wjpmr, 2025, 11(7), 362-370

SJIF Impact Factor: 6.842

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN (O): 2455-3301

ISSN (P): 3051-2557

STUDY OF DRUG SAFETY ALERTS DESCRIBED BY PHARMACOVIGILANCE PROGRAMME OF INDIA IN A TERTIARY CARE HOSPITAL

Janhavi Kadam*, Vaishnavi Khatate, Adnan Patwekar and Dr. Nupuri Joshi

Abhinav Education Society's College of Pharmacy, Pune.

***Corresponding Author: Janhavi Kadam**

Abhinav Education Society's College of Pharmacy, Pune.

Article Received on 05/05/2025 **Article Revised on 27/05/2025** **Article Accepted on 16/06/2025**

ABSTRACT

A prospective observational study was carried out in the tertiary care hospital setting. A total of 301 patients were studied over a period of 8 months for occurrence of ADRs as per the drug safety alerts issued by PvPI. The objectives are to assess the occurrence of ADRs mentioned in drug safety alerts issued by PvPI and to classify them and assess their causality and severity. Data were collected from the medical records of tertiary care hospitals from September 2023 to April 2024.The ADRs were assessed using WHO causality scale and Hartwig and Siegel scale for causality and severity respectively. A total of 301 patients were included in the study, with 189 (62.8%) males and 112 (37.2%) females.

KEYWORDS- Adverse Drug Reaction (ADR), – Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Pharmacovigilance Programme of India (PvPI), International Classification of Diseases (ICD), Drug safety, World health organization (WHO), FDA Adverse Event Reporting System (FAERS), Hartwig and Siegel Scale, WHO Causality Assessment Scale.

INTRODUCTION

An adverse drug reaction is defined as "an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product.".[1]

Adverse drug reactions (ADRs) present a challenge in modern healthcare, especially with complicated therapies, an aging population, and increased multimorbidity.[2] Important studies conducted in the United States and the United Kingdom in the late 20th and early 21st centuries revealed that adverse drug reactions (ADRs) are often observed in clinical settings, where they might occur during hospital admission, after release, or as a reason for unplanned hospitalizations. Research indicates that between 5% and 10% of patients may experience an ADR at admission, during hospitalization, or after discharge, despite numerous preventive measures. Nevertheless, because of the related morbidity and mortality, potential financial burden, and possible injury to the prescriber-patient relationship, this frequency of potential harm must be carefully examined.[2] Patients experiencing ADRs typically see an increase in total medical costs[3] The following advantages can be obtained with an ADR monitoring and reporting program.

1. It provides data regarding the safety and quality of pharmaceutical products.
2. It commences the preparations for risk management.
3. It assists in calculating the incidence of ADRs and avoids the predictable adverse effects.
4. It raises awareness of adverse drug reactions (ADRs) and provides knowledge concerning them to patients, pharmacists, nurses, and the health care team.[9]

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine/vaccine related problem.[3] Modern pharmacovigilance began following the incident of thalidomide tragedy. Thalidomide, a sedative medicine, was initially sold as an over the counter (OTC) medication following extensive animal testing. During the late 1950s and early 1960s, pregnant women worldwide took it to alleviate morning sickness, but it was observed that the foetuses born suffered from Phocomelia, a condition characterized by limb deformities such as shortening or missing arms, missing thumbs and lower arm bones, and other lower extremity issues. Over 10,000 children were born with phocomelia by the time the drug was banned. Following the Thalidomide tragedy of the 1960s, pharmacovigilance programs were established in several industrialized nations.[4] In the 1980s, India launched its initiative.

Although the idea of drug safety monitoring has taken several incarnations, the current Pharmacovigilance Program of India (PvPI) was founded in 2010 by the Central Drugs Standard Control Organization (CDSCO). The initiative is now fully integrated with government laws, a research facility under the Indian Pharmacopoeia Commission, and a regulator acting as a leader.[5] The PvPI makes sure that the benefits of medications outweigh the risks involved in using them in order to protect the health of the Indian population. With the establishment of 250 PvPI-established adverse drug monitoring centres throughout India and the training of medical practitioners, the culture of reporting adverse drug reactions has seen remarkable developments.[5]

The examination of "signals" forms the foundation of PV research. Signals are unreported claims about a direct correlation between a drug's adverse event-inducing effects on the human body and the World Health Organization (WHO). In order to produce extensive signal databases, researchers and physicians utilize spontaneous reporting systems, or SRS.[6] PvPI releases drug safety alerts which are prompted by signals from pharmacovigilance system databases and signals alerting to adverse drug reactions (ADRs) found in post-marketing studies and/or clinical trials.[5] The generated alerts inform patients or medical professionals about the required regulatory actions based on signals like new limitations on the use of medicine in specific populations, the requirement to monitoring for certain signs and symptoms, or the removal of the drug from the market. As the signal is generated it is also important to monitor the signal in the hospital setting to ensure the patient safety by further assessing the causal relationship of the suspect with the occurred event.

There are two basic measures that can be taken in order to prevent occurrence of ADR.

1. Determine which patient subgroup is most likely to have the negative impact and modify the course of therapy accordingly.
2. Make sure the treatment strategy minimizes any potential adverse effects.[2]

Understanding the susceptibilities of patients can help physicians prescribing decision and lower the probability of an adverse drug reaction. Any prior ADRs can be identified by a patient's medication history, preventing re-exposure to the drug. In other situations, risk variables for adverse drug reactions (ADRs) such age, gender, pregnancy status, and ethnicity might be used to estimate the likelihood of an event. Plans for treatment should take into accountancy possible ADRs and minimize any potential negative effects.[2]

The majority of case reports in pharmacovigilance involve possible adverse medication responses, which presents a challenge. In reality, most unfavourable reactions fall somewhere between these two extremes, that is, they are either possible or probable. Very few are certain or unlikely. Numerous systems have been created in an effort to address this issue. In pharmacovigilance, the assessment of causality has become a standard operating process.

WHO Causality Assessment Scale was created as a useful tool for evaluating case reports after collaboration with the National Centres taking part in the Programme for International Drug Monitoring. In essence, it is a combination evaluation that considers the case history's clinical-pharmacological elements as well as the standard of the observation documentation. This approach provides direction for the broad justifications that ought to be applied when choosing one category over another. The Naranjo algorithm is preferred by many primary care physicians due to its simplicity, however the PvPI suggests using the WHO-UMC scale because of its comprehensive approach and it is suitable for various types of data.[7]

Causality Assessment can reduce discord among the evaluators, assess the likelihood of the relationship, specify each case report individually, establish the link between the drug and the event and can lead to development of scientific and educational assessment. The term "severity" is regularly utilized to depict the intensity of a medical event. Severity evaluation classifies ADRs as mild, moderate, or severe based on the measures taken for their management. Hartwig et al. in his Hartwig and Siegel Severity Assessment Scale successfully categorized ADR severity into seven levels concurring to clinical result, counting resultant harm along with intensity of medical intervention required.[8]

PvPI has been releasing signals for ADR since March 2016 out of which a few were selected and observed for the specified ADR.

DRUG NAME	INDICATION	ADR
Meropenem	Nosocomial infections like septicaemia, febrile neutropenia, intraabdominal and pelvic infection etc., caused by cephalosporin's resistant bacteria, meningitis cystic fibrosis	Hypokalaemia
Metoprolol	For the treatment of essential hypertension in adults, functional heart disorders, migraine prophylaxis, cardiac arrhythmias, prevention of cardiac death and reinfarction after the acute phase of myocardial infarction, stable symptomatic CHF.	Hyponatremia
Losartan	For the treatment of hypertension	Muscle Spasm
Amikacin	Indicated in the treatment of serious infections due to amikacin sensitive	Blurred Vision

	organisms	
Cefuroxime	Antibiotic- Indicated for lower & upper respiratory tract infection, UTI, gynaecological infection, skin or soft tissue infection etc. • Antibiotic- Indicated in the treatment of respiratory tract infections, UTI, ENT soft tissue infections etc.	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
Ceftriaxone	For the treatment of urinary tract infections, lower respiratory tract infections, bacteraemia, septicaemia, meningitis, abdominal infections and infections caused by pseudomonas species.	ECG QT prolonged
Torsemide	For the treatment of oedema associated with congestive heart failure & hypertension.	DRESS Syndrome
Diclofenac	For the treatment of RA, OA, ankylosing spondylitis, gout, painful post-operative pain following dental surgery, migraine attack and postoperative inflammation in patients who have undergone cataract operation.	Skin hyper - pigmentation

METHODS AND MATERIALS

1) **Study Site:-** Sahyadri Specialty Hospital, Deccan, Pune- 411004 India.
2) **Study Design:-** Prospective Observational study
3) **Duration of study:-** 8 months
4) **No. of Subject:-** 301 Patients

STUDY CRITERIA

➢ ***Inclusion***

1. Inpatients of either gender of age >18 years.
2. Patients who have been prescribed with any of the following drugs which have PvPI drug safety alerts.

Ceftriaxone	Amikacin
Meropenem	Cefuroxime
Losartan	Metoprolol
Diclofenac	Torsemide

➢ ***Exclusion***

1. Patients who have not been prescribed with the drugs included in the inclusion criteria.
2. Pediatric patients(Age<18)
3. Patient from the out patient department.

➢ ***Materials***

1. Patients Information Sheet (English and Marathi)
2. Patient Consent Form (English and Marathi)
3. Data Collection Form
4. Standard Scales Used

• **For ADR Assessment**

a. WHO Causality Assessment Scale
b. Hartwig and Siegel Scale

RESULTS

This study was a prospective observational study. On admission of the patient, the variables recorded were age, gender, lab reports, medications prescribed during the hospital stay, medication history, ADRs observed and their causality and severity. A total of 301 patients were included out of which 189 (62.8%) were Males and 112(37.2%) were Females.

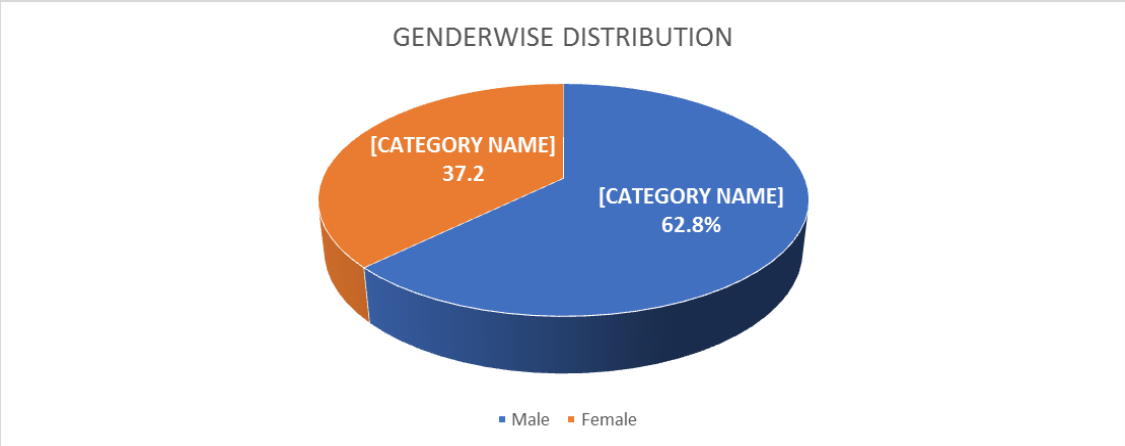

Fig. 1: Genderwise Distribution.

Age distribution of patients revealed that the maximum patient belongs to the age group between 40 to 60 years (41.2%) with 124 patients, followed by elderly age group above 60 years (36.8%) with 111 patients, lastly age distribution of patients revealed that the age group of 18 to 40 years had only 66 patients (21.9%). The average age of the patient was 53.44 ± 17 Years.

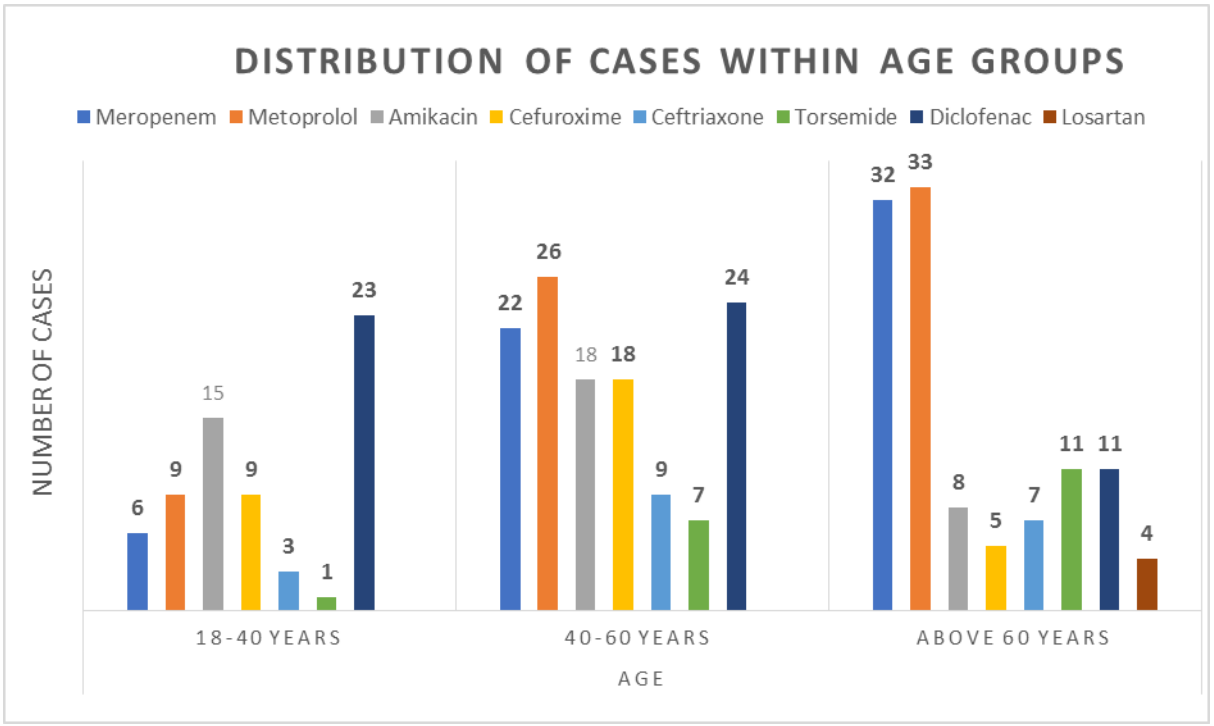

Fig. 2 – Distribution Of Cases Within Age Groups.

Out of 301 patients included in the study, 66 patients were prescribed Metoprolol, 60 with Meropenem, followed by 58 with Diclofenac, 41 prescribed with Amikacin, 34 patients with Cefuroxime, 19 patients were given Torsemide, 19 were given Ceftriaxone, whereas 4 patients were prescribed Losartan.

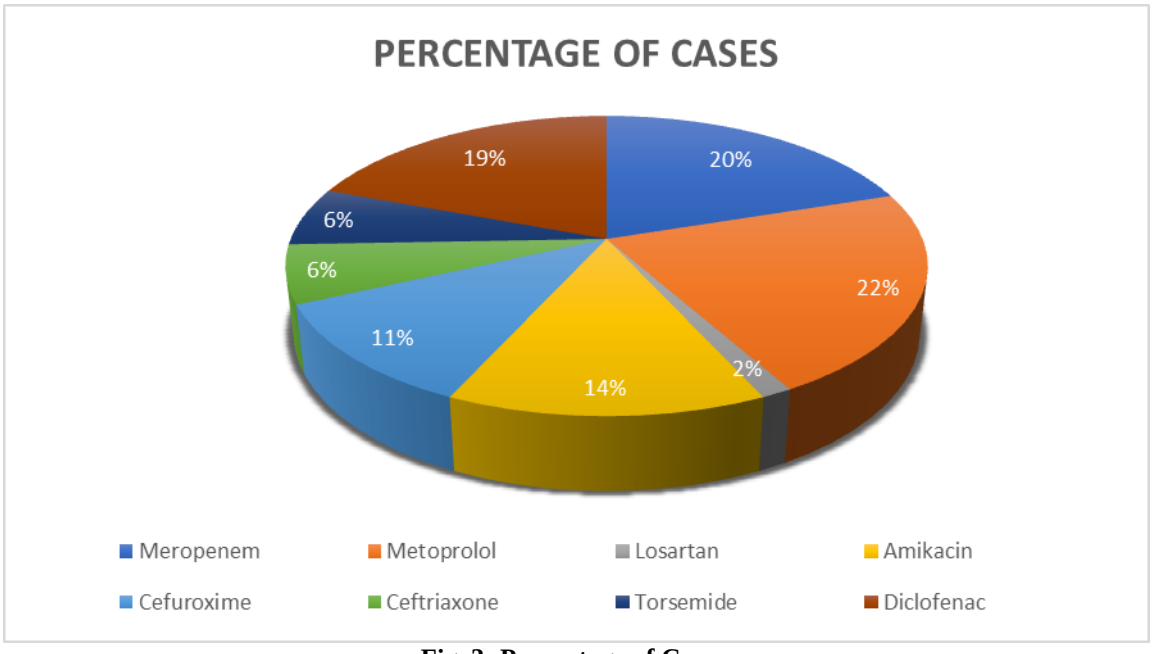

Fig. 3: Percentage of Cases.

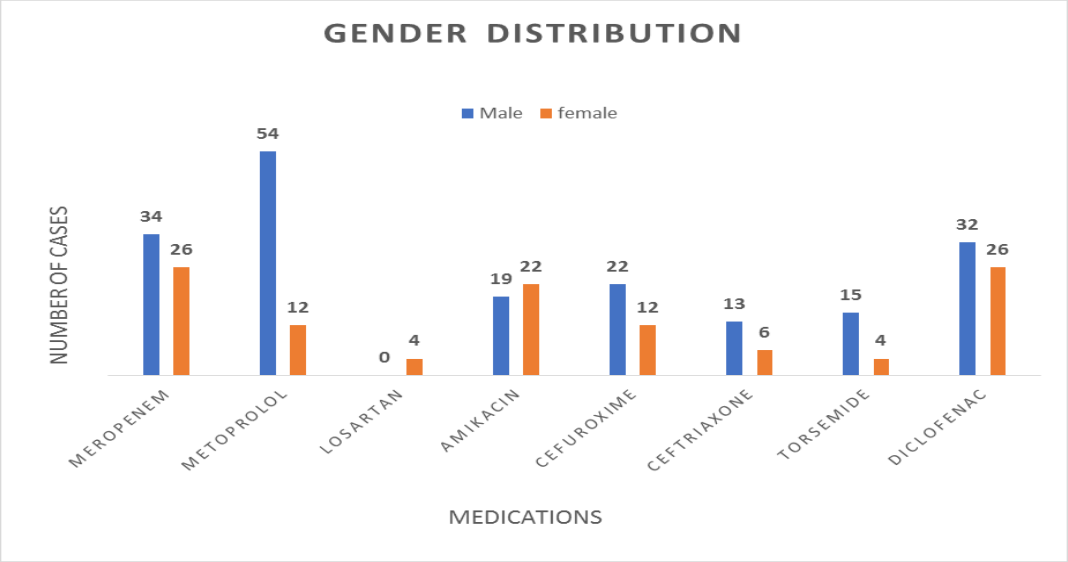

Fig. 4: Gender Ratio.

The PvPI released a drug safety alert concerning Meropenem on December, 2016 which suggested that it may cause hypokalaemia in patients. Evaluation of 60 cases of Meropenem was performed out of which 35 cases were positive for the presence of suspected ADR i.e. 58.33% cases showed hypokalaemia as shown in Fig. 5. Out of 35 positive cases, 31.42% cases had moderate severity while 68.59% mild severity. The serum potassium level observed within the study population was 2.975 ± 0.35 mmol/L, which is indicative of hypokalaemia. Causal assessment showed a possible causal relationship between Meropenem use and the observed hypokalaemia cases.

Another drug safety alert by PvPI concerning Metoprolol in March 2023, indicated a potential risk of hyponatremia in patients. From the 66 cases of Metoprolol studied, 66.66% cases showed hyponatremia. Out of 44 positive cases 56.81% cases had moderate severity while 43.18% mild severity. Average value of Serum sodium level that observed was 132 ± 3.45 mmol/L. The causality assessment of observed hyponatremia cases was possible.

Torsemide and its potential association with DRESS Syndrome was a signal in July 2021. Among the 19 cases observed and evaluated, 15.78% showed eosinophilia which indicates that approximately 3 out of the 19 cases exhibited elevated eosinophil count. The possibility of DRESS syndrome in patients presenting with eosinophilia following torsemide initiation increases and monitoring must be done. The severity of eosinophilia in these cases was mild. The average increased eosinophile count is 9.36 ± 1.6%.

In May 2023 a safety signal by PvPI suggested that administration of Ceftriaxone may cause QT prolongation. 19 cases of Ceftriaxone were evaluated, 15.78% cases out of them showed QT prolongation, the ADR observed were of mild severity and showed a possible causal relationship with the drug.

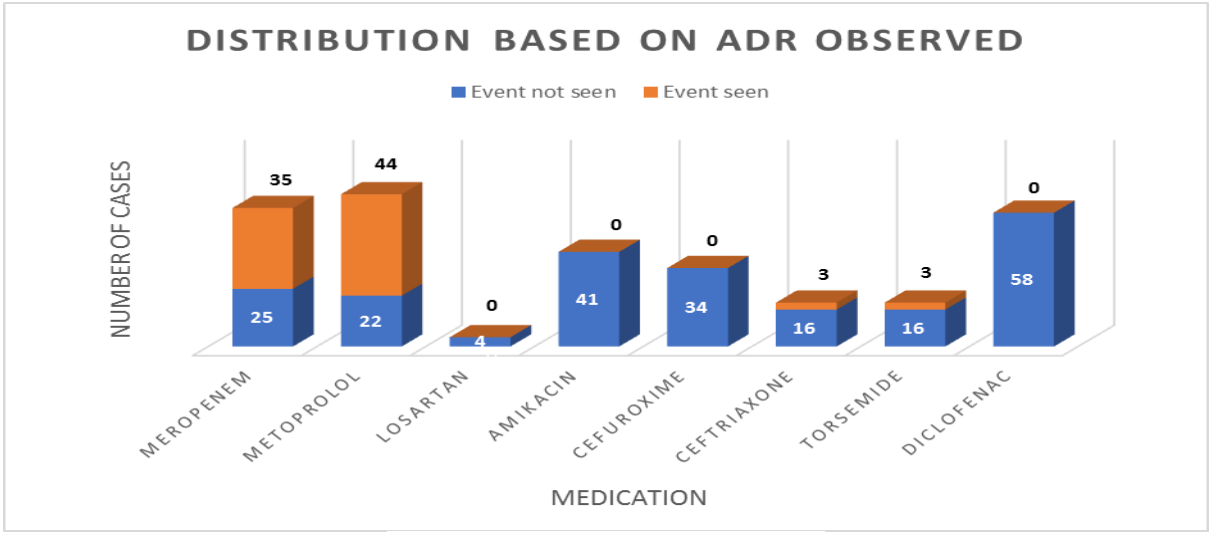

Fig. 5 – Distribution Based On Events.

ICD CLASSIFICATION OF DIAGNOSIS

The International Classification of Diseases (ICD) is an all-inclusive recognized framework for classifying diseases, health conditions, and related variables. By categorizing diseases and health conditions into standardized codes, ICD empowers the collection of precise and comparable health data. This information is pivotal for observing patterns in disease prevalence, mortality rates, and healthcare utilization, which advises healthcare planning, asset allotment, and public health policies. The data shows the distribution of cases over distinctive categories of health conditions. This data can help recognize which types of health conditions are more predominant or have a higher burden within the population. The study observed that most of the cases belonged to the class 16 which is diseases of genitourinary system which indicates that diseases affecting the genitourinary system were prevalent within the population under study. The commonly affected diseases in the study population were acute kidney injury and chronic kidney disease. This was followed by class 11- diseases of the circulatory system. The least number of cases observed was 1 which belonged to class 20 which includes developmental anomalies.

SERIAL NUMBER	ICD CLASS	NUMBER OF CASES
1	Certain infectious or parasitic diseases	13
2	Neoplasms	42
3	Diseases of the blood or blood-forming organs	5
5	Endocrine, nutritional or metabolic diseases	17
8	Diseases of the nervous system	50
11	Diseases of the circulatory system	53
12	Diseases of the respiratory system	16
13	Diseases of the digestive system	25
15	Diseases of the musculoskeletal system or connective tissue	35
16	Diseases of the genitourinary system	60
20	Developmental anomalies	1
21	Symptoms, signs or clinical findings, not elsewhere classified	21
22	Injury, poisoning or certain other consequences of external causes	32
23	External causes of morbidity or mortality	30
24	Factors influencing health status or contact with health services	10

DISCUSSION

This study was prospective observational conducted in a tertiary care facility with 301 inpatients, which includes 189 male patients and 112 female patients. In the study by Grégoire Wuerzner, the study population only included male patients. The possible reason for this could be attributed to men's higher absolute risk compared with women for heart diseases, also men are more responsive to LBNP compared to women, which was parameter focused in the study.[17]

Maximum number of patients included in our study belonged to the age group 40 to 60 years, followed by age group above 60 years, the least patients were from the age group 18 to 40 years. In the study conducted by Manodeep Sen, the most common age group of the patients was 41 to 50 years. The reasons for most patients belonging to age group 40 to 60 as the prevalence of comorbidities increases as per age and the people in this age group tend to neglect their health because of hectic lifestyle, burden of responsibilities and work pressure. All these factors play a crucial role on the patients mental as well as physical health putting them at a potential risk of developing diseases.The age of the patients depended upon the type of patients our tertiary care facility was catering to which did not include pediatric services. The average age of the patient in our study was 53.44 ± 17 years. The study by Anthony D. Bai reported the average age of their study population 73.6 ± 16 years.[21]

Out of 301 patients included in the study, 66 patients were prescribed Metoprolol, 60 with Meropenem, followed by 58 with Diclofenac, 41 prescribed with Amikacin, 34 patients with Cefuroxime, 19 patients were given Torsemide, 19 were given Ceftriaxone, whereas 4 patients were prescribed Losartan. Out of study population we evaluated 68 patients who were prescribed Metoprolol. 33 patients belonged to geriatric population followed by 26 patients in the age group 40 – 60 years. This may be due to the fact that blood pressure is highly age-dependent. Existing literature has documented the age-related trend of absolute BP, which shows a linear rise of SBP with age after 30–40 years old and reaching a plateau in late life.

In our study, the patients receiving Meropenem and Diclofenac were 60 and 58 patients, respectively. The tertiary care facility where our study was conducted demonstrated distinct prescribing practices, with Meropenem predominantly prescribed for ICU patients and Diclofenac for post-operative and orthopedic department patients. The high utilization of Meropenem in ICU settings aligns with its broad-spectrum antimicrobial activity, making it a crucial agent in the management of severe infections. Evaluation of 60 cases of Meropenem was performed out of which 35 cases

were positive for the presence of suspected ADR (Hypokalaemia) out of which 31 cases had other possible risk factors that might also attribute for causing ADR. These factors were concomitant therapy consisting of Torsemide, Furosemide, Hydrocortisone, Lactulose or pre-existing medical conditions like AKI, CKD, etc. Therefore, a comprehensive assessment of patient-specific factors is crucial in elucidating the multifactorial nature of hypokalaemia observed in our study population.

Amikacin and its potential association with blurred vision was a signal in October 2017. The 58 patients evaluated in our study did not experience blurred vision. The study conducted by Galloway and Ramsay primarily focused on ADR caused by Amikacin in patients undergoing an eye surgery or having eye ailments whereas we included all generalised patients above 18 years from inpatient department. The study by Galloway reported the serious retinal toxicity occurring with amikacin use. Dilution errors, increased intraocular pressure after injection, concurrent usage of high quantities of subconjunctival amikacin, and fluctuations in vitreous concentration constitute some of the hypotheses about potential adverse effects. The discrepancy in results of the two studies may possibly be because in the study by Galloway the patients had endophthalmitis, which may contribute to ADR occurrence as loss of vision is one of the symptoms of endophthalmitis.

We studied 19 cases of Ceftriaxone based on safety signal concerning Ceftriaxone and its potential to cause QT prolongation, out of which in 3 patients boderline QT prolongation was observed. Amongst the 3 cases we observed, in 2 patients other factors (pulmonary edema, ischaemia) might have also contributed to QT prolongation. In a retrospective cohort study by Anthoiny D Bai, they studied the association of ceftriaxone and lansoprazole with a prolonged QTc interval whereas we solely focused on Ceftriaxone. It included 27405 patients enrolled in the other PPI group and 3747 participants in the lansoprazole group. In the lansoprazole group, 126 patients (3.4%) experienced ventricular arrhythmia or cardiac arrest, while in the other PPI group, 319 individuals (1.2%) experienced the same event.[21]

Based on the drug safety alert issued by the PvPI regarding Torsemide and its potential association with DRESS Syndrome 19 cases observed and evaluated out of which 3 cases were found to be positive for eosinophilia. Healthcare providers should be attuned to the possibility of DRESS syndrome in patients presenting with eosinophilia following torsemide initiation. Furthermore, underlying medical disorders such allergies, parasite infections, or autoimmune diseases may be linked to eosinophilia. People who are susceptible to eosinophilia because of these underlying diseases might react more strongly to Torsemide, which would intensify the eosinophilic reaction. The duration and dosage of torsemide therapy might potentially have an impact on the onset of eosinophilia.

We studied 4 cases of Losartan out of which none showed muscle spasm.

We classified observed diagnosis by using International classification of diseases (ICD 11 Version). Healthcare providers can use specific ICD codes to identify and document ADRs with varying degrees of detail, enhancing the accuracy and completeness of ADR reporting. The study observed that most of the cases belonged to the class 16 which is diseases of genitourinary system which indicates that diseases affecting the genitourinary system are prevalent within the population under study. These diseases may include conditions such as urinary tract infections, kidney diseases such as chronic kidney disease, Acute kidney injury, urinary incontinence, and reproductive system disorders. This was followed by class 11- diseases of the circulatory system. Certain patient populations may be more vulnerable to ADRs related to circulatory disorders. This includes elderly patients, individuals with pre-existing cardiovascular conditions The least number of cases observed was 1 which belonged to class 20 which includes developmental anomalies also known as congenital anomalies or birth defects.

Overall, our prospective observational study was done in order to identify ADRs, their prevalence, demographic profile of the patients involved, causality and severity assessment of the ADRs. Our study portrays the importance of pharmacovigilance in monitoring drug safety and highlights the multifactorial nature of ADRs. By evaluating and monitoring drugs and their associated ADRs, patient safety in a clinical setting can be achieved.

CONCLUSION

Our study provides information on adverse drug reaction safety alerts for medications such as Meropenem, Torsemide, Diclofenac, Amikacin, Metoprolol, Losartan, Cefuroxime and Ceftriaxone that were released by the Pharmacovigilance Program of India. We followed these alerts from December 2016 to September 2023. We've noted low potassium levels associated with meropenem, decreased sodium levels with metoprolol, elevated eosinophil count with torsemide, and prolonged QT interval with ceftriaxone. The drugs safety alerts by PvPI serve as important tools for enhancing drug safety monitoring, promoting informed decision-making, and ultimately improving patient outcomes. Even though our study was for a period of 8 months, pharmacovigilance and ADR monitoring are continuous process which contribute significantly to the ongoing efforts to ensure the safe and effective use of medicines.

REFERENCES

1. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet [Internet]. 2000 Oct 1; 356(9237): 1255–9. Available from: https://pubmed.ncbi.nlm.nih.gov/11072960/#: ~: text=Adverse%20drug%20reactions%20are%20classified,failure%20of%20therapy%20(Failure).
2. Coleman JJ, Pontefract SK. Adverse drug reactions. Clinical Medicine [Internet]. 2016 Oct 1; 16(5): 481-5. Available from: https://doi.org/10.7861/clinmedicine.16-5-481
3. Kengar MD, Patole KK, Ade AK, Kumbhar SM, Patil CD, Ganjave AR. Introduction to pharmacovigilance and monitoring. Asian Journal of Pharmaceutical Research [Internet]. 2019 Jan 1; 9(2): 116. Available from: https://doi.org/10.5958/2231-5691.2019.00019.4
4. Kim JH, Scialli AR. Thalidomide: The tragedy of birth defects and the effective treatment of disease. Toxicological Sciences [Internet]. 2011 Apr 19; 122(1): 1–6. Available from: https://doi.org/10.1093/toxsci/kfr088
5. Kalaiselvan V, Srivastava S, Singh A, Gupta S. Pharmacovigilance in India: present scenario and future challenges. Drug Safety [Internet]. 2018 Sep 29; 42(3): 339–46. Available from: https://doi.org/10.1007/s40264-018-0730-7
6. Suke SG, Kosta P, Negi H. Role of Pharmacovigilance in India: An overview. Online Journal of Public Health Informatics [Internet]. 2015 Jun 22; 7(2). Available from: https://doi.org/10.5210/ojphi.v7i2.5595
7. Shukla AK, Jhaj R, Misra S, Ahmed SN, Nanda M, Chaudhary D. Agreement between WHO-UMC causality scale and the Naranjo algorithm for causality assessment of adverse drug reactions. Journal of Family Medicine and Primary Care [Internet]. 2021 Jan 1; 10(9): 3303. Available from: https://doi.org/10.4103/jfmpc.jfmpc_831_21
8. Srisuriyachanchai W, Cox AR, Kampichit S, Jarernsiripornkul N. Severity and management of adverse drug reactions reported by patients and healthcare professionals: a Cross-Sectional survey. International Journal of Environmental Research and Public Health/International Journal of Environmental Research and Public Health [Internet]. 2023 Feb 20; 20(4): 3725. Available from: https://www.mdpi.com/1660-4601/20/4/3725#
9. Sahu RK, Yadav R, Prasad P, Roy A, Chandrakar S. Adverse drug reactions monitoring: prospects and impending challenges for pharmacovigilance. SpringerPlus [Internet]. 2014 Nov 26; 3(1). Available from: https://doi.org/10.1186/2193-1801-3-695
10. Kalaiselvan V, Thota P, Singh G. Pharmacovigilance Programme of India: Recent developments and future perspectives. Indian Journal of Pharmacology/the Indian Journal of Pharmacology [Internet]. 2016 Jan 1; 48(6): 624. Available from: https://doi.org/10.4103/0253-7613.194855
11. Thota P, Thota A, Medhi B, Sidhu S, Kumar P, Selvan VK, et al. Drug safety alerts of pharmacovigilance programme of India: A scope for targeted spontaneous reporting in India. Perspectives in Clinical Research [Internet]. 2018 Jan 1; 9(1): 51. Available from: https://doi.org/10.4103/picr.picr_29_17
12. Shalom G, Khoury R, Horev A. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Associated with Mycoplasma pneumoniae Infection. Case Reports in Dermatology [Internet]. 2020 Nov 12; 12(3): 225–30. Available from: https://doi.org/10.1159/000510706
13. Yıldırım Y, Kara AV, Yılmaz Z, Yıldırım R, Yılmaz S, Kadiroglu AK, et al. Cefuroxime Axetil Related DRESS (drug reaction with eosinophilia and systemic symptoms) Syndrome. Electronic Journal of General Medicine [Internet]. 2016 Apr 6; 13(2). Available from: https://doi.org/10.15197/ejgm.1462
14. Singh A, Gainder S. Cefuroxime axetil induced DRESS in a pregnant patient. New Indian Journal of OBGYN [Internet]. 2023 Aug 1; 10(1): 215–7. Available from: https://doi.org/10.21276/obgyn.2023.10.1.38
15. Anuhya TV, Acharya R, MadhyasthaA S, Bhat R, Nayak V. Meropenem induced hypokalemia. Journal of Clinical and Diagnostic Research [Internet]. 2017 Jan 1; Available from: https://doi.org/10.7860/jcdr/2017/27584.10387
16. Zaki S, Shanbag P. Meropenem-induced hypokalemia and metabolic alkalosis. Indian Journal of Pharmacology/the Indian Journal of Pharmacology [Internet]. 2012 Jan 1; 44(2): 276. Available from: https://doi.org/10.4103/0253-7613.93872
17. Wuerzner G, Chiolero A, Maillard M, Nussberger J, Burnier M. Metoprolol prevents sodium retention induced by lower body negative pressure in healthy men. Kidney International [Internet]. 2005 Aug 1; 68(2): 688–94. Available from: https://doi.org/10.1111/j.1523-1755.2005.00447.x
18. Lodhi S a. K, Reddy GAK, Sunder CA. PostoperativeNocardiaEndophthalmitis and the Challenge of Managing with Intravitreal Amikacin. Case Reports in Ophthalmological Medicine [Internet]. 2016 Jan 1; 2016: 1–6. Available from: https://doi.org/10.1155/2016/2365945
19. Galloway G. Macular infarction after intravitreal amikacin: mounting evidence against amikacin. British Journal of Ophthalmology [Internet]. 2002 Mar 1; 86(3): 359–60. Available from: https://doi.org/10.1136/bjo.86.3.359
20. Bains A, Rajagopal SV, Rao M. DRESS syndrome secondary to spironolactone with atypical presentation. Indian Dermatology Online Journal [Internet]. 2020 Jan 1; 11(6): 1022. Available from: https://doi.org/10.4103/idoj.idoj_279_20

21. Bai AD, Wilkinson A, Almufleh A, Rai M, Razak F, Verma AA, et al. Ceftriaxone and the risk of ventricular arrhythmia, cardiac arrest, and death among patients receiving lansoprazole. JAMA Network Open [Internet]. 2023 Oct 26; 6(10): e2339893. Available from: https://doi.org/10.1001/jamanetworkopen.2023.39893
22. Teng C, Walter EA, Gaspar DKS, Obodozie-Ofoegbu OO, Frei CR. Torsades de pointes and QT prolongation Associations with Antibiotics: A Pharmacovigilance Study of the FDA Adverse Event Reporting System. International Journal of Medical Sciences [Internet]. 2019 Jan 1; 16(7): 1018–22. Available from: https://doi.org/10.7150/ijms.34141
23. Lorberbaum T, Sampson KJ, Chang JB, Iyer V, Woosley RL, Kass RS, et al. Coupling data mining and laboratory experiments to discover drug interactions causing QT prolongation. Journal of the American College of Cardiology [Internet]. 2016 Oct 1; 68(16): 1756–64. Available from: https://doi.org/10.1016/j.jacc.2016.07.761