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Original Article

# A Prospective Study on Tracking and Reporting of Adverse Medication Responses in Patients Referred to a Teaching Hospital for Tertiary Care

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**ABSTRACT**

Adverse medication responses are one of the major factors contributing to morbidity and mortality. Every time a patient is exposed to a medicinal product, it's a special circumstance, and there's no way to predict what might happen. Aim was to identify and report adverse medication responses. This prospective, observational, spontaneous reporting study was carried out at HSK Hospital in Bagalkot, Karnataka, India, over the course of six months. During the course of the trial, 114 patients reported a total of 154 ADRs. Male patients (54.54%) reported a greater percentage of adverse drug reactions than female patients (45.46%). The most frequently encountered ADRs in the study population were hypotension, nephrotoxicity, constipation, and loose stools. Antihypertensive (20.7%), Anti-TB (17.5%), and Antibiotic (14.93%) medication classes caused more Adverse Drug Reactions (ADRs) than others. The organ system mostly affected by Adverse medication responses was the Gastrointestinal system (17.53%), followed by the Endocrine system (16.23%), Dermatology (14.28%). By this, we conclude that regularly tracking and reporting adverse medication responses can reveal information about their efficacy and pattern of occurrence. Similar reporting initiatives are required to inform and raise awareness about the reporting of ADRs among hospital medical staff. Studies of this nature that report Adverse medication responses will aid in promoting the safety of medication therapy.

**Keywords:** Adverse medication responses, Pharmacovigilance, Safety of medication therapy.

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## INTRODUCTION

According to the WHO, pharmacovigilance is a practice that focuses on identifying, evaluating, comprehending, treating, and avoiding adverse drug reactions to promote the safe and responsible use of medications. ADR reporting is still a relatively new idea in India, even though ADRs are of major concern to the general public, the medical community, the pharmaceutical sector, and regulatory agencies. The Pharmacovigilance Programme of India was also launched by the Indian government under the direction of the Ministry of Health and Family Welfare, and centers for the monitoring of Adverse Drug Reactions (ADRs) were set up at several tertiary care institutions across the nation.[1]

The global burden of adverse medication responses, which are frequently preventable, includes consequential morbidity and mortality. Because they reduce patients' quality of life and create a huge financial burden on healthcare systems at a time when many of them are already under considerable financial stress, ADRs have a significant detrimental effect on public health. A known risk of pharmacological therapy is ADRs. Even though some ADRs are small and go away on their own, others can result in death or permanent impairment and increase the likelihood of adverse drug reactions, which drives up healthcare costs.[2]

ADRs are thought to be the cause of roughly 10% of hospital admissions, and about 5-20% of hospitalized patients have a significant ADR.[3-5] A significant part of monitoring and evaluation efforts carried out in hospitals now includes reporting ADRs. Such ADR reporting initiatives support ADR reporting, enhance ADR surveillance, and improve health professionals' training on probable ADRs.[6]

A serious adverse reaction, according to the FDA, is one in which the patient experiences one of the subsequent: "death, life-threatening (real risk of death), hospitalization (initial or prolonged), disability (significant, persistent, or permanent), congenital anomaly, or required intervention to prevent permanent impairment or damage".[7] An adverse medication

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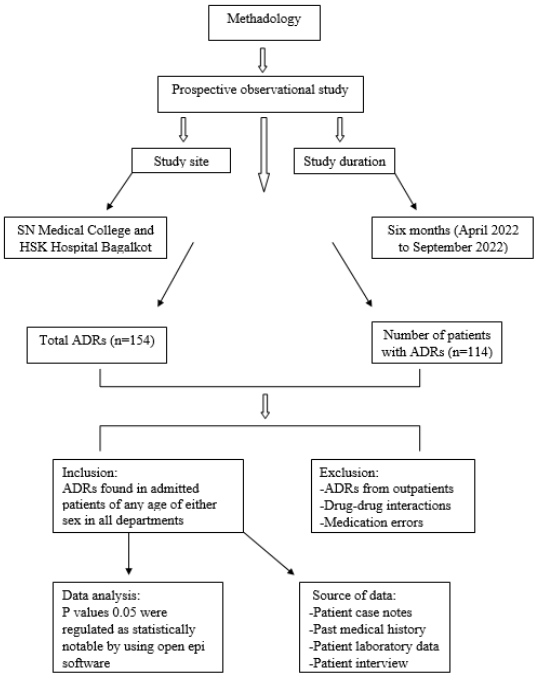
response is "any response to a drug, which is toxic and unintended, and which occurs at doses used in man for prophylaxis, diagnosis, or therapy, or for modification of physiologic function",[8] as per the World Health Organisation (WHO). The term does not include instances of drug abuse or accidental overdose.[9]

In North Karnataka, India, H.S.K Hospital is an 820-bed tertiary care teaching hospital. In structured healthcare systems, chemists should create extensive, continuing programs for tracking and reporting adverse drug reactions.[10] Reporting any suspected ADRs is the chemist's responsibility and professional obligation. Programs for ADR monitoring and reporting enhance ADR surveillance, make ADR recording easier, encourage ADR reporting, offer a way to keep track of the safety of medication usage in high-risk patient populations, and encourage health professionals to become more knowledgeable about possible ADRs.[11] We conducted research based on ADR reports gathered as part of the prospective active pharmacovigilance initiative on tracking ADRs in hospital wards. The primary goals of the current study were to identify and report ADR, determine the kind of ADR, study the pattern of ADR, and assess the Causality, Preventability, Predictability, and management of ADR patients in all departments.

The causality of the reported Adverse medication responses was detected using the Naranjo causality assessment scale, and WHO causality assessment scale.[12-14] The Hartwig scale is used to determine severity,[15] while the Shumock and Throntan scale is used to determine preventability.

## MATERIALS AND METHODS




## RESULTS

Together 154 ADRs were reported from 114 patients during 6-months study period. There were 23,157 patients in total during the trial period. In this patient group, the overall incidence of ADRs during hospitalization was 0.66%. Males (53.25%) had higher ADRs than females (46.75%). However, during the hospital stay, no association between ADRs and gender was seen ($p$ = 0.9661). The rates of ADRs were 7.84% in pediatric patients (under 12 years), 3.50% in adolescents (ages 12 to 18 years), 15.78% in young adults (ages 19 to 30 years), 26.3% in adults (ages 31 to 45 years), 26.38% in older adults (ages 46 to 60 years), 0.16% in elderly patients (age 61 to 75 years), and 2.57% in geriatric patients (age 76 years and older). Compared to pediatric and geriatric patients, the rate of ADRs was substantially higher in adult patients. Considering the evaluation described in Table 1.

The majority of the reactions in the current study 86.34% were of type A, while type B accounted for 13.66%. ADRs that occur most frequently in type A reactions are common (42.1%), infrequent (52.6%), and rare (5.2%), whereas ADRs that occur most frequently in type B reactions are common (3.25%), infrequent (47.6%), and rare (28.5%).

The bulk of ADRs among reported ADRs is from the following classes: Antibiotics (14.93%), and Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) (8.44%) following other classes of drugs of which Considering evaluation presented in Figure 1. Gastrointestinal

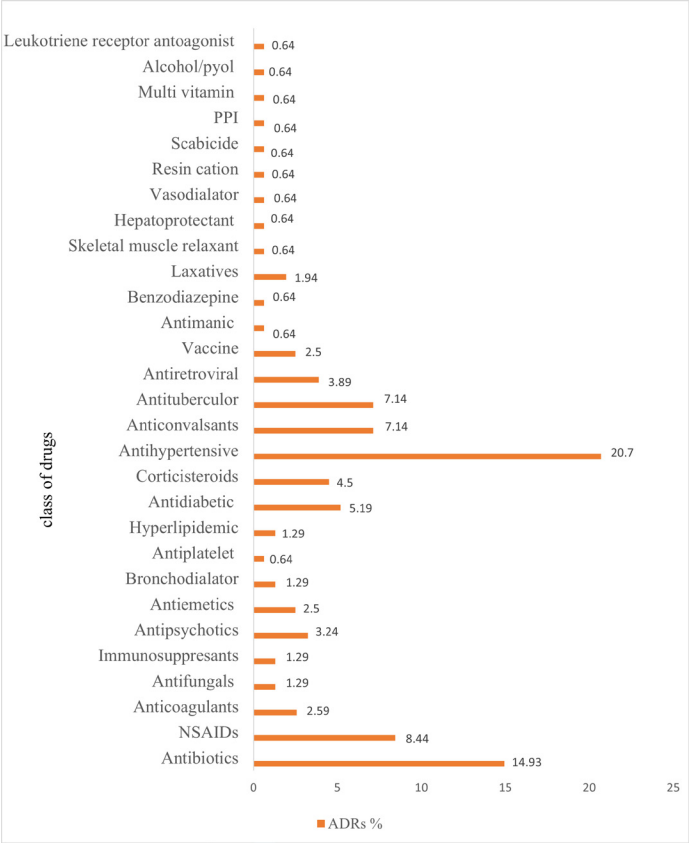



**Figure 1:** Percentage of a class of drug-causing ADRs.

**Table 1: Percentage of the patients and patient characteristics.**

| Age group | Gender | Number of ADR (*n*=154) | Number of patients with ADR (*n*=114) | Percentage of patients with ADR |
|---|---|---|---|---|
| 0-24 month | Male | 02 | 02 | 1.75 |
| | Female | 01 | 01 | 0.87 |
| 2-11 Year | Male | 03 | 03 | 2.61 |
| | Female | 04 | 03 | 2.61 |
| 12-18 Year | Male | 05 | 04 | 3.50 |
| | Female | 0 | 0 | 0 |
| 19-30 Year | Male | 08 | 07 | 6.14 |
| | Female | 14 | 11 | 9.64 |
| 31-45 Year | Male | 26 | 17 | 14.9 |
| | Female | 18 | 13 | 11.40 |
| 46-60 Year | Male | 20 | 14 | 12.28 |
| | Female | 17 | 13 | 11.40 |
| 61-75 Year | Male | 16 | 11 | 9.64 |
| | Female | 17 | 12 | 10.52 |
| 76 and above year | Male | 02 | 02 | 1.7 |
| | Female | 01 | 01 | 0.87 |
| TOTAL | Male | 82 | 61 | 53.50 |
| | Female | 72 | 53 | 46.50 |

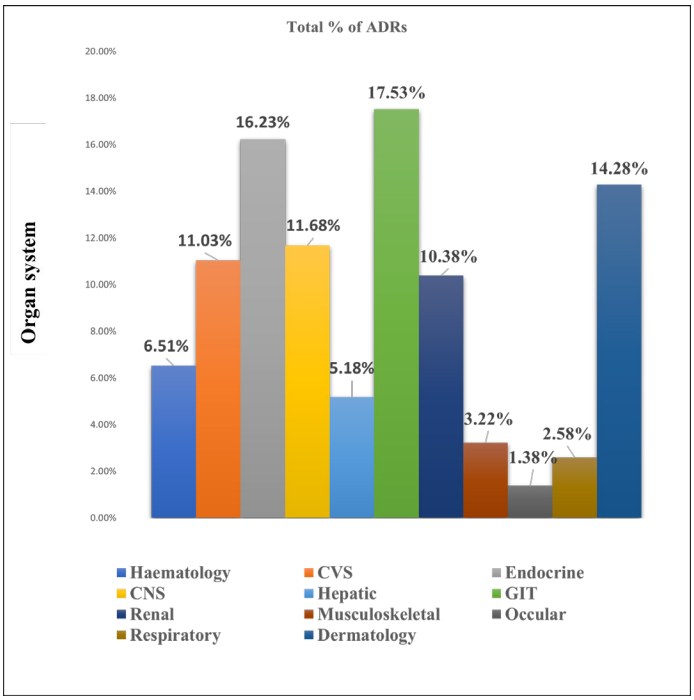



**Figure 2:** Organ systems affected by ADRs.

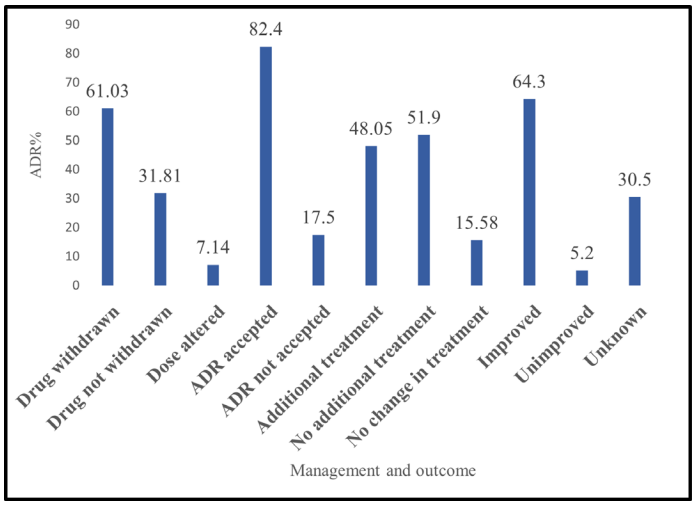



**Figure 3:** Management and outcome of ADRs.

system (17.53%), followed by the Endocrine system (16.23%), Dermatology (14.28%), followed by the other organ system most frequently impacted by ADRs in our study. Considering the evaluation presented in Figure 2. According to the WHO scale, the reports were given the following causality ratings: Certain (1.94%), Probable (64.28%), Possible (32.5%), Unlikely (1.28%), and Conditional/Unclassified (1.2%). According to the Naranjo probability scale, Definite (27.2%), Probable (35.7%), Possible (31.1%), and Unlikely (5.8%). According to the Hartwig and Siegel scale, mild and moderate reactions made up 24.6% and 59.0%, respectively, whereas severe reactions made up 16.2%. According to the Schumock and Thornton scale used to evaluate preventability, 82.4% of ADRs were preventable, 11.6% were Possibly preventable, and 5.8% were Not preventable. The majority of reports found that polypharmacy serves as an ADR predisposing factor after evaluating the types of prescriptions

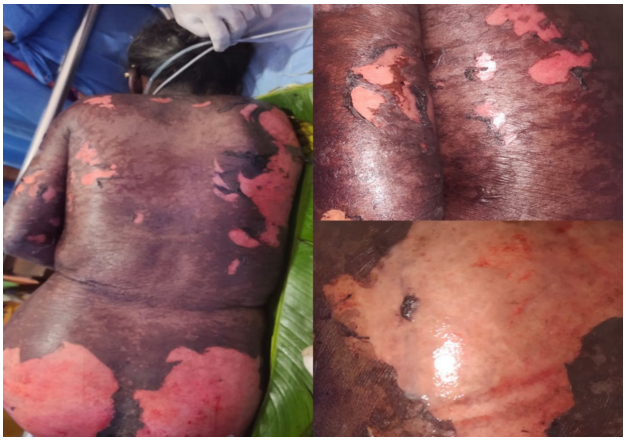


**Figure 4:** Phenytoin: Toxic epidermal necrolysis.

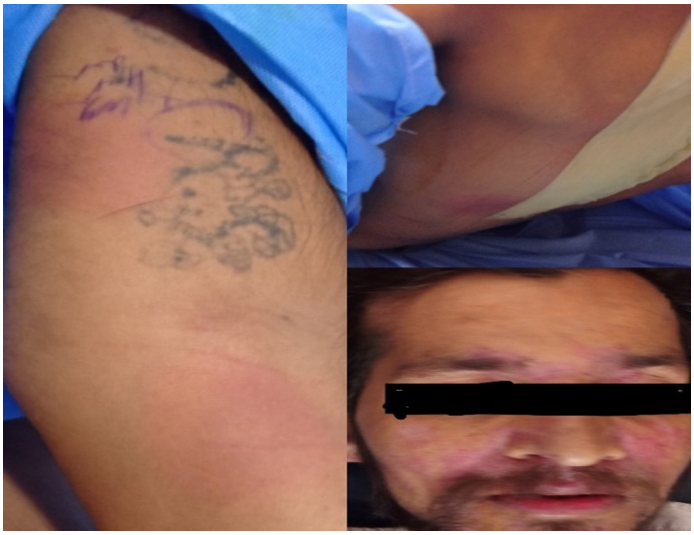


**Figure 5:** Pneumococcal vaccine: Urticaria and Pruritis.

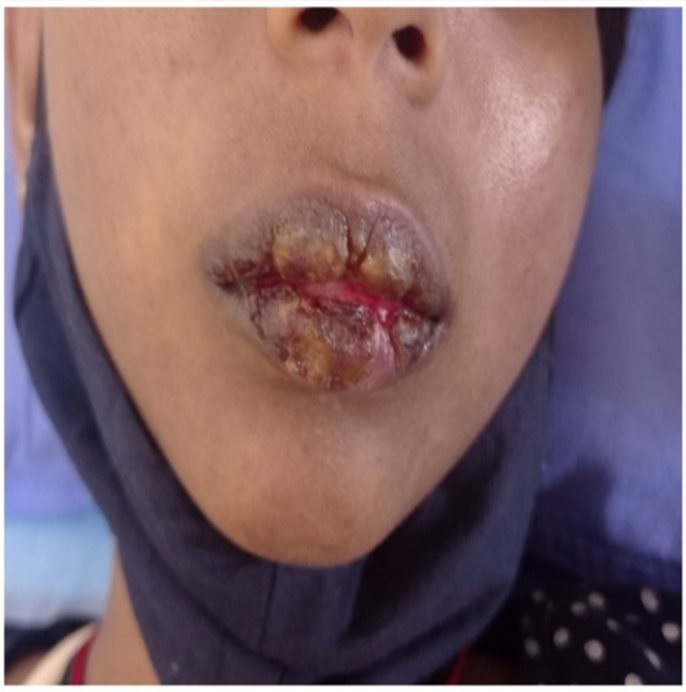


**Figure 6:** Clotrimazole: Blister and Burning.

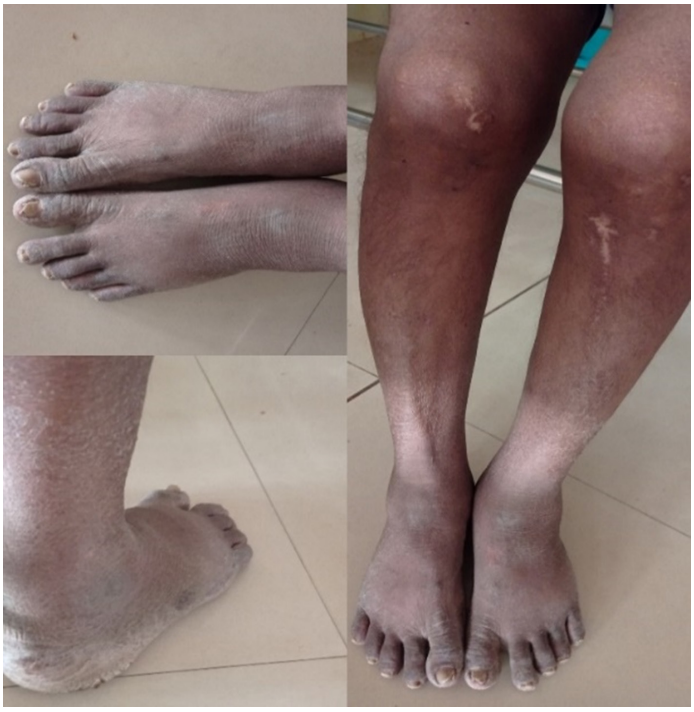


**Figure 7:** Atorvastatin: Rhabdomyolysis.

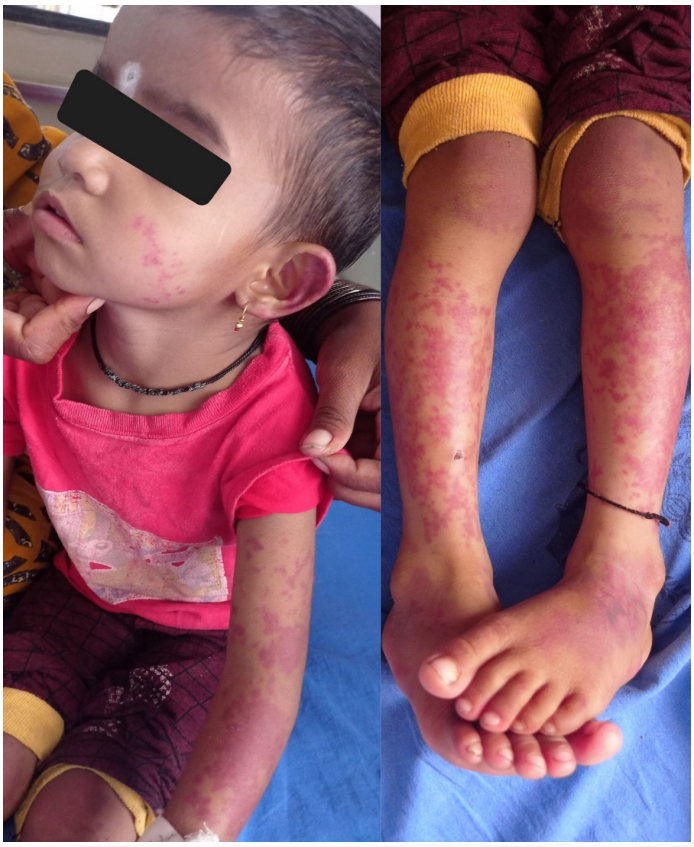


**Figure 8:** Levetiracetam: Vasculitis.

that result in ADRs. The impact of polypharmacy was statistically insignificant in both adults and children ($X^2 = 1.15$ and $p = 0.286$). In our study, the suspicious drug was discontinued in (61.03%) of the complaints. There were two treatment outcomes: Additional

treatment (48.05%) and no extra treatment (51.9%). The patient showed improvement as a result of the ADRs in 64.3% and this was made feasible since the medicine that was causing the adverse drug reactions in these patients was removed or the amount was lowered, considering the evaluation presented in Figure 3.

## DISCUSSION

ADRs may significantly impact both the general health care system and the well-being of a patient.[16] In the present study, a greater number of patients with suspected ADRs were found between the age group of 31-45 years followed by 46-60 years, which is consistent with other studies, The majority of adult patients were taking numerous medications and had concomitant diseases like stroke, diabetes, hypertension, and atherosclerosis, which was the cause of this. This enables us to comprehend that polypharmacy and numerous disease conditions, which are present in the majority of patients, are the predisposing variables most frequently linked to the observed responses.

The majority of ADRs in the current research are Type A responses, which is similar to findings from another investigation. as a result of the fact that the majority of ADRs were dose-related, predictable, and high morbidity, low mortality, and recovered following the dosage decrease.

The gastrointestinal system, followed by the endocrine system, the dermatologic system, and the GI system, are the organ systems most impacted by ADRs in the current study. This is different from another study, which found that the organ systems most affected by ADRs were the dermatologic system, the GI system, and the central nervous system. This result is because the majority of drugs were distributed, metabolized, and absorbed through the GI system. As a result, the system is frequently exposed to all chemicals and drugs, which causes GI symptoms to develop. In addition, the skin is the primary organ of the body to experience cutaneous drug reactions, photosensitivity reactions, and fixed drug eruptions.

In the present study class of drug frequently caused ADRs is the Anti-hypertensives, for example, Enalapril an ACE inhibitor increases the sensitivity of bradykinin' dependent airway sensory nerve fibers by that causes cough and wheezing[17] also by reducing glomerular filtration pressure due to hemodynamics when the efferent arterioles from the glomeruli relax it causes nephrotoxicity,[18] Amlodipine a calcium channel blocker by increased urinary calcium excretion confers an increased risk of kidney stones.[19] Followed by Antibiotics like Ceftriaxone a cephalosporin which shows a direct effect on mucous membranes and disturbs the gut microflora which results in the accumulation of high molecular carbohydrates in the colon and causes loose stools[20] and Cefixime by the production of IgE antibodies this this this this this this this fixed this to mast this ell then again pre-expose to the same antigen-antibody reaction occurs on the mast cell surface then release of inflammatory mediators like histamines, PGs, LTs, causes skin rashes.[5] Such as antitubercular medications INH's metabolite acetyl diazine may be hazardous by itself or may degrade into reactive acetyl radicals, acetyl ions, and ketone that may bond covalently with hepatic macromolecules and cause damage to the liver. Rifampicin: potentiates the hepatotoxicity of anti-TB drugs. Pyrazinamide: hydroxy pyrazinamide and pyrazinoic acid are responsible for hepatotoxicity. Ethambutol: unknown,[21] with contrast to other studies showing the that class of drug frequently causing ADR was the Antibiotic drug class (Ceftriaxone, Linezolid) followed by Antitubercular drugs (HRZE).

The majority of the Adverse Drug Reactions (ADRs) in the current study fell into the probable group, followed by the potential category, by prior studies that also showed the probable category, followed by the possible category. In the present study Most of the reactions were treated by withdrawing the offending drugs, additional treatment followed by dose reduction. Similar findings were observed in another study.

We have shown some photographs of ADRs in the present study which were collected during the study period (Figure 4) Phenytoin induced toxic epidermal necrosis which is categorized as a type B reaction. Causality according to the WHO scale revealed that it falls into certain groups (Figure 5).[2] Pneumococcal vaccine-induced pruritis and urticaria categorized as type B reaction. Causality according to the WHO scale revealed that it falls into certain group Figure 6.[23] Clotrimazole-induced blister and burning, categorized as type B hypersensitivity reaction. Causality according to the WHO scale revealed that it falls in the probable group (Figure 7).[24] Atorvastatin-induced rhabdomyolysis is categorized as a type A reaction. Causality according to the WHO scale revealed that it falls into certain groups Figure 8.[25] Levetiracetam-induced vasculitis is categorized as a type B Hypersensitivity reaction. Causality according to the WHO scale revealed that it falls into certain groups.[26]

## CONCLUSION

Every drug will cause ADRs, some are harmful, and some are negligible, so the early detection and reporting of such reactions by healthcare professionals will aid in promoting the safety of the patient's medication therapy. Along with that major predisposing factor for ADRs is polypharmacy, so physicians should give much attention to the reduction of polypharmacy as much as possible, as well as prolonged usage of antihypertensive will lead to nephrotoxicity (AKI).

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**ADR:** Adverse drug reaction; **WHO-UMC:** World Health Organization-Uppsala Monitoring Centre; **FDA:** Food and Drug Administration; **NSAID:** Non-steroidal anti-inflammatory drugs; **ACE inhibitors:** Angiotensin-converting enzyme (ACE) inhibitors; **OBG:** Obstetrics and Gynecology; **SPSS software:** Statistical Package for Social Sciences; **HRZE:** isoniazid, rifampicin, pyrazinamide, and ethambutol; **AKI:** Acute kidney injury; **GI:** Gastrointestinal; **CNS:** Central Nervous System.

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