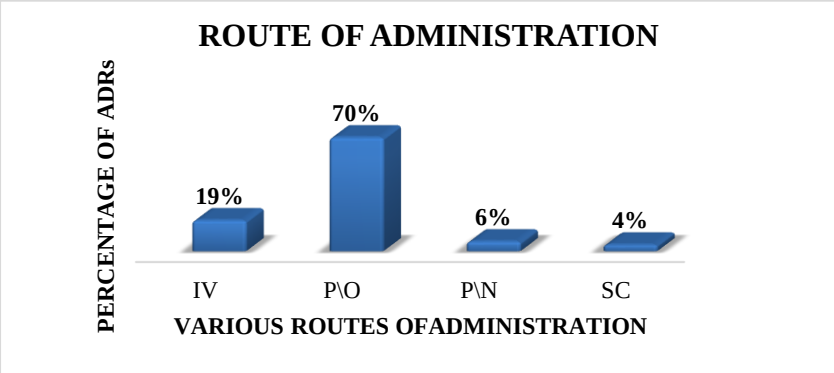

FIG 6: Route of Administration

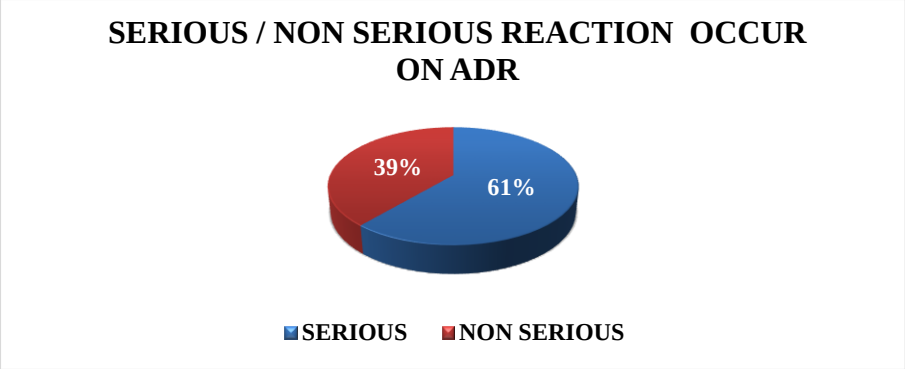

FIG 7: Distribution of ADRs based on Seriousness or Non-Seriousness of the reaction

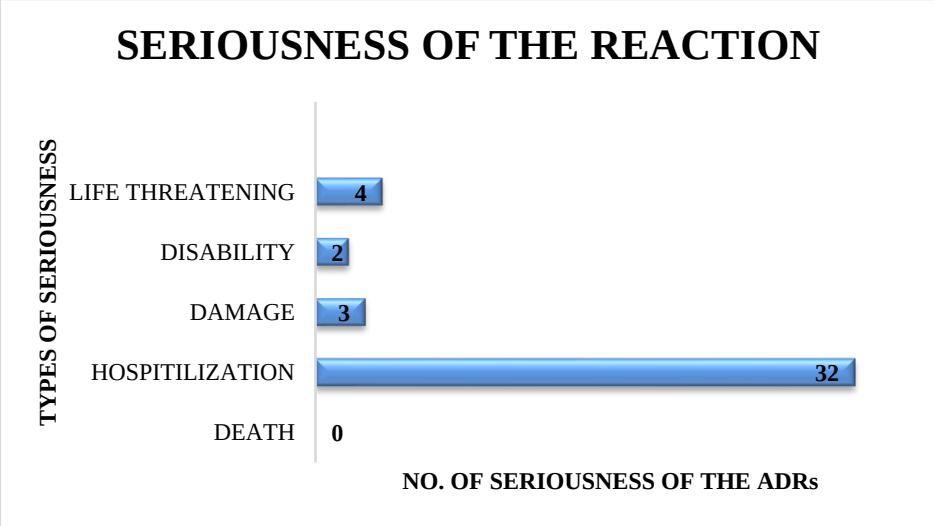

FIG 8: Distribution of ADRs based on Seriousness of the reaction

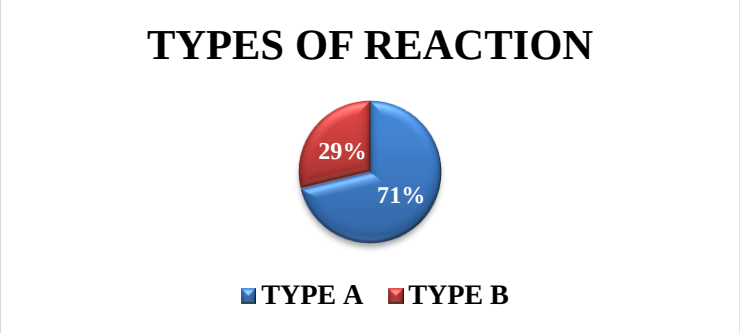

FIG 9: Distribution of ADRs based on Type of A and B reactions

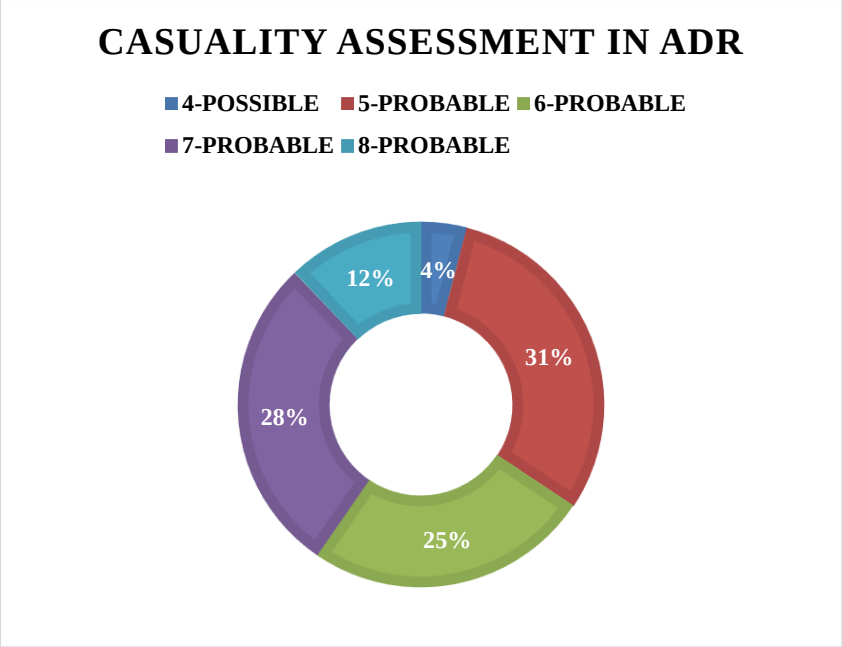

FIG10: Distribution of ADRs based on the Causality assessments

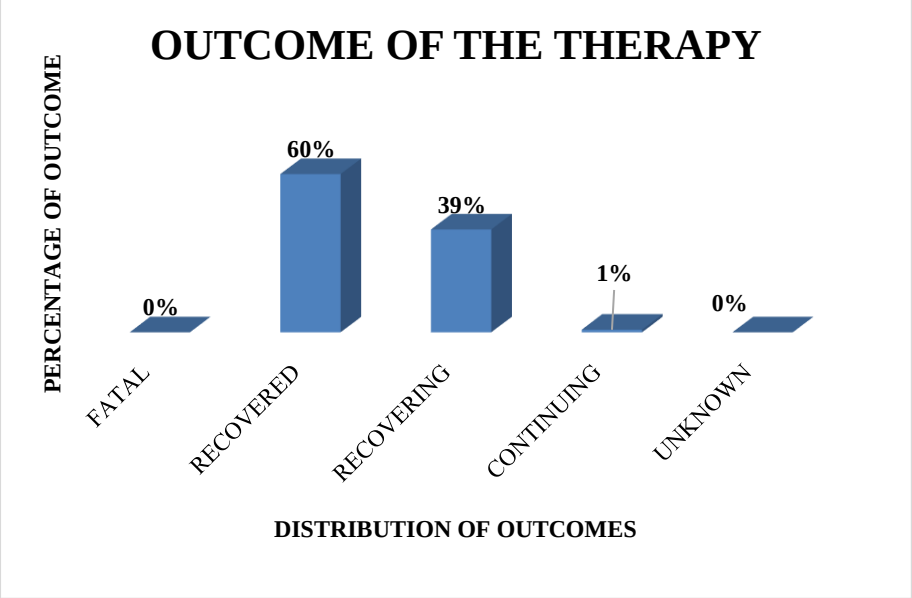

FIG 11: Outcome of ADRs reported In-patients

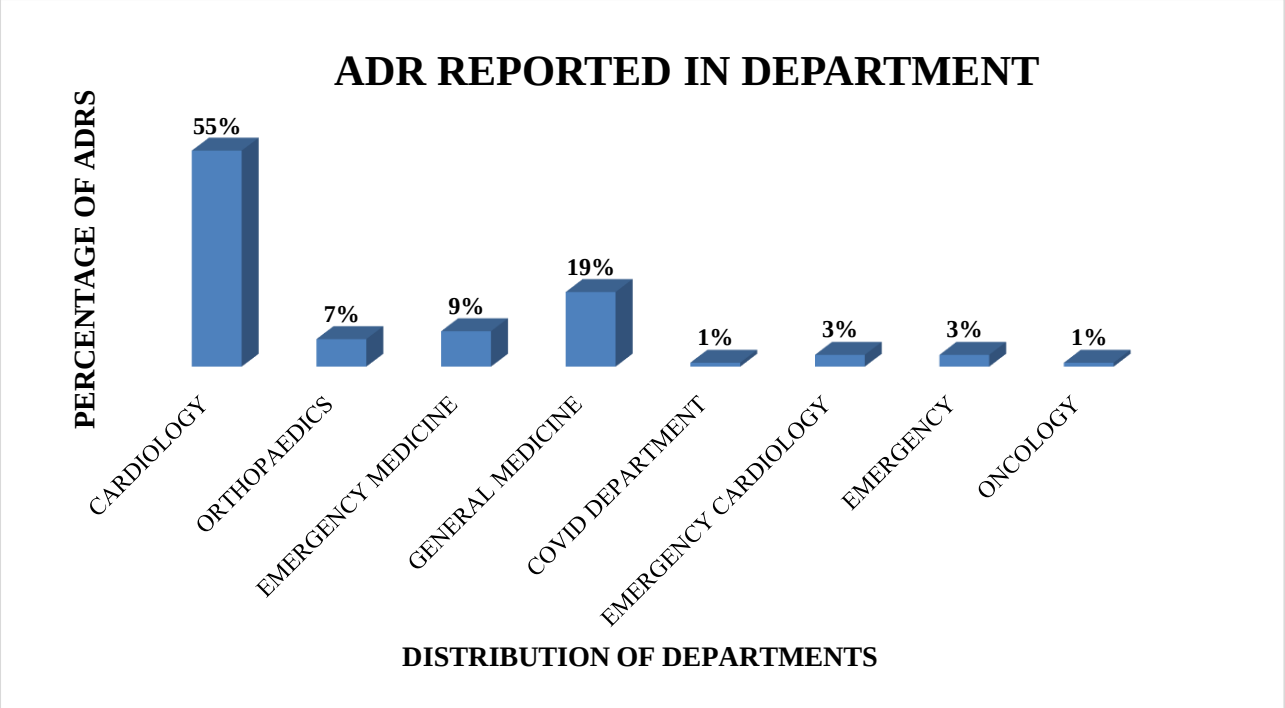

FIG 12: ADR on different departments

DISCUSSION:

Adverse drug reaction has been occurring for many years as medicines play an important role in the life of the patient as well as in the health care system. An Adverse drug monitoring centre in a hospital can be helpful in the prevention of ADRs by continuous surveillance of the drug's effect on patients and by giving awareness to the healthcare professionals regarding the drugs that have the susceptibility to cause ADRs. Our study reported that the percentage of ADR occurring in men was greater than in females, this coincides with the study of Nouf Alayed et al conducted in Saudi Arabia. [(11)] Most of the ADRs usually occur in patients who are above the age of 40 and the maximum of the ADRs occurred in the Cardiology department, this finding is similar to the study of Sara Pourseyed MD et al. [(12)] In our hospital, the majority of the ADRs were caused due to the administration of Antibiotic medications which is also observed in the study of Atul J Rajparaetal. [(13)] Beta lactam antibiotic was responsible for highest number of ADRs among the antibiotics, as shown by another study of Kavita Dhar et al. [(14)] When the seriousness of all the ADRs was assessed, it indicated the hospitalization status of the patients, and this data coincides with the study of Claudia Giardiana et al. [(1)] A study of Meena Shrivastava et al conducted in Nagpur, reports that the oral route was the commonest for ADRs, our study also reports the same. [(10)] Analysis of the type of reaction of ADRs revealed that the maximum of the reaction was of type A and the causality assessment conducted by using the Naranjo scale showed that most of the reaction were of a probable score, and it correlates with the data of M. Shamna et al. [(15)] The system of the body that mostly got affected was blood with 54% and was like the study of Jayesh M Kathiria et al where the second highest system affected due to ADR was the blood system. [(16)] Evaluation of the outcome of ADRs was done to understand the conditions of the patient after the management

of ADRs and it was founded that maximum of the patients got recovered which is concurrent with the study of T. M. Vijayakumar et al. [17]

The strength of this research is to mainly emphasis the occurrence of adverse drug reactions in a tertiary care hospital, especially in a rural area of south India. The main limitation of our study was spontaneous reporting i.e. Under-reporting practice by the healthcare professionals because all the ADRs of our study were reported by the pharma students during their ward rounds. This study highlights the ADRs of cardiac patients which will be helpful for physicians in the careful selection of drugs.

CONCLUSION:

Our study concludes that it is an observational study of a period of 2 years and six months. Maximum of the patients recovered from the adverse drug reaction and did not cause any harm to the patient's life. This study was done to monitor the occurrence of adverse drug reactions in patients which will help in improving the quality care of the patients by enhancing the knowledge of the physicians by promoting the safer use of drugs. It will also promote awareness to the health care professionals on how to report the ADRs in most of the hospitals in India particularly in rural India as well as in other developing countries. A systematic monitoring and documentation of the ADRs must be done to promote a decrease in the occurrence of ADRs. A proper medication review and patient counseling could help in the elimination of adverse drug reactions. Monthly reporting of ADRs to the regional adverse drug monitoring center must be implemented.

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