

Adverse Medication Response Recorded in a Referral Health Facility: An Observational Study

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Abstract:-

➤ Introduction:

The incidence of adverse drug reactions (ADRs) has significant implications for patient safety and public health. In 1937, the introduction of sulphanilamide for streptococcal infections marked a pivotal moment in drug safety. Present study assessed the pattern, causality and severity of the ADRs reported from a tertiary referral centre.

➤ Materials and Methods:

Study conducted at the Mahatma Gandhi Mission Medical College and Hospital Kamothe Navi Mumbai recorded the pattern of ADRs between January 2021 and December 2022. The data was collected from the ADR Monitoring Center using the suspected ADR reporting form, version 1.4 of IPC, Ghaziabad, India. The suspected ADR forms were assessed to understand the pattern of ADRs regarding the completeness score of the ADR form.

➤ Findings and Discussion:

A total of 111 ADRs were recorded, with 43.24% of cases falling within the age range of 21 to 40. Antimicrobial medications were the main culprits behind the majority of ADRs reported by the departments of dermatology and general medicine. Rashes, edema, and urticaria are among the skin-related symptoms among the most frequently reported adverse drug reactions (ADRs). 72.9% of instances were classified as mild, according to severity assessment, whereas 57.65% of ADRs were found to be likely.

➤ Conclusions:

Because ADRs represent a serious threat to public health, our study highlights the significance of pharmacovigilance in tracking and preventing them. Databases on a national and international level are enhanced by systematic, regular reporting and monitoring of ADRs. In order to raise awareness of ADRs among patients and healthcare professionals, spontaneous reporting is still essential.

Keywords:- Adverse Drug Reactions, Pharmacovigilance, Causality Assessment, Severity Assessment, Completeness Score.

I. INTRODUCTION

Sulphanilamide's 1937 discovery as a treatment for streptococcal infections marked a turning point in the advancement of patient safety. In order to gather international data on adverse drug reactions (ADRs), the World Health Organization (WHO) established the "Plan for International Drug Monitoring," or Pharmacovigilance, in 1968. In 1998, India became a member under the supervision of the Uppsala Monitoring Centre, which is based in Sweden¹.

"The science and activities relating to the Detection, Assessment, Understanding, and Prevention of adverse drug effects or any other possible drug-related problems" is the definition of pharmacovigilance, or PV².

In 2010, the Indian Ministry of Health launched the Pharmacovigilance Programme of India. For the Central Drugs Standard Control Organization (CDSCO) initiative, the Indian Pharmacopoeia Commission, Ghaziabad, has functioned as a National Coordinating Center (NCC) since April 15, 2011. In India, tertiary care facilities have established pharmacovigilance centers to track and prevent adverse drug reactions.³ Based on adverse drug reactions, pharmacovigilance is a scientific approach to evaluate the safety and effectiveness of drugs and other medical supplies.³ Because new medications are tested on small numbers of patients, their safety is uncertain at launch. However, adverse drug reactions (ADRs) are not identified until after a significant number of patients have been exposed to them during clinical trials.⁴

Any unwanted change brought on by a medication that occurs at normal human dose levels and requires therapy or dosage decrease is referred to be an adverse drug reaction. It might also function as a warning not to take the same medication in the future. Adverse drug reactions (ADRs) are the fourth most common cause of morbidity worldwide and the fifth most significant predictor of mortality in hospitals. 3.7% of all hospital admissions are caused by ADR. Of these, 1.8% are deadly.³ In India, the rate of ADR reporting is less than 1%, while the global rate is between 6 and 10%.⁴

ADRs are a serious public health concern in terms of mortality, morbidity, and costs. Adverse drug reactions (ADRs) are a potential with every new prescription a patient is prescribed. These reactions are unexpected. Because of

this, no drug is completely risk-free, even when used as prescribed by a physician.⁵ Therefore, it is essential to identify and document any adverse drug reactions observed during regular prescription use. The information gathered from this kind of systematic, ongoing ADR monitoring aids in building a national and eventually global ADR database with the goal of improving patient safety and serving as a resource for product labeling, modification, and ongoing patient education.⁴

Therefore, in a tertiary referral center, the current study evaluated the pattern of adverse drug responses, the cause of the reported ADRs, and their severity.

II. MATERIALS AND METHODS

➤ *This is a Cross-Sectional, Retrospective Study*

A. Inclusion Criteria

- All types of ADRs reported to the AMC, Mahatma Gandhi Mission Medical College, Kamothe, Navi Mumbai.
- All inpatient and outpatient ADRs were reported from various Mahatma Gandhi Mission Medical College and Hospital, Kamothe, Navi Mumbai departments during the period January 2021 to December 2022.

B. Exclusion Criteria

ADRs reported before January 2021 and after December 2022 shall be excluded.

This study was conducted in the Department of Pharmacology, Mahatma Gandhi Mission Medical College, Kamothe, Navi Mumbai. Approval of Institutional Ethics Committee and permission from the ADR Monitoring Centre of Mahatma Gandhi Mission Medical College, Navi Mumbai, were obtained before the initiation of the study.

ADRs recorded from the different clinical departments of Mahatma Gandhi Mission Medical College, Kamothe, Navi Mumbai were 111 in number. The ADR data, obtained from the AMC, using the suspected Adverse Drug Reaction reporting form, Version 1.4, IPC, Ghaziabad, India was collected during the period January 2021 to December 2022.

The suspected ADR forms were assessed to understand the pattern of the ADRs concerning completeness score of the ADR form, patient demographics, type of the reactions, department-wise reporting, ADRs reported as per drug categories and organ systems affected, various ADRs reported and Type of ADR reaction.

The reported ADR forms were also analyzed for their causality and severity associated with the ADRs. WHO UMC ASSESSMENT SCALE (categorized as Certain, Probable, Possible, or Unlikely) was used to assess the causality and Modified Hartwig and Siegel Severity Scale (broad categorized as "mild," "moderate," and "severe") was further used to assess the severity of each reported ADR.

The data was analyzed and entered into the Microsoft-Excel Sheet. The completeness score of the Individual case safety report (ICSR) was done by adopting a scale derived by Sachin Kumar Kuchya et al.⁶ (August 2017)

III. RESULTS AND DISCUSSIONS

In the current study, 111 ADRs were reported from the Mahatma Gandhi Mission Medical College & Hospital, Kamothe, Navi Mumbai clinical departments between January 2021 and December 2022. Distribution pattern of the patients reported males 58 (52.25%) to be in majority than females 53 (47.74%) (**Figure 1**).

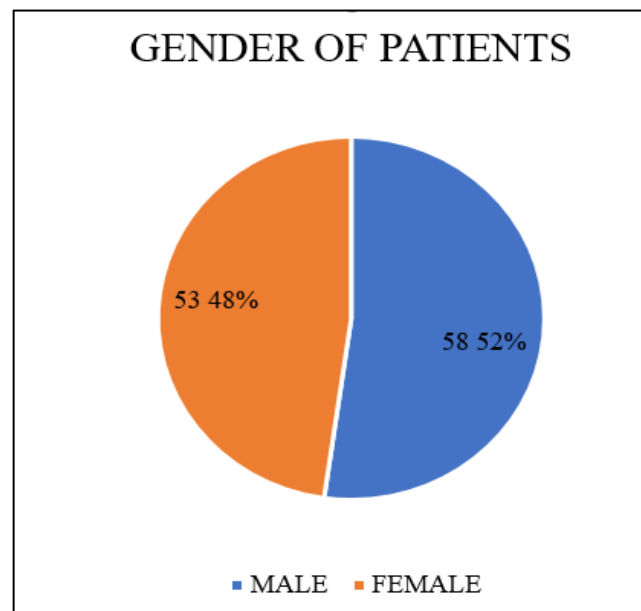


Fig 1: Gender of Patients

The age distribution in reported cases of ADRs observed in the range of ≤ 20 years of age (7.20%), 21-40 years age group (43.24%), 41-60 years of age group (33.33%), while in > 60 years of age group (16.21%). (**Figure 2**). The mean age of patients was 42.47.

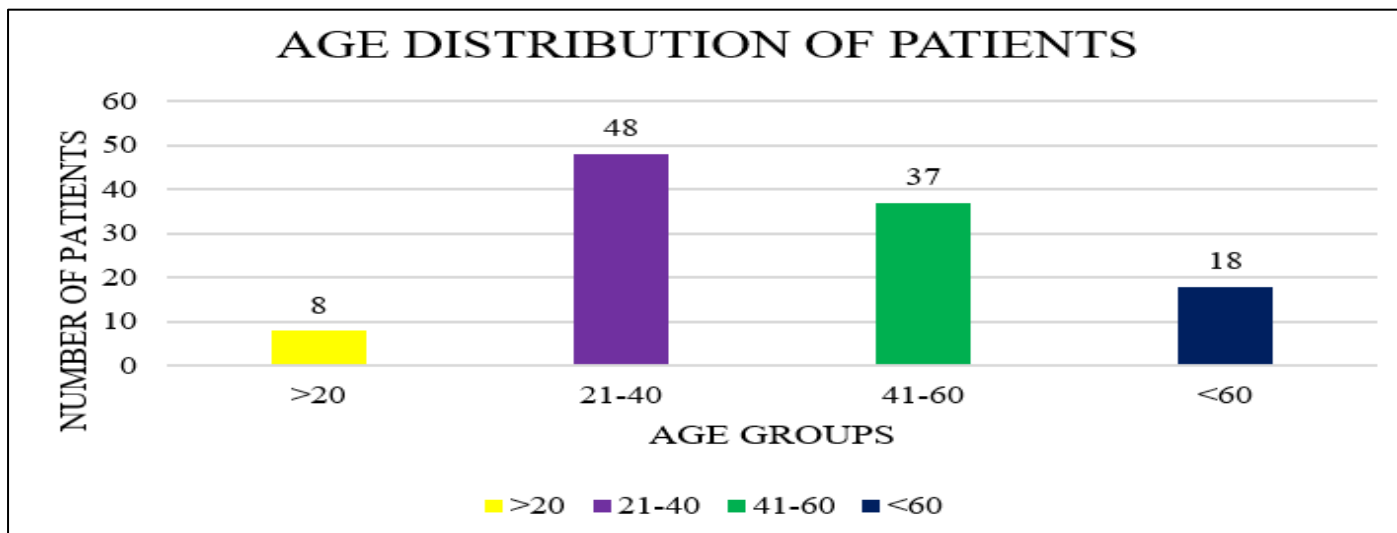


Fig 2: Age Distribution of Patients

Out of 111 ADRs, the majority of ADRs were implicated in Department of Dermatology 47 (42.34%), followed by of General Medicine 33 (29.72%), General Surgery 14 (12.6%), Psychiatry 7 (6.4%), Emergency Medicine 4 (3.60%), Respiratory 3 (2.70%), Nephrology 2 (1.8%), Cardiology 1 (0.9%). (**Figure 3**). The outcome observed in 111 patients who suffered ADRs was 20 Recovered, and 91 recovered.

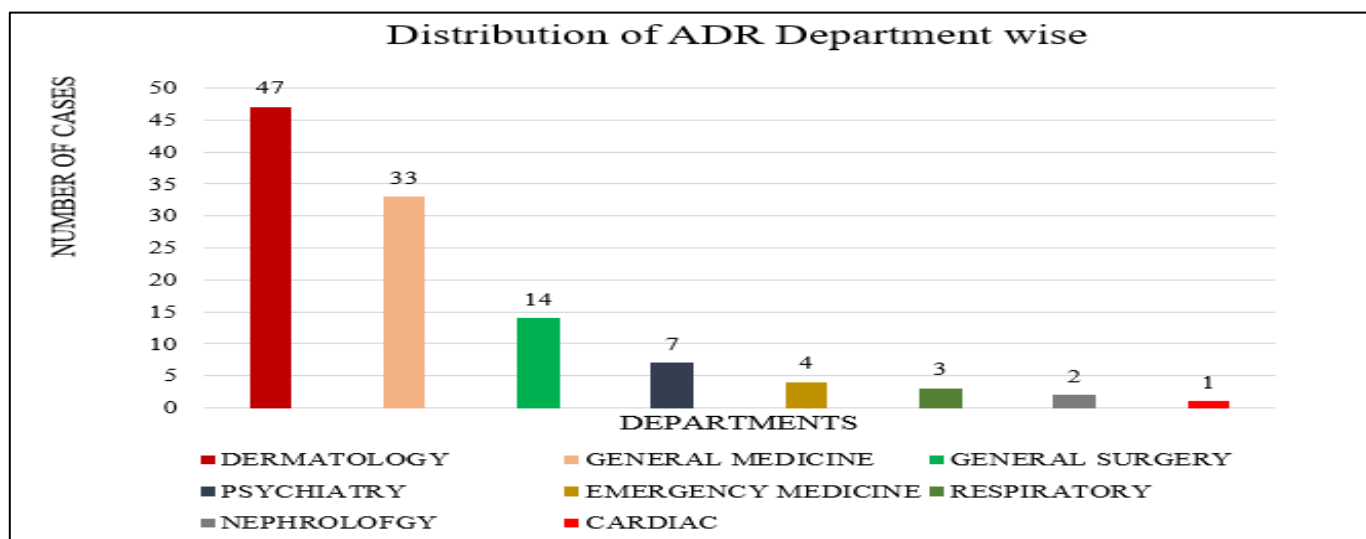


Fig 3: Distribution of ADRs

The most common drug class associated with ADRs were Antimicrobials 42 (37.8%). The other classes of drugs with ADRs includes NSAIDs 18 (16.2%), Anti-Tubercular 10 (9%), Anti-diarrheal 10 (9%), Anti-Psychotics 7 (6.3%), Anti-Epileptics 5 (4.5%) and Anti-Hypertensives 5 (4.5%).

The most commonly used drug associated with ADRs was Metronidazole 8 (7.2), followed by Amoxicillin and Clavulanic Acid 7 (6.3%), Diclofenac 6 (5.4%), Ceftriaxone 6 (5.4%), Ethambutol 5 (4.5), Isoniazid 5 (4.5%), Paracetamol 5 (4.5%), Cefixime 4 (3.6%), Phenytoin 7(6.3%), Ofloxacin 4 (3.6%), Metformin 3 (2.7%), Telmisartan 3 (2.7%), Rifampicin 3 (2.7%), Teneligptin 2 (2.7%), Atropine 2 (2.7%), Ciprofloxacin 2 (1.8%), Cefuroxime 2 (1.8%), Amikacin 2 (1.8%), Cycloserine 1 (0.9%).

The most common type of ADRs observed was Maculopapular Rash 17 (15.3%), followed by Vomiting 16 (14.4%), Headache 14 (12.6%), Dizziness 12 (10.8%), Nausea 10 (9%), Erythematous Papules 8 (7.2%), Diarrhea 7 (6.3%), Skin Lesions 5 (4.5%), Swelling of lips-face 5 (4.5%), Constipation 4 (3.6%), Epigastric Pain 3 (3.6%), Erythema 2 (1.8%), Indigestion 2 (1.8%), Gum Hyperplasia 2 (1.8%), Oedema 2 (1.8%), Urticaria 1 (0.9%). Further data were also analyzed for the Type of ADR collected (54, 48.6%), Type-1 (51, 45.9%), Type-2 (6, 5.4%), and Others.

The most affected Organ System due to ADRs was Skin 62 (58%), GIT 25 (22%), CNS 21 (18%) and Genitourinary tract 3 (2%).(**Figure 4**) According to WHO-UMC Causality Assessment Scale 2 (1.8%), sure, 64 (57.65%) probable, and 45 (40.54%) possible.(**Figure 5**).

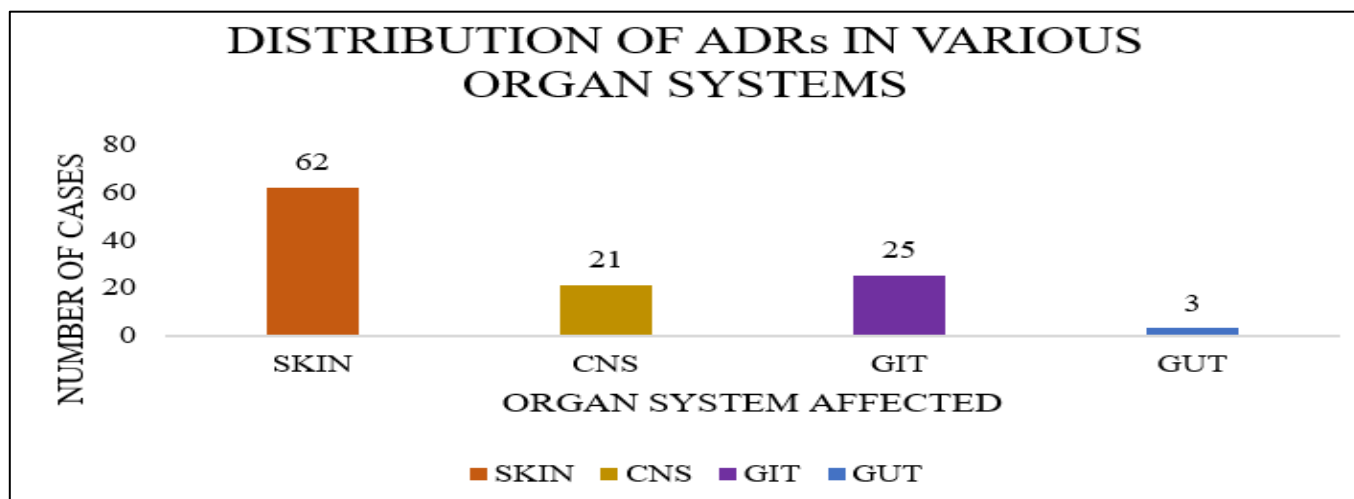


Fig 4: Distribution of ADRs in Various Organ System

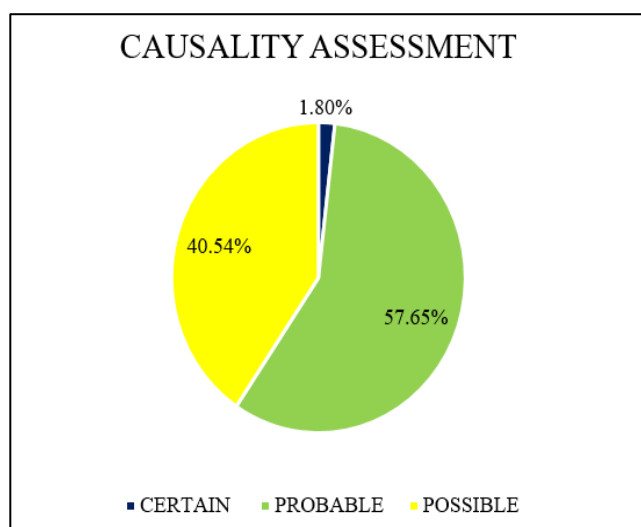


Fig 5: Causality Assessment

Most of the ADRs that were reported in the study were Mild 81 (72.9%), followed by Moderate 24 (21.6%), and 6 (5.4%) were Severe. The completeness score of the suspected adverse drug reaction reporting form was observed with an average of 35.29 ± 1.16 . (Figure 6)

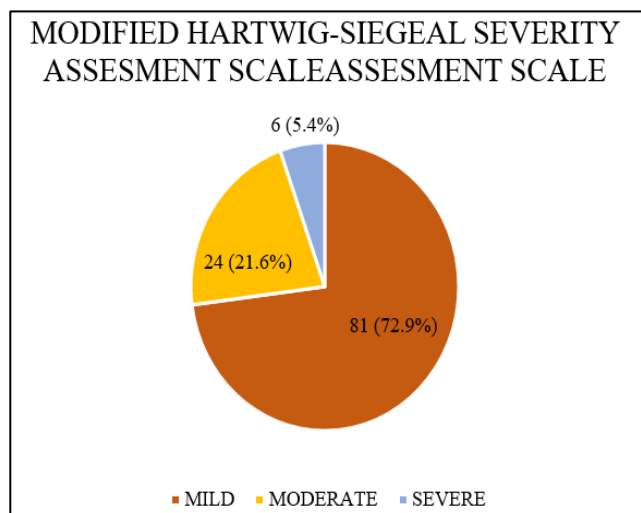


Fig 6: Modified Hartwig-Siegeal Severity Assessment Scale

The majority of drugs used in the pharmacotherapy of different disorders are probably going to have side effects in addition to benefits. A hospital's ability to gather data on adverse drug reactions (ADRs) can help to improve medication safety over time, analyze the frequency of ADR reports, and raise awareness of the issue among medical staff.

In the present study of 111 study participants, the mean age of patients was 42.47 years. The majority of the patients (43.24%) were in the age group of 21–40 years, which is similar to a study conducted by Vaishali S Thakare *et al.*⁷ Gender distribution of the patients were 58 Male (52.25%) and 53 (47.74%) female as reported by Rangeel Singh Raina *et al.*⁸, whereas Vaishali S Thakare *et al.*⁷ indicating female preponderance which is in contrast to most of the studies where there was male preponderance.

In the present study, the majority of the ADRs were from the Department of Dermatology 47 (42.34%), closely followed by General Medicine 33 (29.72%), General Surgery 14 (12.6%), Psychiatry 7 (6.4%), Emergency Medicine 4 (3.60%), Respiratory 3 (2.70%), Nephrology 2 (1.8%), Cardiology 1 (0.9%) were the least. This was observed to be similar to Rangeel Singh Raina *et al.*⁸ and Ankitha L⁹ studies, and this was in contrast to the Vaishali S Thakare *et al.*⁷ in which majority of the ADRs belonged to the Pulmonary Medicine Department.

According to Anjan Adhikari *et al.*, antimicrobials, which are the most prescribed medications, are also the main source of adverse drug reactions.¹⁰ On the other hand, anti-inflammatory drugs and immunosuppressive therapies were identified as the primary sources of adverse drug reactions (ADRs) in a different investigation⁽¹¹⁾.

In the present study, compiled data revealed that the most commonly used drug associated with ADRs was Metronidazole (7.2%), followed by Amoxicillin and Clavulanic Acid (6.3%), Ceftriaxone (5.4%), was the most used antimicrobial class used in the study, followed by Diclofenac (5.4%). Majority of the ADRs were mainly due to cephalosporins (36.5%), whereas fluoroquinolones were

accountable in 17 cases (20%)⁸. Another study conducted by Gupta AK et al.⁴ indicated maximum ADRs were due to anti-neoplastic and antimicrobials.

The majority of adverse drug reactions (ADRs) were dermatological, affecting both the skin and the appendages. These responses accounted for 58% of all reported cases and included the following main symptoms: urticaria, swelling of the lips and face, erythematous papules, skin lesions, and maculopapular rash. This study and the one by Ankitha L. et al. are comparable.⁹ AKT-induced hepatitis, AKT-induced hyperuricemia, and iron hypersensitivity were the most common adverse drug reactions (ADRs) in the study by Vaishali S. Thakare et al.⁷, which differed from ours in that it included GI disturbances such as vomiting, nausea, diarrhea, constipation, and indigestion. The results aligned with the research conducted by Gupta AK et al.⁴.

The Causality Assessment of the reported ADRs was done according to the WHO-UMC Scale., of which 2 (1.8%) were Certain, 64 (57.65%) were Probable, and 45 (40.54%) Possible, which differs from the study conducted by Moounika Nirumalla et al.¹², with (66.15) Possible, (29.23%) Probable, (4.6%) Certain.

Modified Hartwig and Siegel scale was used to assess severity of ADR and it was found that most of the ADRs were Mild 81 (72.9%), followed by Moderate 24 (21.6%) while 6 (5.4%) were Severe. A study by Vaishali S Thakare *et al.*⁷ observed that 58% of the patients had mild ADRs, followed by severe (30%) and moderate (13%).

The completeness score of the suspected adverse drug reaction reporting form was reported with an average of 35.29 ± 1.16 , which was similar to the study conducted by Vaishali S Thakare et al.⁷ in which they observed the completeness score with an average of 32.2 ± 2.6 .

The public health implications of a study on hospital-based surveillance of suspected ADRs are substantial. However, the main flaw in it is that it doesn't give precise adverse drug reactions for a given medication. But a better approach to get data would be through active surveillance. In order to inform and increase awareness among medical professionals, nurses, pharmacists, and even patients, spontaneous adverse drug reaction reporting is mandated in our nation.

IV. CONCLUSION

This was a retrospective study conducted at the author's institute (an AMC under PvPI, IPC, Ghaziabad, India) on the ADR reports received from January 2021 to December 2022.

ADR poses a serious obstacle to the effectiveness of treatment. To deal with this problem, a pharmacovigilance program was established. The Indian Pharmacovigilance Programme suffers from a significant underreporting problem. Creating long-term pharmacovigilance programs in hospitals and promoting awareness campaigns among healthcare workers at all levels are necessary in order to solve

this. Physicians should place a strong emphasis on anticipating, avoiding, identifying, reporting, and monitoring adverse drug reactions (ADRs) in order to reduce their frequency. The medical professional must always be on the lookout for adverse drug reactions (ADRs) and have a rigorous system in place for reporting them.

Furthermore, patients must be counselled for awareness on the understanding of ADRs and the timely medical attention needed for the same. Our study's shortcomings included its brief duration with a small sample size. We conclude that Anti-microbial, NSAIDs, Antitubercular, Anti-diarrheal, and psychotropic drugs are responsible for most of the ADRs, and the 21-40-year-old population is most commonly affected by ADR.

The average completeness score was 35.29. The completeness score can increase if the reporter considers their moral obligation.

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- **Conflicts of Interest:** There are no conflicts of interest.

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