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Original Article

Predictability, Severity and Causality Assessment of Adverse Drug Reactions Reported at a Tertiary Care Hospital in Belagavi, North Karnataka: A Prospective Observational Study

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ABSTRACT

Introduction: Adverse Drug Reactions (ADRs) present major challenges in healthcare, contributing significantly to hospital admissions and impacting a large number of inpatients. Monitoring ADRs often relies on electronic health records or specialized surveillance programs. Issues such as underreporting and delays highlight the need for robust ADR tracking, while advancements in technology offer new opportunities to enhance this process. Effective ADR monitoring and analysis are essential for ensuring patient safety and supporting regulatory decision-making. **Objectives:** To assess the predictability, severity and causality of ADRs using various scales. **Materials and Methods:** A Prospective Observational Study was conducted for a year at the ADR Monitoring Center (AMC) in a tertiary care hospital at Belagavi, under the PvPI. ADRs reported from both outpatient and inpatient departments were included, except those due to drug poisoning, blood products and alternative medicines. Data were collected and evaluated for causality, predictability and severity using appropriate scales. Descriptive statistics were employed for analysis. **Results:** A total of 706 ADRs were reported, with 56% in adults and 24% in the elderly. Males constituted 51.2% of the cases. Severity assessment using the Hartwig and Siegel Scale showed 63% mild, 35% moderate and 2% severe ADRs. Predictability assessment revealed 74% were predictable. Causality assessment based on the WHO-UMC scale classified 50.2% as probable, 38.9% as possible and 10.3% as certain. Gastrointestinal disorders were the most common ADRs (19.87%), followed by skin and subcutaneous tissue disorders (14.74%). Drug withdrawal was the most common action taken (52.92%), with 39.6% fully recovered patients. **Conclusion:** The study underscores the importance of comprehensive ADR monitoring and management. High predictability suggests many ADRs can be anticipated and prevented through meticulous risk assessment and patient monitoring. Personalized approaches to drug therapy and holistic patient monitoring are crucial to ensure patient safety and well-being.

Keywords: Adverse Drug Reactions, Causality, Hartwig and Siegel Scale, Predictability, Severity.

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INTRODUCTION

Adverse Drug Reactions (ADRs) described as "a 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" (Edwards and Aronson, 2000).

ADRs are significant in healthcare, accounting for 5% of all hospital admissions and affecting 10-20% of hospitalized patients. Among these patients, the total occurrence of serious ADRs is 6.7%, with fatal ADRs accounting for 0.32%. A study conducted in a tertiary care hospital in South India revealed that drug-related Adverse Drug Reactions (ADRs) accounted for 0.7% of total admissions, with 1.8% of these ADRs being fatal (Einarson, 1993; Lazarou *et al*., 1998; Kalaiselvan *et al*., 2016).

Reporting mechanisms encompass spontaneous reporting systems, enabling voluntary reporting of suspected ADRs by doctors, nurses, pharmacists and patients to regulatory agencies or drug manufacturers. Active surveillance involves systematic and proactive monitoring of patients for ADRs, often utilizing electronic health records or dedicated surveillance programs.

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Pharmacovigilance, a scientific discipline, focuses on detecting, assessing, understanding and preventing ADRs and other drug-related issues. Tracking and analysis involve causality assessment to evaluate the likelihood that a drug caused an ADR, signal detection to identify potential safety signals from reported ADRs and data analysis to uncover patterns, trends and correlations informing regulatory decisions or further research. Challenges like underreporting and timeliness, alongside opportunities from technology, underscore the importance of comprehensive ADR monitoring and analysis in ensuring patient safety and guiding regulatory decisions (Fossouo *et al.*, 2023; Sahu *et al.*, 2014).

The Pharmacovigilance Programme of India (PvPI), coordinated by the Indian Pharmacopoeia Commission, monitors drug safety and Adverse Drug Reactions (ADRs) nationwide. By collecting and analyzing ADR data, PvPI ensures safe medication use, promotes awareness, trains healthcare professionals and involves the public in enhancing drug safety measures (IPC, 2024).

Objectives

Study was conducted to monitor adverse drug reactions reported from various departments of a tertiary care hospital in Belagavi Karnataka. To analyze the Predictability, Severity and Causality assessment of ADRs as per various Scales.

MATERIALS AND METHODS

Study procedure

A prospective observational study was carried out at the ADR Monitoring Center (AMC) in a tertiary care hospital in Belagavi, North Karnataka. This center operates under the PvPI. The study spanned from January 2023 to December 2023. Permission was obtained from the PvPI chief Coordinator of the tertiary healthcare center to conduct this study. Ethical clearance was obtained from the Ethics committee (KLE/COP/EC/710/2022-23). Data pertaining to the adverse drug reactions, including seriousness, recovery status, drug details and outcomes, were evaluated and collected from the ADR reports. The collected data underwent evaluation for causality, predictability, seriousness, severity and outcome utilizing appropriate scales. Analysis was conducted employing descriptive statistics to summarize and interpret the findings.

Inclusion criteria

- ADRs from OPD and IPD departments of a Tertiary care hospital, Belagavi, Karnataka, India.
- ADRs observed across all age groups.

Exclusion criteria

- ADRs resulting from the use of blood or blood products.
- ADRs associated with alternative medicine systems such as Homeopathy, Ayurveda and Unani.

RESULTS

The demographic distribution of ADRs, as depicted in Table 1, underscores the varied susceptibility across different age groups. Adults comprise 56% of the reported ADR cases, followed closely by the elderly, constituting 24% of the total. Notably, while infants and adolescents exhibit lower incidences at 2% and 4% respectively, neonates are least affected at 0.42%. The gender distribution of ADRs shows a nearly equal representation between males and females. Specifically, males constitute 51.2% of the reported ADR cases, while females represent 48.72% of the total.

The severity assessment was conducted using modified Hartwig and Siegel Scale, indicates that the maximum of the ADRs were categorized as mild, accounting for 63% of cases. Moderate severity ADRs comprised 35% of the total, while severe ADRs were less frequent at 2% (Table 2).

The predictability of ADRs, categorized based on the types of reactions, indicates a significant proportion of ADRs were

Table 1: Details of demographic data of ADRs.

	Demographic variables	No of Patients (%) *n*=706
Age Group	Neonates	3 (0.42%)
	Infants	15 (2%)
	Child	90 (13%)
	Adolescent	31 (4%)
	Adult	397 (56%)
	Elderly	170 (24%)
Gender	Male	362 (51.2%)
	Female	344 (48.72%)

Table 2: Predictability, Severity, Causality Assessment.

Scales	Types	No. of ADRs (%)
Severity assessment by Hartwig and Siegel Scale	Mild	445(63%)
	Moderate	244 (35%)
	Severe	16(2%)
Predictability as per types of ADRs.	Non-Predictable	185 (26%)
	Predictable	521 (74%)
Seriousness as per WHO-UMC Scale.	Serious	269 (38.01%)
	Non-serious	437 (61.9%)
Causality Assessment as per WHO-UMC scale.	Certain	73 (10.3%)
	Probable	355 (50.2%)
	Possible	275 (38.9%)
	Unlikely	3 (0.004%)

Table 3: Action taken following the occurrence of adverse drug reaction.

Action Taken	ADRs
Drug Withdrawn.	383
Dose of the drug not changed.	211
Dose of the drug reduced.	57
Dose of the drug increased.	4
Not applicable.	51

Table 4: Outcomes of Adverse drug reactions.

Category	No of ADRs
Recovered	280 (39.6%)
Not recovered	85 (12%)
Recovering	333 (47%)
Resolved with sequelae	3 (0.004%)
Unknown	6 (0.008%)

predictable, comprising 74% of cases. Conversely, non-predictable ADRs accounted for 26% of instances. This distribution suggests that a substantial majority of ADRs can be anticipated based on known drug effects or patient characteristics, underscoring the importance of risk assessment and monitoring in clinical practice (Table 2).

According to the WHO-UMC Scale, Adverse Drug Reactions (ADRs) were categorized based on seriousness, revealing a notable proportion of serious cases at 38.01%. Conversely, non-serious ADRs constituted the majority, comprising 61.9% of the total (Table 2).

The causality assessment of ADRs based on the WHO UMC scale reveals a spectrum of causal relationships. The majority of ADRs were classified as probable, accounting for 50.2% of cases, followed by possible ADRs at 38.9%. Smaller proportions were deemed certain (10.3%), while only a negligible fraction was categorized as unlikely (0.004%) (Table 2).

The actions taken following the occurrence of Adverse Drug Reactions (ADRs) are crucial for patient safety and management. The data indicates that the most common action taken was withdrawing the drug, accounting for 52.92% of cases. In contrast, the dose of the drug remained unchanged in 29.63% of instances, while it was reduced in 7.98% of cases and increased in 0.56%. Additionally, in 9.22% of cases, no specific action was applicable. These percentages reflect the diverse approaches taken by healthcare professionals in response to ADRs, emphasizing the importance of tailored interventions based on the severity and nature of the adverse event (Table 3).

The outcomes of ADRs, as outlined in Table 4, demonstrate various states post-ADR occurrence. The majority of ADR cases, accounting for 333(47%) of instances, were classified as "Recovering," indicating ongoing improvement. Additionally,

Table 5: Classification of ADRs as per systemic class.

Adverse Event (SOC)	Number of reports
Gastrointestinal disorders.	155
Skin and subcutaneous tissue disorders.	115
Nervous system disorders.	98
General disorders and administration site conditions.	81
Metabolism and nutrition disorders.	61
Respiratory, thoracic and mediastinal disorders.	42
Blood and lymphatic system disorders.	37
Investigations.	30
Musculoskeletal and connective tissue disorders.	23
Vascular disorders.	23
Renal and urinary disorders.	22
Infections and infestations.	18
Eye disorders.	12
Psychiatric disorders.	15
Injury, poisoning and procedural complications.	10
Endocrine disorders.	10
Hepatobiliary disorders.	10
Cardiac disorders.	8
Immune system disorders.	5
Ear and labyrinth disorders.	3
Reproductive system and breast disorders.	2
	780

a significant portion, comprising 280(39.6%) of cases, were "Recovered" from the ADRs. Conversely, a smaller fraction, at 85(12%), remained "Not recovered." Furthermore, a small number of cases, 3(0.004%), resolved with sequelae, while the outcome was categorized as "Unknown" in 6(0.008%) of instances (Table 4).

The classification of adverse drug reactions based on systemic classes provides valuable insights into the diverse physiological systems affected by medication use. Gastrointestinal disorders stand out as the most frequently reported ADR, comprising 19.87% of the total reports. Underscoring the frequent occurrence of gastrointestinal symptoms such as nausea, vomiting and diarrhea. Skin and subcutaneous tissue disorders follow closely behind, representing 14.74% of the reports, indicating a substantial incidence of dermatological reactions like rash and itching. Nervous system disorders such as giddiness and headache and general disorders/administration site conditions account for 12.56% and 10.38% respectively. Other notable System Organ

Class (SOC) includes metabolism and nutrition disorders (7.82%), respiratory disorders (5.38%) and blood and lymphatic system disorders (4.74%). Collectively, this data underscores the diverse range of ADRs affecting patients and the importance of systematic monitoring and management across various systemic classes to ensure patient safety and well-being (Table 5).

DISCUSSION

The analysis of ADRs in this study provides significant insights into their demographic distribution, severity, predictability, causality and the affected systemic classes. In total of 706 ADRs, around 397 ADRs were observed in adults, followed by the elderly population. This observation contrasts with previous studies that reported a higher incidence of ADRs at a young age (S P *et al.*, 2013; Kumar *et al.*, 2017). The gender distribution in this study showed a greater occurrence of ADRs in males (362, 51.2%), aligning with findings from a study by Jindal *et al.* (55.86%) (Jindal *et al.*, 2023). However, Verma *et al.* (2014) reported a higher incidence in females (56%) (Verma *et al.*, 2014).

Regarding the outcomes of ADRs, most patients showed recovery after the offending drug was withdrawn and the ADRs were treated. This is consistent with the general approach to managing ADRs, where drug withdrawal is a primary intervention.

Causality assessment by the WHO-UMC scale revealed that, 355 (50.2%) were probable and 275 (38.9%) ADRs were possible. This distribution is in contrast to a finding by Venkatsubbaiah *et al.*, who reported 48.82% of ADRs were possible and 27.17% were probable ADRs (Meda *et al.*, 2018). Similarly, Mahesh N. Belhekar *et al.* found 68.8% possible ADRs and 24% probable ADRs (Belhekar *et al.*, 2019).

The severity assessment using the Modified Hartwig and Siegel scale indicated that 244 (35%) ADRs were moderate, 445 (63%) were mild and 16 (2%) were severe. Comparable results were shown by a study conducted by Kechi *et al.*, with 53.81% moderate and 1.39% severe ADRs as per the Modified Hartwig and Siegel Severity Scale (Keche *et al.*, 2021). Similar conclusions was stated in a study carried out by (Palappallil *et al.*, (2016).

Antimicrobials were associated with the highest number of ADRs (32.29%). This finding is in line with Palappallil *et al.*, study where antibiotics were causing ADRs in 33% of patients (Palappallil *et al.*, 2017).

In the present study, 74% of ADRs were predictable, according to the types of ADRs. This predictability rate is supported by previous studies, which reported 96.1%, 53% and 7.4% predictable ADRs, respectively (Du *et al.*, 2019; Rabbur *et al.*, 2005; Raut *et al.*, 2012). The classification of ADRs based on systemic classes showed that gastrointestinal disorders were the most common (19.87%), followed by skin and subcutaneous tissue disorders (14.74%) and nervous system disorders (12.56%). This differs from the findings of Ratan J. Lihite *et al.*, who reported 63.52% skin-related ADRs and 15.29% nervous system-related ADRs (Lihite *et al.*, 2017).

Routine monitoring of patients, early diagnosis and selecting the best possible drugs from different groups can significantly minimize adverse drug reactions. Patients prescribed with a narrow therapeutic index and medicines affecting vital functions should be monitored strictly to ensure safety (Badar *et al.*, 2018).

CONCLUSION

The analysis of adverse drug reactions across various demographics provides crucial insights into the patterns and implications of these reactions, which are vital for enhancing patient safety and optimizing pharmacological interventions. The high predictability of ADRs suggests that many reactions can be anticipated and prevented through diligent risk assessment and patient monitoring. The demographic variations in ADR susceptibility underscore the necessity for personalized approaches to drug therapy. The diverse systemic classes affected by ADRs highlight the importance of holistic patient monitoring to ensure safety and well-being. Additionally, strengthening pharmacovigilance systems and promoting patient education on ADRs can contribute to early detection and timely intervention.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

ABBREVIATIONS

ADR: Adverse Drug Reaction; **OPD:** Outpatient Department; **IPD:** Inpatient Department; **PvPI:** Pharmacovigilance Programme of India; **AMC:** Adverse Drug Reaction Monitoring Center; **WHO-UMC:** World Health Organization-Uppsala Monitoring Centre; **IPC:** Indian Pharmacopoeia Commission; **SOC:** System Organ Class.

ETHICAL STATEMENT

Permission was obtained from the AMC - PvPI chief Coordinator of the tertiary healthcare center to conduct this study. Ethical clearance was obtained from KLECOPBGM Ethics committee (KLE/COP/EC/710/2022-23).

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