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Original Article

Strengthening Adverse Drug Reaction Reporting: Integrating Pharmacists with Physicians and Educating Future Healthcare Professionals on Pharmacovigilance

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Abstract

Underreporting of adverse drug reactions (ADRs) due to time constraints, limited awareness, reluctance, and legal fears demands integrating pharmacists with physicians and implementing an extensive continuing education module on pharmacovigilance for application-based learning. Our study aimed to integrate a pharmacist with a treating physician to enhance patient safety by facilitating ADR reporting, providing a continuing education module on pharmacovigilance to senior residents and interns, and providing an ADR alert card to patients. We carried out a cross-sectional study over ten months in the general medicine department of a tertiary care hospital. We integrated Doctor of Pharmacy intern students with treating physicians to facilitate easy identification of ADR and for issuing ADR alert cards. We provided a seven-day continuing education module on pharmacovigilance concepts for senior residents and final-year medical interns. We distributed an ADR alert card to 180 patients. The largest groups of patients affected by ADRs in our study were aged between 41-50 and 51-60 years, collectively accounting for nearly 50% of the affected population. Our study reported a slight female predominance (51.1%). The gastrointestinal system (31.1%), nervous system (20%), and skin and subcutaneous tissue (13.9%) were the most frequently affected organ systems, accounting for 65% of the ADRs. Most ADRs (92.2%) were not serious. Analgesics (aspirin), HMG-CoA inhibitors (atorvastatin), and antiepileptics (phenytoin) were the top three drug classes most associated with ADRs. Out of 23 participants, 21 (91.3%) correctly completed the reporting of ADR into the ADR form from anonymous case reports, identified predisposing factors, assessed causality correctly, and suggested prevention and management strategies according to the clinical scenario. Most participants (95.7%) indicated that the module significantly enhanced their awareness and comprehension of Pharmacovigilance concepts, with only a small percentage (4.3%) expressing neutral sentiment and none disagreeing. Integrating pharmacists, continuing pharmacovigilance education, and issuing ADR alert cards significantly enhanced ADR reporting, comprehension of pharmacovigilance concepts, and patient safety measures in the healthcare setting.

Keywords: Pharmacovigilance, World Health Organization-Uppsala Monitoring Center (WHO-UMC) scale, Continuing education, Underreporting, Aspirin, Phenytoin.

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1. Introduction

Healthcare professionals (HCPs) are the mainstay of the pharmacovigilance system and thus have a prominent role in it. However, not implementing adverse drug reaction (ADR) reporting as part of their daily practice is a major drawback of this system [1]. Sensitizing them by providing adequate knowledge and skills could play an important role in successfully implementing the program [2, 3]. Corrective measures for improving awareness and knowledge through continuing medical education (CME) [2] would help improve the reporting rates of ADRs.

Adverse drug reactions (ADRs) represent a major concern for patient safety, particularly within general medicine departments. The incidence rates range from 27% to 68% in these settings [4, 5]. Although these ADRs may not be fatal, they frequently contribute to extended hospital stays, patient suffering, and increased healthcare costs [4]. Underreporting of these ADRs by healthcare professionals hinders drug safety measures [5]. However, nurses and pharmacists are more proactive in reporting ADRs than physicians [6]. This is further supported by an increase in the reporting rates of ADRs by empowering pharmacists in ADR reporting [7]. Therefore, when pharmacists report adverse drug reactions, it helps to decrease underreporting and lessens the burden on physicians.

Apart from communicating the ADRs to the adverse drug reaction monitoring center (AMC), it is equally important to communicate the same information to the patient. An ADR alert card can play an essential role here. These cards will inform healthcare providers of the patient's susceptibility to certain ADRs, particularly in emergencies, and influence the choice of therapy [8]. Studies have also shown that these interventions can significantly improve the reporting and management of ADRs and thus contribute to better clinical outcomes [8].

Considering the underreporting of ADRs due to physicians' time constraints, limited awareness of reporting protocols, reluctance to report known reactions, and fear of legal consequences [9], integrating a pharmacist with a physician is beneficial. Additionally, studies from India have examined the knowledge, attitudes, and practices regarding pharmacovigilance among various groups, including resident doctors [1], postgraduate medical students [3], and undergraduates and interns [10]. Notably, these studies did not include a continuing education module for participants. Recent studies have begun addressing this gap: Shenoy et al. [11] introduced a one-hour educational program for doctors and nurses, while Hingorani et al. [2] implemented a two-hour training session for resident doctors. However, to adequately cover the essential concepts of pharmacovigilance and ensure practical, application-based learning, a continuing education module necessitates a significant time allocation. Therefore, our study aimed to integrate a pharmacist with a treating physician to enhance patient safety by facilitating ADR reporting, providing a continuing education module on pharmacovigilance to senior residents and interns, and providing an ADR alert card to patients.

2. Materials and Methods

2.1. Study Design and Setting

We carried out a cross-sectional study over ten months, from August 2023 to March 2024, in the general medicine department of a tertiary care hospital. We used convenience sampling to collect data on adverse drug reactions (ADRs) from 180 patients. Participants were adults aged 18 or older, of any gender, who were taking at least one medication and had experienced a likely ADR related to their medication.

2.2 Seriousness of Adverse Drug Reaction

An ADR is considered serious if it satisfies any of the following criteria:

a) The ADR is the cause of death

b) The ADR causes life-threatening conditions

c) The ADR is the cause of hospitalization or prolongation of hospitalization

d) The ADR is the cause of congenital anomaly

e) The ADR is the cause of the disability

f) The ADR causes any other medically important event

2.3 Outcomes of the adverse drug reaction

We considered the following outcomes of an ADR:

(a) Recovered (b) Recovering (c) Not recovered

(d) Fatal (e) Recovered with sequelae

(f) Unknown

2.4 Causality of the adverse drug reaction

The causality of the adverse drug reaction was assessed using the World Health Organization Upsala Monitoring Center (WHO-UMC) causality scale. This causality assessment scale is widely used to assess causality in individual case safety reports (ICSR). The various causality categories of the WHO-UMC scale are as follows: "certain," "probably/likely," possible," “unlikely,” “conditional/unclassified,” and “unassessable/unclassifiable.” One author (MVK) trained on the signal detection and causality assessment from the WHO-UMC online course and assessed the causality of reports. When we encountered uncertainty in determining the causality, a pharmacovigilance associate from the nearby adverse drug reaction monitoring center (AMC) and a physician guided us through the process.

2.5. Integrating a pharmacist with a treating physician

We integrated each Doctor of Pharmacy intern student with a treating physician. There are four general medicine outpatient departments. The primary responsibility of these students was to identify any ADRs by taking the best possible medication history from the patients. Once they identified any ADR, they would discuss it with the treating physician and team and provide an ADR alert card to the patient. The identified ADR would be reported on a suspected adverse drug reaction reporting form and submitted to the nearby adverse drug reaction monitoring center (AMC).

2.6 Adverse Drug Reaction Alert Card

Patients who experienced an ADR received an alert card containing their name, OP number, age, gender, blood group, contact number, the date the card was issued, the date of reaction, description of the reaction, suspected drugs, and the name and signature of the doctor or reporter. Patients can use this alert card during subsequent visits to any physician. This helps the physician identify drug allergies, a predisposing factor for an ADR and allows for the selection of a more suitable medication for the patient.

2.7 Continuing education on the prevention of ADRs

We sent the proposal for a continuing education module to senior residents and final-year intern students (39) in various departments. Only 23 of them actively participated in the module. We tested their knowledge of the pharmacovigilance concepts using a descriptive question. After completing the education module, we assigned two case reports on drug-induced ADR to each student. We asked them to report the ADR in an ADR reporting form to identify predisposing factors, causality, prevention, and management of ADRs. We then gathered feedback from them on the education module.

We provided a continuing education module (CEM) for the senior residents and intern students (MBBS final year) on the pharmacovigilance concepts for seven days (two hours each day). We adopted the educational content for CEM based on Herrera [12]. We provided a case study-based adverse drug reaction (ADR) reporting system and a real-time ADR reporting system for senior residents and interns. We also included educational content on identifying potentially inappropriate drugs using potentially inappropriate medications (PIM) list/criteria. For example, we provided information on the Screening Tool of Older Persons' Prescriptions (STOPP) criteria to identify PIM in the elderly.

2.8 Data collection and data analysis

We collected information on age and gender from the patient's case sheet. The information on the suspected drug of the ADR, description of the reaction, seriousness, and outcomes of the reaction, and causality of the reaction were collected in a suspected adverse drug reaction reporting form to report to the nearby AMC. Data were analyzed and presented as frequencies, percentages, and visual graphs where applicable.

2.9 Ethical approval

The Institutional Ethical Committee approved the study (VIPT/IEC/346/2023). We obtained written informed consent from the participants. We assured the participants about the confidentiality and privacy of their data.

3. Results and Discussion

The largest groups of patients experiencing adverse drug reactions were between the ages of 41-50 (n=42) and 51-60 (n=43), together accounting for nearly 50% of the affected population. Females (51.1%) slightly outnumbered males (48.9%) (**Figure 1**). The organ systems with the most adverse drug reactions (ADRs) were the gastrointestinal system (31.1%), followed by the nervous system (20%), and the skin and subcutaneous tissue (13.9%). These organ systems collectively comprised 65% of the ADRs. The top three drugs most associated with different ADRs were aspirin, atorvastatin, and phenytoin (**Table 1**, **1a**, and **1b**). Most ADRs were not serious (92.2%), and 36.1% of patients recovered.

Table 1. Adverse drug reactions (ADR) based on organ system and the suspected drug**.**

Organ System	Name of the ADR	Name of the suspected drug	Total
Cardiovascular System	Ankle edema (1) Tachycardia (1) Pedal edema (4) Embolic stroke (1)	Labetalol Cilostazol Amlodipine, Atorvastatin, Enalapril, Aceclofenac Nicoumalone	7
Ocular System	Redness of eye (3) Blurred vision (1) Ocular toxicity (1) Ocular gyrus (1)	Paracetamol Mannitol Ethambutol Risperidone	6
Urinary System	Dysuria (5) Haematuria (1)	Amitriptyline, Diclofenac Nicoumalone	6
Endocrine System	Polydipsia (3) Hypoglycemia (2)	Furosemide Insulin, Mixtard	5
Hematologic System	Petechiae (3) Neutropenia (1)	Doxycycline Clozapine	4
Reproductive System	Erectile Dysfunction (1) Vaginal discharge (2)	Risperidone Prednisolone, Azithromycin	3

Table 1a. Adverse drug reactions (ADR) based on organ system and suspected drug**.**

Organ System	**Name of the ADR**	**Name of the suspected drug**	**Total**
Gastrointestinal System	Constipation (10) Diarrhea (7) Epigastric pain (7) Bloating (6) Abdominal Pain (5) Dyspepsia (4) GERD (3) Gastritis (3) Vomiting (3) Hepatitis (2) Sialorrhea (2) Xerostomia (2) Anorexia (1) Severe Nausea (1)	Ondansetron, Pregabalin, Sucralfate, Fluconazole, Itraconazole Amoxicillin, Sitagliptin, Spironolactone, Pantoprazole, Sodium valproate Aspirin, Clopidogrel, Atorvastatin Atenolol, Enalapril, Sitagliptin Pantoprazole, Aspirin , Cefixime, Azithromycin Aspirin, Ondansetron, Cefoperazone + Sulbactam Aspirin, Pantoprazole Aspirin, Amoxicillin Pantoprazole, Metronidazole HRZE Carbamazepine, Domperidone Cetirizine, Chlorpheniramine, Atorvastatin, Aspirin	56
Nervous System	Paresthesia (8) Dizziness (9) Acute Dystonia (1) Drowsiness (1) Dystonia (3) Headache (1) Slurred Speech (2) Somnolence (2) Tinnitus (1) Tremors (5) Vertigo (3)	Amlodipine, Methyl cobalamine, Ondansetron, Furosemide, Metoprolol Amlodipine, Quetiapine, Chlorpheniramine Olanzapine Chlorpheniramine Chlorpromazine, Haloperidol Sodium Valproate Carbamazepine, Risperidone Cetirizine Streptomycin Lithium Carbonate, Olanzapine, Risperidone, Chlorpromazine, Pregabalin	36

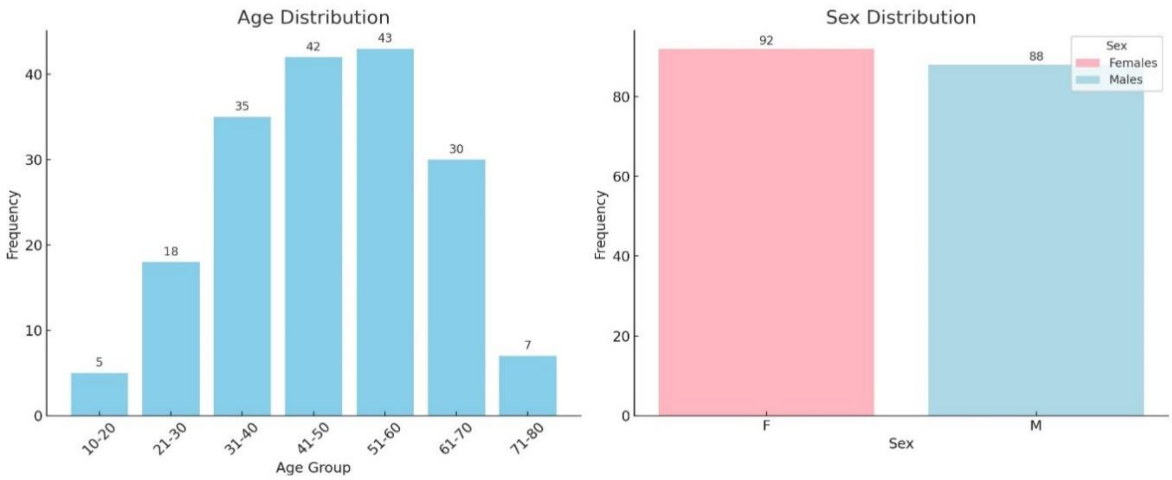

Figure 1. Age-wise and Sex-wise distribution of patient population.

Table 1b. Adverse drug reactions (ADR) based on organ system and suspected drug**.**

Organ System	Name of the ADR	Name of the suspected drug	Total
Skin and Subcutaneous Tissue	Skin rashes (5)	Hydroxyurea, Rifampicin, Prednisolone, Olanzapine	25
	Itching (5)	Aspirin, Ciprofloxacin, Phenytoin	
	Exfoliative dermatitis (4)	Phenytoin	
	Erythema (2)	Phenytoin, Aspirin	
	Facial Edema (2)	Atorvastatin	
	Urticaria (2)	Pantoprazole	
	Itchy rash (2)	Clexane	
	Palmar erythema (1)	Phenytoin	
	Diaphoresis (1)	Glimepiride	
	Severe itching (1)	Phenytoin	
Respiratory System	Non-productive cough and Cough (12)	Enalapril	19
	Pharyngitis (5)	Formoterol fumarate dihydrate + Budesonide	
	Rhinitis (1)	Teneligliptin	
	Sleep Apnea (1)	Tramadol	
Musculoskeletal System	Myalgia (7)	Metformin, Atorvastatin	13
	Arthralgia (4)	Amlodipine	
	Polyarthritis (1)	Atorvastatin	
	Pain in upper limbs (1)	Risperidone	

The causality of more than half of the cases (57.2%) was possible (**Figure 2**). Most participants (95.7%) indicated that the module significantly enhanced their awareness and comprehension of Pharmacovigilance concepts, with only a small percentage (4.3%) expressing neutral sentiment and none disagreeing (**Table 2**).

The largest groups of patients affected by ADRs in our study were aged between 41-50 and 51-60 years, collectively accounting for nearly 50% of the affected population. Studies have reported different age groups ranging from 19-39 years [13], 30-60 years [14], the adult age group [15], and patients over 60 years of age [16]. It is well established that comorbidity, geriatric syndromes, cognitive and functional deficits, and pharmacokinetic and pharmacodynamic changes predispose the elderly to an increased risk of iatrogenic illness [17].

However, in our study, 40-60 years are more affected due to health conditions, healthcare-seeking behavior, and compliance and adherence. For example, cognitive impairment in the elderly can lead to underreporting of ADRs [18].

Our study reported a slight female predominance. In contrast, other studies have reported varying degrees of predominance, including contrasting male predominance [13] and similar female predominance [15].

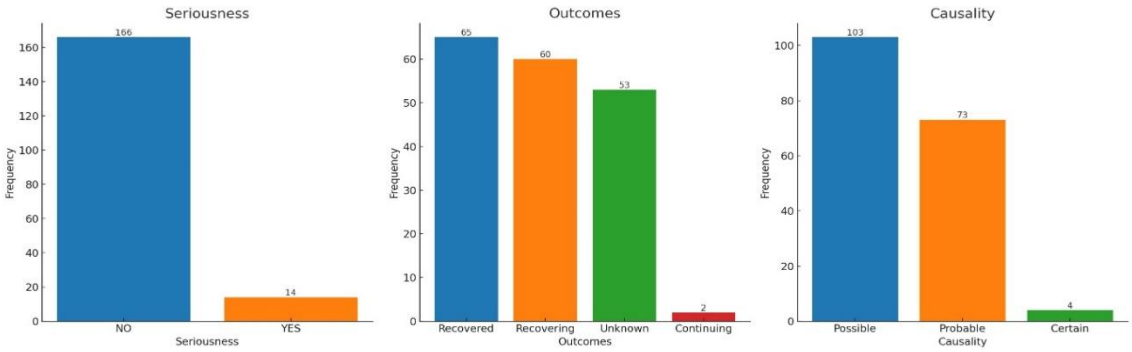

Figure 2. Seriousness, Outcomes, and Causality of adverse drug reactions.

Table 2. Feedback survey on the effectiveness of the continuing education module among the senior residents and final-year intern students (n=23)**.**

Question	Agree	Neutral	Disagree
The module provided a comprehensive understanding of the scope and aims of Pharmacovigilance	22 (95.7%)	1 (4.3%)	0
The classification of Adverse Drug Reactions (ADRs) was explained in a clear and understandable manner	20 (87%)	1 (4.3%)	2 (8.7%)
The predisposing factors for ADRs were adequately covered, and their importance was highlighted	21 (91.3%)	0	2 (8.7%)
The module helped me understand the basic principles of Causality Assessment and its significance in Pharmacovigilance	19 (82.6%)	2 (8.7%)	2 (8.7%)
The WHO algorithm and Naranjo's Causality Assessment Scale were explained in detail, ensuring a thorough understanding of their applications	18 (78.3%)	3 (13.0%)	2 (8.7%)
The process and importance of reporting ADRs were effectively communicated through the module	22 (95.7%)	0	1 (4.3%)
The Pharmacovigilance Programme of India and its role were adequately covered in the module	23 (100%)	0	0
The module provided valuable insights into Drug Therapy Problems and their impact on patient safety	18 (78.3%)	3 (13.0%)	2 (8.7%)
The discussion on Potentially Inappropriate Medications lists for special populations was informative and relevant	21 (91.3%)	1 (4.3%)	1 (4.3%)
The module's coverage of the severity and preventability of ADRs, along with the associated scales, was comprehensive and practical	20 (87%)	2 (8.7%)	1 (4.3%)
Overall, the module improved my awareness and understanding of Pharmacovigilance concepts	22 (95.7%)	1 (4.3%)	0

There are gender-based differences in biological, psychological, and cultural factors, including sex differences in pharmacokinetics (PK) and pharmacodynamics (PD), endogenous sex-specific hormone exposure, exogenous steroid administration, genetics, immunity, and polypharmacy, women being more affected than men [19, 20]. This is further supported by higher blood drug concentrations and longer drug elimination times in women when administered a standard adult dose of the drug [20].

In our study, the gastrointestinal system (31.1%), nervous system (20%), and skin and subcutaneous tissue (13.9%) were the most frequently affected organ systems, accounting for 65% of the ADRs. Similarly, a few studies reported gastrointestinal disorders as predominant ADRs [16, 21]. However, other studies have highlighted varying patterns, such as metabolic and hepatic systems [14], skin-related reactions [13, 15], and cutaneous disorders followed by general, vascular, and cardiac disorders [22]. The intimate contact between drugs and food in the GI tract contributes to the increased susceptibility of the gastrointestinal system to adverse drug reactions. Phytochemicals from the food have been shown to inhibit drug metabolism and active efflux mechanisms in the GI tract and lead to increased systemic drug exposure, consequently enhancing the therapeutic effects and potential toxicity of drugs [23]. Additionally, drugs can induce changes in gastric motility, affecting the rate of gastric emptying, which contributes to the susceptibility of the gastrointestinal system to adverse drug reactions [24].

Most ADRs (92.2%) were not serious in our study. Similarly, a few studies reported no fatal ADRs [16, 25]. In contrast, other studies reported the incidence of severe ADRs [14, 22]. Tongaonkar et al. [14] reported a higher recovery rate (54%) than our study (36.1%). More than half of the cases in our study (57.2%) showed “possible” causality using the WHO-UMC scale. However, many studies used Naranjo’s scale and reported “probable” causality as a predominant category [14, 15, 25]. Completing causality assessment using the WHO-UMC scale is shorter than the Naranjo scale [26, 27]. Furthermore, the simplicity and ease of use of WHO-UMC criteria make it preferable to the Naranjo scale by clinicians in day-to-day practice [26].

Our study identified analgesics (aspirin), HMG-CoA inhibitors (atorvastatin), and antiepileptics (phenytoin) as the top three drug classes most associated with ADRs. In contrast, other studies have reported oral hypoglycemics and antitubercular drugs [14], antibiotics [13,15, 16, 21, 22], antithrombotic agents [22], and cardiovascular agents and central nervous system agents [21] as the most associated drugs with ADRs. The class of drugs most frequently associated with adverse drug reactions (ADRs) varies based on factors such as the hospital's formulary, prevalent disease conditions, and patients' clinical status. For example, James et al. [15] reported beta-lactam antibiotics as the most implicated drug class of ADRs because they were widely used in general medicine and as prophylaxis for various infections in their study. Similarly, in our study, the age group between 40 and 60 comprises a significant portion of the population. This group is at a higher risk of developing lifestyle-related diseases like hyperlipidemia, for which atorvastatin is a commonly prescribed treatment. Therefore, atorvastatin is likely to be one of the main drugs contributing to ADRs in this age group.

In our study, we distributed an Adverse Drug Reaction (ADR) alert card to 180 patients. The cases that were deemed preventable had a history of similar reactions following the intake of the same drug, indicating a lack of awareness. This could have been mitigated through patient education and the issuance of a drug alert card [28]. An ADR alert card is a form of risk communication whereby any HCPs communicate an ADR episode in a written form to the patient or family. It is an important aspect of ADR management. The key goal is to eliminate or minimize re-exposure to the offending and structurally related medications [29]. ADR alert cards enhance patient safety by providing critical information on known drug allergies or adverse drug reactions [30]. They are vital in emergencies where patients cannot communicate [31]. Additionally, introducing ADR alert cards can increase the number of reported ADRs, as evidenced in a few studies [32, 33].

However, if ADR alert cards are not kept up-to-date or are incomplete, they can lead to miscommunication and potentially harmful clinical decisions. For instance, if a new allergy develops and is not recorded, healthcare providers might unknowingly prescribe a harmful medication [34]. The HCPs may overly rely on the ADR alert cards and neglect thorough patient interviews, which can be problematic if the card is lost, damaged, or not updated.

After completing the continuing education module, the participants' understanding and knowledge were assessed. Out of 23 participants, 21 (91.3%) correctly completed the reporting of ADR into the ADR form from anonymous case reports, identified predisposing factors, assessed causality correctly, and suggested prevention and management strategies according to the clinical scenario. Furthermore, most participants (95.7%) indicated that the module significantly enhanced their awareness and comprehension of Pharmacovigilance concepts, with only a small percentage (4.3%) expressing neutral sentiment and none disagreeing.

Shenoy et al. [11] provided only one hour of educational training on Pharmacovigilance concepts and reported a statistically significant improvement in the knowledge of doctors on pharmacovigilance. However, some questions, like the number of medical device monitoring centers in India and the phases of clinical trials, may be less directly related to pharmacovigilance and more broadly to healthcare systems and research. Hingorani et al. [2] provided two hours of educational training and reported a statistically significant improvement in the knowledge of resident doctors. However, the authors did not specify any information about the scoring of the knowledge domain and the validity and reliability of the questionnaire used to assess the knowledge. Our study provided a 14-hour continuing education on Pharmacovigilance concepts with case-based and real-time ADR reporting. Additionally, we assessed their knowledge using activity-based learning rather than administering a questionnaire. This approach improves knowledge retention and recall abilities and enhances problem-solving skills [35].

Our study has a few limitations. We only assessed the knowledge of few senior residents and final year intern students. The low participation rate in the continuing education module could affect the generalizability of the findings related to the module's effectiveness in improving knowledge of pharmacovigilance concepts. The study does not include a control group for comparison, which limits the ability to assess the impact of the educational intervention on improving knowledge and reporting of adverse drug reactions compared to standard practices.

4. Conclusion

We provided drug alert cards to every patient with an ADR. Most participants (91.3%) successfully reported an ADR in the ADR form, identified predisposing factors, assessed causality correctly, and suggested strategies for prevention and management according to the scenario. Integrating pharmacists, continuing pharmacovigilance education, and issuing ADR alert cards significantly enhanced ADR reporting, comprehension of pharmacovigilance concepts, and patient safety measures in the healthcare setting.

Conflict of interest

The authors declare to have no conflict of interest.

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