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IMPACT OF PHARMACOVIGILANCE IN MONITORING ADVERSE DRUG REACTIONS: A RETROSPECTIVE STUDY

Ali Hassan[1], Azra Batool[2], Ahmed Sadiq Sheikh[3], Hashmat Ullah[4], Muhammad Masoom Akhtar[5], Aziz Ur Rahman[6], Tehmina Rabbani[7], Mobina Manzoor[8], Sidra Mumtaz[9], Pervaiz Akhtar Shah[10*], Tariq Javed[11], Sheikh Abdur Rashid[12*]

[1,4,9,12*] Gomal Centre of Pharmaceutical Sciences, Faculty of Pharmacy, Gomal University, Dera Ismail Khan, 29050, Pakistan; [1]Email: alihassanch34@gmail.com ;
[4]Email: drhashmat28@gmail.com; [9]Email: dr.sidraimran85@gmail.com;
[12*]Email: sheikhabdurrashid11@gmail.com
[2] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hamdard University, Islamabad Campus, Pakistan 44000; [2]Email: azra.batool@hamdard.edu.pk
[3]Faculty of Pharmacy, My University, Islamabad 44000; [3]Email: dean.pharmacy@myu.edu.pk
[5]Department of Pharmacology, Faculty of Pharmacy, Hamdard University, Islamabad Campus, Pakistan 44000; [5]Email: m.masoom@hamdard.edu.pk
[6]Department of Pharmacy, University of Malakand, Pakistan; [6]Email: azizuom123@gmail.com
[7]Department of Pharmaceutics, Balochistan University, Quetta, Pakistan; [7]Email: achakzai.tehmina@gmail.com
[8]Lahore College for Women University; [8]Email: mobina_star@hotmail.com
[10*] Punjab University College of Pharmacy, University of the Punjab, Lahore, Pakistan, Allama Iqbal Campus, Lahore 54000; [10*]Email: pervaiz.pharmacy@pu.edu.pk
[11]Margalla College of Pharmacy, Margalla Institute of Health Sciences, Rawalpindi 46000 Pakistan; [11]Email: tariqbaghi@gmail.com

***Corresponding Authors:** Sheikh Abdur Rashid, Pervaiz Akhtar Shah
*Email: sheikhabdurrashid11@gmail.com, pervaiz.pharmacy@pu.edu.pk

Abstract

Adverse drug reactions (ADRs) are a major problem for healthcare systems around the world. Effective pharmacovigilance is therefore necessary to ensure patient safety. The purpose of this retrospective observational study, which ran from March to August 2023 in a tertiary care hospital for six months, was to evaluate the frequency, trends, and features of adverse drug reactions. There were 115 ADRs in all, with an average of 11 cases reported per month and an incidence of 0.95 cases per 1,000 patients. Skin/subcutaneous tissues (24.34%) and the gastrointestinal system (38.26%) were the most frequently affected organs, with adult patients aged 18-65 accounting for the majority of cases (64.34%). The most common mode of administration (72.17%) was oral. The severity assessment classified the ADRs as follows: 16.52% as severe, 36.53% as moderate, and 46.95% as mild. The causality analysis yielded 10.43% certain, 39.1% probable, and 30.43% plausible ADRs. Antihypertensives (25.2%), antimicrobials (39.13%), and antidiabetics (16.52%) were the most implicated drug classes. These results highlight the need for enhanced ADR reporting protocols and ongoing surveillance to improve patient safety, especially with regard to focused interventions for

high-risk populations such as women and adults.

Keywords: Adverse drug reactions, Pharmacovigilance, Causality assessment, Patient safety

1. Introduction

According to the World Health Organization (WHO) adverse drug reactions describe hazardous and unexpected drug reactions that happen at normal human dose levels. The existing body of research has a large number of studies that highlight the importance of reporting and assessing ADRs and their results. Studies have indicated that the incidence of adverse drug reactions (ADRs) resulting in hospitalization varied between 1.0% and 16.8% in the United States and between 0.5% and 12.8% in European nations (1). Due to the introduction of numerous highly harmful substances as medications in the last two or three decades, the identification of ADRs has gained increased importance. WHO took a significant interest in this issue and set up an international monitoring center for adverse drug reactions in Uppsala, Sweden. This center works with national monitoring centers in about 70 countries (2).

ADRs represent unintentional and harmful reactions to medications taken at recommended dosages for diagnosis or treatment. They require particular treatment, dose modification, withdrawal, or prevention and are divided into six categories. Type A pertains to dose, Type B is unrelated to dose, Type C is related to time and dose, Type D is related to time, and Type E is withdrawal-related and Type F highlights therapy failure (3).

To ensure patient safety, pharmacovigilance aims to prevent ADRs. The identification of adverse drug events (ADEs) remains a serious challenge for healthcare professionals. ADEs are widespread throughout the world; among hospitalized patients, their prevalence rates are 3.2% in England, 4.8% in Germany, and 5.6% in the USA. Due to inadequate monitoring and reporting systems, ADEs rank as the fifth most common cause of mortality worldwide (4). The overall cost of healthcare as well as the financial burden on individual patients is increased by ADRs. According to estimates, each ADR will cost Rs. 690 (US $15) in medication-related morbidity and mortality. Furthermore, the quality of life (QoL) of patients may be adversely affected by eight ADRs (5).

ADR reporting has grown in importance as a part of hospital monitoring and assessment procedures . These ADR reporting initiatives support ADR reporting, enhance ADR surveillance, and advance health professionals' education about potential ADRs (6). In a hospital setting, ADRs could be tracked using either voluntary reporting or active surveillance. In Western countries, there are a variety of reporting systems in place, most of which are spontaneous reporting systems with or without mandatory legal obligations (7).

The main component of a pharmacovigilance program is the spontaneous reporting of ADRs by medical professionals engaged in clinical practice. Despite the most conventional and straightforward approach of ADR reporting, it has been shown to be inadequate, primarily as a result of underreporting. Other techniques for pharmacovigilance, referred to as active surveillance, include computer monitoring, clinical records, ward rounds, telephone structured interviews, chart review, and clinical records (8).

Mapping the various reaction patterns in a hospital is aided by routine reaction monitoring. This aids in the development of strategies for teaching hospitals how to safely use medications and in individualized patient care. Thus, the study was conducted to examine the frequency, trends, and evaluation of the pharmaceuticals causing and body systems impacted, as well as the causation, severity, preventability, and result of the many adverse reactions recorded.

2. Materials and Methods

A retrospective, observational study on ADR monitoring was conducted in all departments of a Quaid e Azam International Hospital, a tertiary care hospital over a six-month period from March 2023 to August 2023. Patients who reported adverse drug reactions gave their informed agreement to participate in the trial. Following the Institutional Review Board's approval of the study protocol (191/pharm/GU, dated 01/07/2022) the investigation got underway.

2.1 Inclusion Criteria

This study's inclusion criteria were all potential adverse drug reactions (ADRs) that were eventually recorded and reported and may have been caused by prescription as well as non-prescription medications that patients, whether inpatients or outpatients, utilized.

2.2 Exclusion Criteria

Overdosing, overprescribing, and overconsumption, individuals taking over ten prescription drugs and patients who were unconscious or unable to react to questions verbally as well as any intellectually impaired individuals or drug users were not included in the study.

2.3 Making adverse medication reaction reporting forms (yellow cards)

Yellow cards were created according to WHO guidelines with the intention of including all pertinent information, like the patient's name, age, sex, height, and weight; the date of the adverse event; a brief description of the reaction; the name of the suspected drug; the length of the reaction; and the identity of the reporting clinician.

2.4 Data Collection

The investigator acquired the necessary data from the relevant ward or department. The patient profile form was used to collect data when a suspected adverse drug response (ADR) was discovered. The patient's personal information as well as details about their medications, including over-the-counter medications, alternate treatments and recently discontinued medications were recorded. Similarly, a thorough record of all adverse reactions, completed with the reaction's description, timing, duration, and treatment administered, as well as relevant investigation reports were also recorded.

The Hartwig severity assessment scale was used to measure severity, and the Naranjo causality evaluation scale was used to assess causality, in compliance with the guidelines provided by the WHO Uppsala Monitoring Center (9). Two investigators extracted the data independently, and they were analyzed using a random-effects model. The incidence of ADRs that occurred during the patient's stay in the hospital was combined with the incidence of ADRs that resulted in admission to determine the overall incidence of ADRs in hospitalized patients. We did not include medication administration problems, noncompliance, overdoses, drug addiction, treatment failures, or potential adverse drug reactions.

3. Statistical Analysis

Data were fitted into IBM SPSS (Statistical Package for the Social Sciences) version 20. Descriptive statistics were computed to calculate mean, standard deviation and percentage. Similarly, chi-squared ($\chi 2$) test was employed to determine any relation among parameters. P-values were considered significant if they were less than 0.05.

4. Results

4.1 Monthly reported cases of ADRs

There were thousands of patients who visited the hospital between March 2023 and August 2023, including both outpatients and inpatients. However, a total of 115 ADRs were reported spontaneously from different hospital departments throughout that same time period. The number of ADRs reported varied, averaging about 11 (9.56%) reports per month, with July (27), the highest reporting month, and April (11), the lowest reporting month . Throughout the course of the trial, the hospital's overall ADR incidence was 0.95 per 1,000 patients.

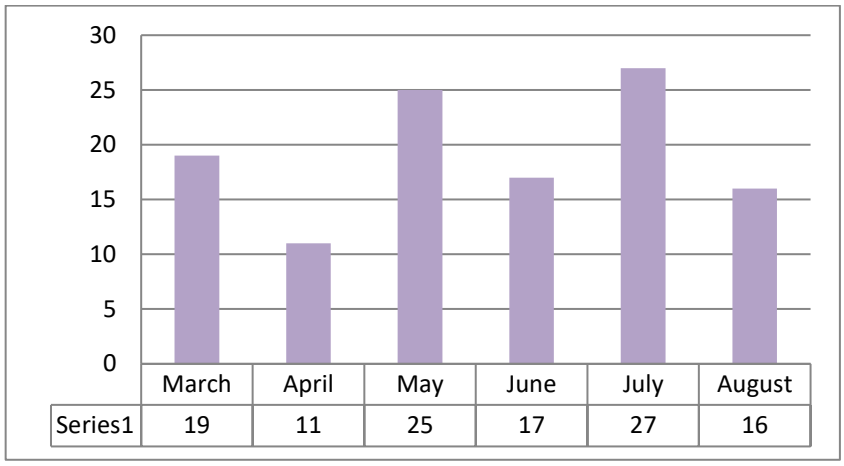

Figure 1. Monthly reported cases of ADRs

4.2 Adverse drug reactions reports and patient demographics

About 115 individual ADR reports were examined over the course of the research period of monitoring. Table 1 revealed interestingly, more ADR reports (n = 74, 64.34%) came from female patients than from male patients (n = 36, 31.30%). Adult patients between the ages of 18 and less than 65 made up the majority of ADR reports (n = 82, 71.30%). Additionally, in terms of the seriousness criteria, the majority of ADRs did not result in significant consequences; this is demonstrated by the absence of reports involving fatalities, life-threatening events, or effects that were incapacitating or disabling; only 6.08% (n = 07) of the reports included hospitalization or prolonged hospitalization. A statistically significant relation was found to be among ADRs and age as well as gender attributes (chi-squared ($\chi 2$) test, $p<0.05$).

Table 1. Frequencies of patient characteristics

Parameter	n(%)
Gender	
Male	36 (31.30%)
Female	74 (64.34%)
Age Group	
< 18 years	12(10.43%)
18 to < 65 years	82(71.30%)
≥ 65 years	21(18.26%)
Seriousness Criteria	
Caused/prolonged hospitalisation	07(6.08%)
Death	0(0)
Life threatening	02(1.7%)
Disabling/incapacitating	0(0)
Congenital anomaly/birth defects	0(0)

Age vs ADRs ($p<0.05$, $\chi 2$ test)
Gender vs ADRs ($p<0.05$, $\chi 2$ test)

4.3 Adverse drug reaction related to route of drug administration

The route of drug administration is pivotal factor determining ADR prevalence in health care setting. The frequency of adverse drug reactions linked to various administration routes as presented in the figure 2 highlighted that oral route was reported to be the major prevailing route of drug administration associated with ADRs.

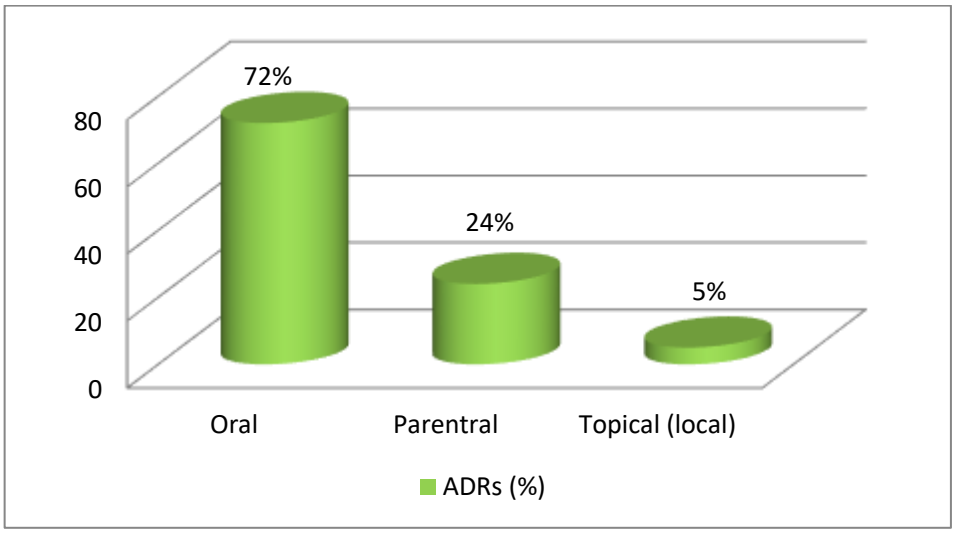

Figure 2. %age prevalence of ADRs with respect to the routes of drug administration

4.4 Adverse drug reaction and organ system involvement

Figure 3 presents a pictorial display of ADRs affecting various organ systems of the body. Gastritis and dysphagia were the most frequent gastrointestinal side effects, making up 38.26% (n=44) of the cases. Skin and subcutaneous disorders accounted for 24.34% (n=28) of the cases and were the next in line. Additional noteworthy classifications were of respiratory ailments, which were documented in 13.04% (n=15) of the instances, and central nervous system (CNS) and neurological diseases, which represented 8.69% (n=10) of the cases. Cases related to blood were 3.47% (n=4), Hepatic system 2.60% (n=3) and others of unknown origin were 9.56% (n=11). The data displayed a thorough description of the organ systems impacted by ADRs.

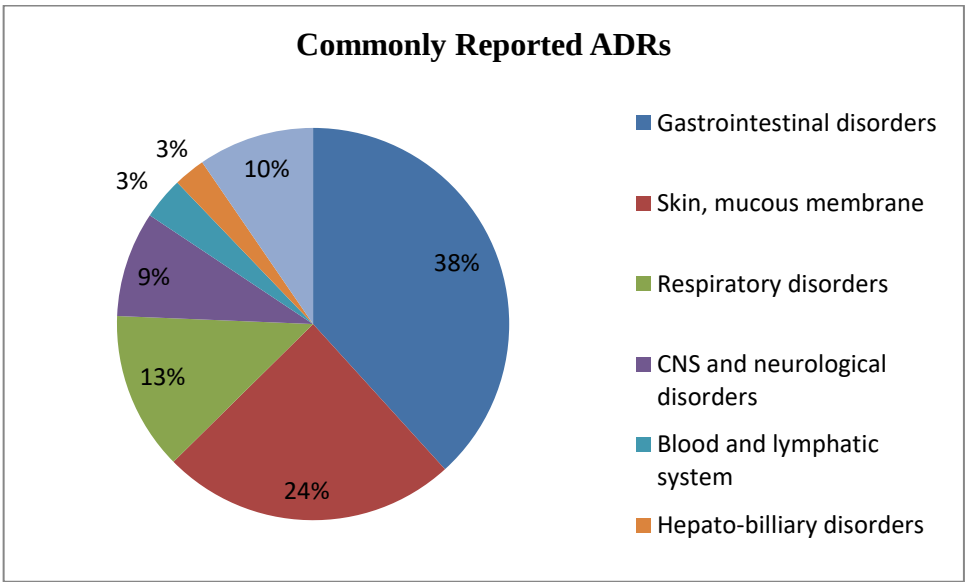

Figure 3. Pictorial display of ADRs affecting various organ systems

4.5 Causality assessment of adverse drug reactions on Naranjo Scale

The data shown in table 2 describes causality assessment of ADRs based on Naranjo Scale. Out of a total of 115 cases, about 12 ADRs (or 10.43 %) were categorized as certain. including skin reactions to ceftriaxone injections, itching and dermatitis to Statins , and hypoglycemia to glimepiride tablets. About 45 ADRs (39.1%) were deemed likely, such as dysphasia with bumetanide pills and dry cough with lisinopril. Additionally, 35 (30.43%) were categorized as possibly occurring, such as anorexia, abdominal pain treated with antihypertensive medications, dyspnea treated with metoprolol. Likewise, 10 ADRs (8.69%) were classified as un-assessable because they were unable to be further

classified, such as itching when taking antitubercular medications and mental depression while taking atenolol. Table 2 presents Naranjo scale data.

Table 2. Causality assessment of adverse drug reactions on Naranjo Scale

Scale of probability	**ADRs (%)**
Certain	12 (10.43)
Probable	45 (39.1)
Possible	35 (30.43)
Unlikely	05 (4.34)
Conditional	08 (6.95)
Un-assessable	10 (8.69)
Total	115

4.6 Severity threshold of ADRs

Out of 115 ADRs reported over the past six months, the severity of 54 cases (46.95%) was of mild range. Moderate cases were relatively less than the mild one and they constituted 42 cases (36.53%) of all the 115 ADRs reported. The number which was less was of severe cases and the reported severe cases were 19 (16.52%). As described in the figure 4, the antimicrobials appeared to produce mild nature ADRs of high frequency as compared to antihypertensives and anti-diabetics.

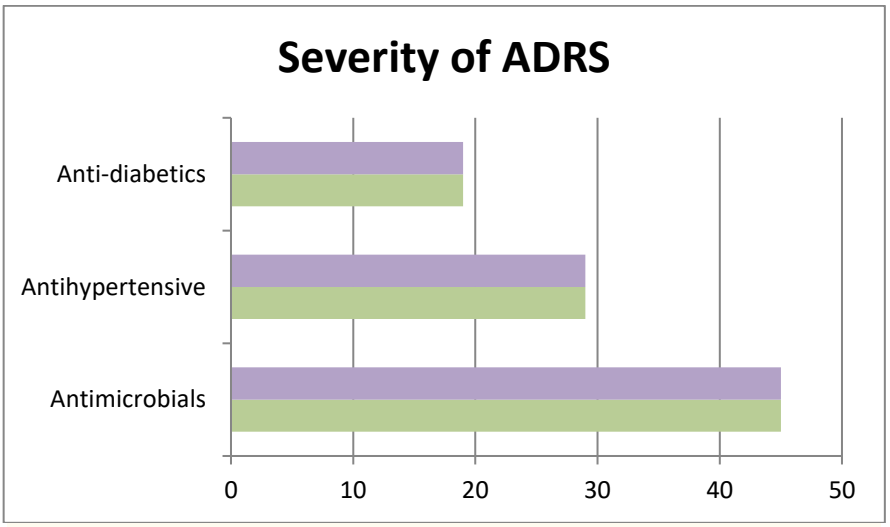

Figure 4. Severity threshold of ADRs from different drug categories

4.7 ADRs association with various drug classes

Figure 5 reveals an association of ADRs with notable medications of various pharmacological classes. Out of 115 ADRs most of the ADRs were caused by Antimicrobials i.e. 45 (39.13%) followed by Antihypertensive 29 (25.2%), Antidiabetic 19 (16.52%), NSAID 12 (10.43%), Blood and blood products 11 (9.56%), CNS drugs 05 (4.34%), Anticoagulants 03 (2.60%) and others 02 (1.73%).

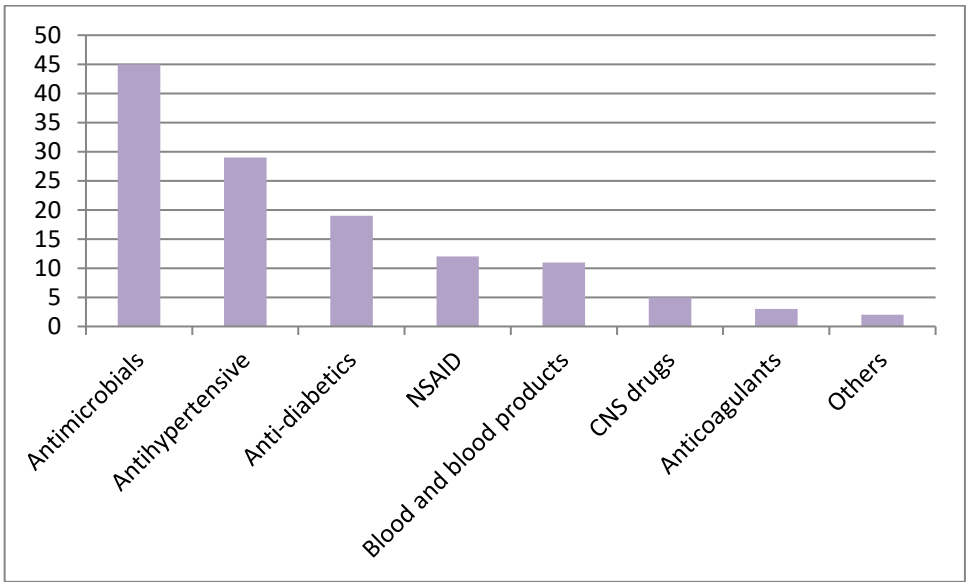

Figure 5. ADRs occurrence with respect to drugs of various pharmacological groups.

5. Discussion

Adverse drug reactions are noxious one and should be prevented. A strong pharmacovigilance is necessitated to monitor ADRs in order to improve patient care, reducing unwanted objectionable outcomes, and becoming cost effective healthcare modality. Keeping in view aforementioned parameters, this study was executed in tertiary care hospital. Between March and August 2023, the hospital saw thousands of patients; hence, 115 ADRs from various departments were documented on their own initiative. The average monthly reporting rate was 9.56%, with July having the most reports (27), and April having the fewest (11). Overall, there were 0.95 ADRs for every 1,000 patients. These results highlight the irregularities in ADR reporting and the need for continuous monitoring in addition to targeted actions to improve patient safety. Throughout the monitoring period, 115 distinct ADR reports were analyzed for our investigation. Female patients were more as compared to male population. This is consistent with a larger study that discovered that, across all locations and reporter types, there were more female reports involving ADRs compared to men. Adult patients between the ages of 18 and 65 accounted for ADR complaints in our study which is consistent with the comparative study's finding that female reports accounted for a higher proportion of all reports in all age groups from 12 to 17 years old and older especially in 18-44 age range (10). In terms of ADR severity, our analysis revealed that the majority of ADRs were not significant, with no reports of fatalities, life-threatening occurrences, or incapacitating effects, and just 6.08% (n = 7) necessitating hospitalization or prolonged hospitalization. Males had a higher percentage of serious and fatal ADRs, according to the comparison analysis. Overall, our investigation demonstrates the generally lower severity of ADRs in our study population when compared to the global data and confirms the tendency of a higher incidence of ADR reports among female patients, especially in adults. According to our research, topical, oral, and parenteral delivery methods were associated with the highest prevalence of adverse drug reactions (ADRs). Based on this distribution, oral administration accounted for the most often associated route with adverse drug reactions (ADRs). This result aligns with that of another study that found that 271 (72.3%) of the 375 major adverse drug reactions (ADRs) were associated with oral delivery, 36 (9.6%) with intravenous administration, and 58 (15.5%) with intramuscular administration. In addition, 10 (2.7%) patients received the medication by a method other than intramuscular, intravenous, or oral (11).

Oral administration is the route most frequently linked to adverse drug reactions (ADRs), according to both studies, underscoring the significance of regularly monitoring this route. Our study's parenteral ADR proportions (23.48%) are comparable to the comparative study's combined intravenous and intramuscular ADR proportions (25.1%), indicating similar trends in the prevalence of ADRs across all administration routes. Our study's results provide a detailed overview of the organ systems affected by adverse drug reactions (ADRs). Gastritis and dysphagia were found to be the most common

gastrointestinal side effects, skin and subcutaneous disorders were the next most common. Other noteworthy categories included diseases of the respiratory system and neurological and central nervous system (CNS) disorders.

In contrast, 170 putative ADRs were recorded over the course of six months among 101 patients (35.9%) in another study that evaluated ADRs in hospitalized adult patients in an infectious diseases referral unit in Tehran. According to this study, the gastrointestinal system was most frequently impacted (47.5%), and anti-infectives were implicated in 93.1% of these events (12). Although gastrointestinal problems are prominent in both studies, ours covers a wider spectrum of impacted systems, such as skin, respiratory, and central nervous system illnesses. Variations in observed ADR forms and rates may be explained by changes in patient demographics, study locations, and methodology. These results point to the need for improved pharmacovigilance practices for certain patient populations or drug classes, as well as approaches to reduce adverse drug reactions in clinical settings. By contrasting these findings, we are able to obtain a thorough understanding of ADRs and identify areas that require more study and medical intervention.

Our study's findings showed that, out of 115 adverse drug reactions (ADRs) reported in the previous six months, 46.95% had mild severity, 36.53% had moderate severity, and 16.52% had severe severity. By contrast, a high prevalence of adverse drug reactions (ADRs) was discovered in a different study on chronic obstructive pulmonary disease (COPD), which greatly increased healthcare expenses. According to this study, 4.8% of ADRs posed a risk to life. (13) Hartwig's Severity Assessment Scale was used to classify most ADRs in this study; 32.6% were classified at Level 1, 26.4% at Level 2, and 19% at Level 3. Furthermore, in the COPD trial, almost 22% of ADRs had a significant effect on patients' day-to-day functioning, requiring extra therapy and possibly raising the likelihood of additional ADRs. Novphyllin had the highest relative risk of developing an adverse drug reaction (ADR) at 0.65, followed by aclidinium bromide at 0.09, and salbutamol and indacaterol at 0.07 (14).

In contrast to the COPD study, which stresses the frequent incidence of severe and life-threatening ADRs, our study's results show a higher proportion of mild and moderate ADRs. Our study's severity distribution differs from the COPD study's classification levels in that a larger percentage of ADRs were extremely severe, impairing patients' ability to go about their normal lives and necessitating further interventions. While our study provides a broader view on ADR severity across diverse cases, the COPD study's focus on individual medications and their related hazards offers insightful information about the relative risks of different treatments. In order to lessen the impact of ADRs on healthcare systems and patient well-being, this comparison emphasizes the significance of focused monitoring and treatment measures suited to particular patient populations and drugs (15).

Following antihypertensives (29 cases), antidiabetics (19 cases), NSAIDs (12 cases,), blood and blood products (11 cases), CNS drugs (5 cases), anticoagulants (3 cases), and others (2 cases), our study, which examined 115 adverse drug reactions (ADRs), discovered that antimicrobials were the primary cause of ADRs. By contrast, a different study examined 2571 complaints of adverse drug events (ADRs) and found 415 ADEs that may have been prevented, of which 317 were examined. Ten medications were shown to be responsible for almost 60% of the avoidable adverse drug experiences. Overdosing on anticoagulants that resulted in hemorrhagic episodes, interactions between opiate agonists that caused drowsiness and respiratory depression, and improper insulin dosage that caused hypoglycemia were among the high-priority preventable adverse drug events (16). The other study underscores the essential influence of specific drug mistakes, particularly with anticoagulants, opiates, and insulins, on patient safety, while our study reveals the prevalence of antimicrobials and antihypertensives in ADRs. In order to lower ADRs and ADEs, both studies emphasize the significance of careful medication monitoring and specialized intervention techniques (17).

Numerous suggestions for enhancing patient safety and pharmacovigilance procedures can be made in light of the study's findings and conclusions. First and foremost, it's critical to put in place a strong pharmacovigilance system that promotes patients' and healthcare providers' timely reporting of adverse drug reactions (ADRs). This can be accomplished by making ADR reporting more widely known and by offering user-friendly platforms and tools for reporting. Furthermore, frequent

education and training sessions on recognizing, handling, and disclosing adverse drug reactions (ADRs) for medical professionals can greatly enhance the caliber and volume of reports (18). Improved coordination between hospital divisions and pharmacovigilance units is essential to guarantee thorough ADR data monitoring and analysis. Creating interdisciplinary teams to evaluate and analyze ADR reports and creating uniform procedures for ADR handling are two examples of this. Real-time data collection and analysis can be facilitated and reporting processes streamlined by incorporating pharmacovigilance procedures into clinical workflows and electronic health records. As the main contributors of adverse drug reactions (ADRs) in this study, high-risk drugs like antimicrobials, antihypertensives, and antidiabetics should receive priority attention when it comes to risk assessment and management techniques. Modified dosage regimens, substitute treatments, and improved patient monitoring are examples of tailored interventions that can reduce the dangers connected to these drug types (19).

Programs for patient education should also be created in order to educate people about the possible side effects of their medications and the significance of following doctor's orders. By enabling patients to identify and report ADRs as soon as they occur, this can help with early detection and intervention. Pharmacovigilance data should be used by regulatory bodies to update safety precautions, dosing guidelines, and drug labels. In order to guarantee the safe and efficient use of pharmaceuticals, regulatory decisions might be informed by ongoing monitoring and analysis of ADR trends (20).

Lastly, by routinely analyzing pharmacovigilance data and pinpointing areas for improvement, healthcare organizations should concentrate on continual quality improvement. This entails enhancing patient monitoring procedures, prescribing practices, and healthcare organizations' safety and alertness cultures. Healthcare practitioners can enhance pharmacovigilance procedures, lower the frequency of ADRs, and eventually enhance patient outcomes and safety by putting these suggestions into practice (21). The results highlight how important pharmacovigilance is for identifying, evaluating, and averting ADRs in order to improve patient safety (22). Risks can be reduced by early identification and prompt reporting, especially in high-risk populations. In addition to continuous monitoring, which can influence regulatory changes and enhance healthcare practices, patient education regarding medication dangers and adherence is crucial (23). This study emphasizes how important it is to maintain strong pharmacovigilance in order to enhance patient care, minimize unfavorable outcomes, and save healthcare expenditures (24).

6. Conclusion

This study looks at adverse drug reactions that were recorded in a hospital between March and August of 2023. There were 115 ADRs in total, recorded in different departments, with an average of 11 reports per month. The majority of complaints were from individuals between the ages of 18 and 65 and severity study revealed that 6.08% of them required hospital admissions or prolonged stays. Gastrointestinal issues were the most often affected system, while oral delivery was the most common route linked to adverse drug reactions. The most commonly implicated drug class was antimicrobials followed by antihypertensives.

References

1. Abu Hammour, K., El-Dahiyat, F., Hyari, R., Salameh, S., Manaseer, Q., Farha, R. A., … Zawiah, M. A retrospective analysis of the pharmacovigilance data registry in a tertiary teaching hospital in Jordan. *Journal of Pharmaceutical Policy and Practice*, 2024; *17*(1).
2. Kumar, B.N., Nayak, K., Singh, H., Dulhani, N., Singh, P., Tewari, P. "A pharmacovigilance study in medicine department of tertiary care hospital in Chhattisgarh (jagdalpur), India." *Journal of young pharmacists: JYP* 2010; vol. 2,1, 95-100. doi:10.4103/0975-1483.62222
3. Pathak, A.K., Kumar, M., Dokania, S., Mohan, L. and Dikshit, H. "A Retrospective Analysis of Reporting of Adverse Drug Reactions in a Tertiary Care Teaching Hospital: One Year Survey." *Journal of clinical and diagnostic research: JCDR*, 2016; vol. 10(8). doi:10.7860/JCDR/2016/18826.8284

4. Iftikhar, S., Sarwar, M.R., Saqib, A. and Sarfraz, M. Causality and preventability assessment of adverse drug reactions and adverse drug events of antibiotics among hospitalized patients: A multicenter, cross-sectional study in Lahore, Pakistan. *PLoS One*, 2018; *13*(6), p.e0199456.
5. Gupta, A., Kaur, A., Shukla, P. and Chhabra, H. Adverse Drug Reactions pattern in a tertiary level teaching hospital: A Retrospective Study. *Indian Journal of Pharmacy Practice*, 2017; *10*(1).
6. Jose, J. and Rao, P.G. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Pharmacological research*, 2006; *54*(3), pp.226-233.
7. Gor, A. P.; Desai, S. V.. Adverse Drug Reactions (ADR) in the inPatients of Medicine Department of a Rural Tertiary Care Teaching Hospital and Influence of Pharmacovigilance in Reporting ADR. Indian Journal of Pharmacology, 2008; 40(1):p 37-40, | DOI: 10.4103/0253-7613.40488
8. Arellano, A.L., Alcubilla, P., Farré, M. and Montané, E. Drug-related deaths in a tertiary hospital: Characteristics of spontaneously reported cases and comparison to cases detected from a retrospective study. *Journal of clinical medicine*, 2021; *10*(18), p.4053.
9. Smith CC, Bennett PM, Pearce HM, Harrison PI, Reynolds DJ, Aronson JK, et al. Adverse drug reactions in a hospital general medicine unit meriting notification to the Committee on Safety of Medicines. *Br J Cln Pharmacol.* 1996; 42:423–9.
10. Watson, S., Caster, O., Rochon, P.A., Rujiter, H.D. "Reported adverse drug reactions in women and men: Aggregated evidence from globally collected individual case reports during half a century." *EClinicalMedicine,* 2019; vol. 17. doi:10.1016/j.eclinm.2019.10.001
11. Prajapati, K., Desai, M., Shah, S., Panchal, J., Kapadia, J., Dikshit, R. "An analysis of serious adverse drug reactions at a tertiary care teaching hospital." *Perspectives in clinical research* vol. 2016; 7(4) 181-186. doi:10.4103/2229-3485.192044
12. Kourorian, Z., Fattahi, F., Pourpak, Z., Rasoolinejaf, M., Gholami, K. Adverse drug reactions in an Iranian department of adult infectious diseases. Eastern Mediterranean health journal, 2009; 15. 1351-7.
13. Petrova, G., Stoimenova, A., Georgiev, O., Dimitrova, M., Kamusheva, M., Petrova, D. "Assessment of the expectancy, seriousness and severity of adverse drug reactions reported for chronic obstructive pulmonary disease therapy." *SAGE open medicine,* 2017; vol. 5.
14. Bajracharya, S. R., Ghimire, R., Gyanwali, P. and Khadka, A. "Causality Assessment of Adverse Drug Reaction Using Naranjo Probability Scale: A Retrospective Study", *Medical Journal of Shree Birendra Hospital*, 2020; 19(1), pp. 16–19. doi: 10.3126/mjsbh.v19i1.21573.
15. Hacker, M. Adverse drug reactions. In *Pharmacology,* 2009; pp. 327-352. Academic Press.
16. Winterstein, A.G., Hatton, R.C., Gonzalez-Rothi, R., Johns, T.E. and Segal, R. Identifying clinically significant preventable adverse drug events through a hospital's database of adverse drug reaction reports. *American journal of health-system pharmacy*, 2002; *59*(18), pp.1742-1749.
17. Bailey, C., Peddie, D., Wickham, M.E., Badke, K., Small, S.S., Doyle-Waters, M.M., Balka, E. and Hohl, C.M. Adverse drug event reporting systems: a systematic review. *British journal of clinical pharmacology*, 2016; *82*(1), pp.17-29.
18. Palaian, S. Pharmacovigilance practices and activities: Issues, challenges, and future direction. In *Social and Administrative Aspects of Pharmacy in Low-and Middle-Income Countries*, 2018; pp. 145-162. Academic Press.
19. Kumar, V. Challenges and future consideration for pharmacovigilance. *J Pharmacovigilance*, 2013; *1*(1), pp.1-3.
20. Rohilla, A., Singh, N., Kumar, V., Sharma, M.K., Dahiya, A. and Kushnoor, A. Pharmacovigilance: needs and objectives. *Journal of Advanced Pharmacy Education and Research*, 2012; *2*(4-2012), pp.201-205.
21. Jose, J., Al Rubaie, M.H., Al Ramimmy, H. and Varughese, S.S. Pharmacovigilance: Basic concepts and an overview of the system in Oman. *Sultan Qaboos University Medical Journal*, 2021; *21*(2), p.e161.

22. Khan, L.M., Al-Harthi, S.E., Saadah, O.I., Al-Amoudi, A.B., Sulaiman, M.I. and Ibrahim, I.M. Impact of pharmacovigilance on adverse drug reactions reporting in hospitalized internal medicine patients at Saudi Arabian teaching hospital. *Saudi Med J*, 2012; *33*(8), pp.863-8.
23. Obebi Cliff-Eribo, K., Sammons, H., Star, K., Ralph Edwards, I., Osakwe, A. and Choonara, I. Adverse drug reactions in Nigerian children: a retrospective review of reports submitted to the Nigerian Pharmacovigilance Centre from 2005 to 2012. *Pediatrics and International Child Health*, 2016; *36*(4), pp.300-304.
24. Zheng, L., Jin, H.B., Guan, Y.Y. and Yang, J. Pharmacovigilance of cutaneous adverse drug reactions in associations with drugs and medical conditions: a retrospective study of hospitalized patients. *BMC Pharmacology and Toxicology*, 2022; *23*(1), p.62.