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Enhancing Adverse Drug Reaction Reporting in Tertiary Hospital in Saudi Arabia: An Evaluation of Methods and Strategies

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Abstract

Inadequate reporting of Adverse drug reactions (ADR) is a rampant phenomenon and undermines the hazards associated with it. With appropriate interventions, improved ADR reporting can prevent such untoward medicinal events. The study aimed to evaluate the impact of diverse interventions in improving ADR reporting in Prince Sultan Medical Military City (PSMMC), Riyadh, Saudi Arabia. ***Methods:*** An interventional study was conducted among nurses and pharmacists in *PSMMC*, Riyadh, Saudi Arabia, from January to December 2022. The study interventions included continuous training and education, technology function (trigger tool), patient interviews, and introduction of ADR reporting in annual performance evaluation with weekly feedback reports. A segmented regression analysis of an interrupted time series (12 observation points) established variation in average monthly ADR reporting between the first and second half of 2022. ***Results:*** The study yielded significant results, with 20,942 ADR reported between January 2022 and December 2022. The highest number of ADRs was documented in the second half of 2022 (n=14,555, 69.5%). After the interventions, the average number of reports per month increased by 35.8%**.** Cumulatively, a statistically significant difference was noted in the ADR reporting rate before and after interventions (30.4% versus 59.6%, $P < 0.0001$). The most effective intervention was an annual performance evaluation with weekly feedback reports. Most ADRs reported in 2022 were by pharmacists (76.1%). ***Conclusion:*** In conclusion, all interventions were found to improve the dynamics of pharmacovigilance by enhancing ADR reporting among nurses and pharmacists, with annual performance evaluation with weekly feedback reports being the ideal intervention.

Keywords: Adverse Drug Reaction; Reporting; Monitoring; Pharmacovigilance; Interventions; Saudi Arabia.

INTRODUCTION

Undoubtedly, therapeutic medicines have changed the dynamics of disease management and health and well-being; however, there is every so often a trade-off. With the restorative ability of these medicines, there are adverse effects that might be unwanted or unheard of, commonly called adverse drug reactions (ADR) (Edwards & Aronson, 2000; WHO). ADR substantially impact morbidity and mortality (Osanlou *et al.*, 2022). In 2014, the Alhawassi Study demonstrated that around 10%–20% of inpatients will have at least one ADR during their hospital stay (Bailey *et al.*, 2016). Nevertheless, repercussions of ADRs are fundamentally avoidable with apt measures (Aung *et al.*, 2022). In this regard, several nations have established pharmacovigilance centers, including Saudi Arabia (Alshammari *et al.*, 2017; Khan *et al.*, 2023; Walker *et al.*, 2023). Pharmacovigilance is defined as the *"science and activities relating to the detection, assessment,*

understanding, and prevention of adverse effects or any other medicine/vaccine-related problem" by the World Health Organization (WHO) (WHO). In hospital settings, episodes of ADRs are evaluated and notified to pharmacovigilance centers directly by healthcare providers such as doctors, nurses, and pharmacists, regarded as spontaneous ADR reporting (Aagaard & Hansen, 2009; Gedde-Dahl *et al*., 2007). To this end, several guidelines are present to raise the knowledge and understanding of healthcare providers about the burgeoning issue of poor ADR reporting and its consequences. The WHO's 'Safety of Medicines' manual offers standard suggestions for examining, evaluating, and notifying ADR reports (Organization, 2002). Also, the WHO pharmacovigilance indicators guide exists those aids in managing pharmacovigilance functions in diverse healthcare environments (WHO, 2015). Regardless of the available guidelines, pharmacovigilance has not been given due importance; moreover, numerous aspects of managing ADR reporting depend on human factors, leading to disparities in hospital practices. It has been reported that the attitude of healthcare professionals is a crucial determinant of suboptimal reporting (Lopez-Gonzalez *et al*., 2009).Furthermore, the type, completeness, and correctness of ADR reporting rely on expertise and clinical settings (Aung *et al*., 2018).

To improve the reporting ecosystem of ADR in the hospital setting, it is essential to establish strategies that could drive healthcare professionals' attitudes. While few studies have been conducted in Saudi Arabia to delineate the role of interventions such as incentives in improving ADR reporting (Ali *et al*., 2018), none of the investigations tapped into multifaceted interventions and their impact. Therefore, the present study was designed to evaluate the effect of diverse interventions (continuous training and education, technology function (trigger tool), patient interviews, and introduction of ADR reporting in annual performance evaluation with weekly feedback reports) in improving ADR reporting in Prince Sultan Medical Military City (PSMMC), Riyadh, Saudi Arabia.

MATERIALS AND METHODS

Institutional Ethics Approval and Considerations

The study was reviewed and approved by the Scientific Research Center, Research Ethics Committee of the PSMMC, Riyadh, Saudi Arabia **(IRB Approval No:** E-2373**)**.

Study Design and Setting

An interventional research study was conducted to evaluate the impact of diverse interventions on improvement in adverse drug reaction reporting among nurses and pharmacists in PSMMC, Riyadh, Saudi Arabia, between January 2022 and December 2022. PSMMC, also known as Riyadh Armed Forces Hospital and established in 1978, is one of the advanced hospitals in Riyadh, with a volume of 1,134 admissions. The hospital specializes in oncology, neurology, cardiology, hematology, urology, and bone marrow transplant unit services (Al Qahtani *et al.*, 2021). ADR from both inpatients and outpatients are notified to the Medication Safety Units of the hospital. Seriousness and causality of ADRs are evaluated by *the Medication Safety officer and Drug Posing Information Centre*. Causality is examined through the Naranjo adverse drug reaction probability scale (Naranjo *et al*., 1981).

Inclusion and Exclusion Criteria

All ADR at PSMMC reported by nurses and pharmacists and submitted to the Saudi Food and Drug Authority between January 2022 and December 2022 were included. The exclusion criteria were ADR reported by either patients or physicians and adverse drug reaction reports not submitted to the Saudi Food and Drug Authority.

Study Interventions

- *Continuous Training and Education*

Continuous training and education for all health care providers regarding the ADRs were introduced in June 2022. The training was specifically focused on how to report ADR and the importance of writing adverse drug reactions.

- *Technology Function (Trigger Tool)*

Technology functions to detect adverse drug reactions, such as trigger tool methodology, were also established as an intervention. A preliminary list of trigger tools was designed on the basis of the Institute for Healthcare Improvement (IHI, 2004), which included drug triggers and laboratory triggers. Consenting patients from the Department of Medicine Units were selected, and a list of trigger tools was tested on every alternate patient. Drug charts, laboratory investigations, discharge forms, and complaints by patients were reviewed for identification of triggers till patient discharge from the hospital. Triggers and ADR were documented in case forms and were labeled as positive triggers (triggers associated with adverse drug reactions) and negative triggers (triggers not associated with adverse drug reactions). For the precision of the trigger tool, the sensitivity, specificity, and positive predictive value were estimated and led to the finalization of a list of modified trigger tools (Menat *et al*., 2021).

- *Patient Interviews*

Patient interview is yet another method to monitor and report adverse drug reactions. This was also included in June 2022 as an intervention. Participants were asked to interview patients prior to receiving medication from the outpatient pharmacy.

- *Adverse Drug Reaction Reporting in Annual Performance Evaluation* with Weekly Feedback Reports

In June 2022, ADR reporting was made a key feature of the Annual Performance Evaluation with

weekly feedback reports to promote active adverse drug reaction reporting among nurses and pharmacists. Besides other job-related aspects, health care provider with the greatest number of adverse drug reaction reports were remunerated with certification and award.

Intervention Phase

Consenting nurses and pharmacists were enrolled. Participants were exposed to continuous training and education, technology function (trigger tool), patient interviews, and adverse drug reaction reporting in Annual Performance Evaluation with weekly feedback reports wards; they were followed for adverse drug reaction reporting over a period of ADR reported by nurses and pharmacists were gathered in adverse drug reaction reporting form and examined for seriousness and causality.

Data Collection

The study's first phase involves the implementation of a web-based questionnaire to gather information from patients or patient files through nurses and pharmacists in additional hospital systems. Information included: date and time of adverse drug reaction, name of the pharmacist, pharmacy location, patient name/I.D., gender, age of the patient, name of the drug, dose of the drug, frequency and route of administration, duration of administration, indication, side effect, and an outcome of the adverse drug reactions. Suspected adverse drug reaction reports submitted to the hospital system and compiled by *the Medication Safety officer and Drug Posing Information Centre were assessed*. Then, it was submitted to the Saudi Food and Drug Authority.

Statistical Analyses

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 24.0 (IBM Corp., and Armonk, N.Y., USA) and Stata version 18 for Windows. Descriptive statistics were conducted, and frequencies and percentages for categorical data were reported. A linear model was used to calculate the change in adverse drug reaction reporting over time. Independent samples t-test was utilized to test the difference before and after implementing the incentives. Through segmented regression analysis of an interrupted time series (12 observation points), variation in the level of average monthly adverse drug reaction reporting between the first and second half of 2022 was established. Serial autocorrelation was identified using the partial autocorrelation function plot of the residuals. The Cochrane-Orcutt method was utilized to estimate parameters for first-order autocorrelation. The comparison of severe ADR for every month was conducted via Fisher's exact test. *P-value* <0.05 was considered statistically significant for all statistical tests.

RESULTS

Overall, 20,942 ADRs were reported to the Saudi Food and Drug Authority from January 2022 to December 2022. The highest number of ADRs was documented in the second half (June to December) of 2022 (n = 14,555, 69.5%) (Figure 1).

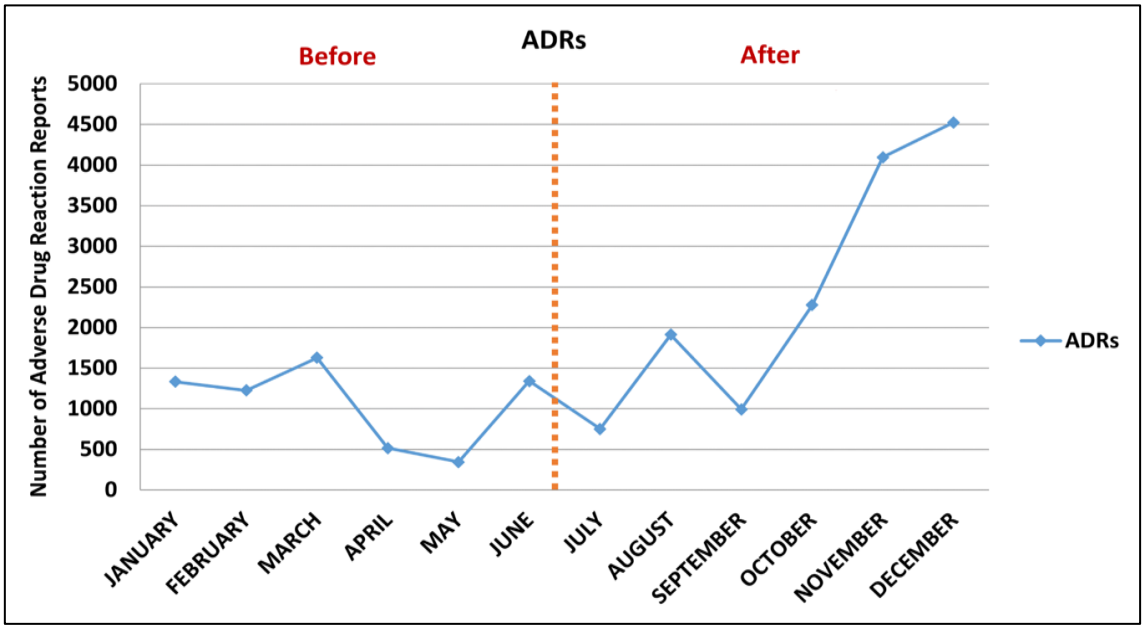

Figure 1: Month-Wise Adverse Drug Reaction Reports Before and After Interventions

The majority of the ADR reports involved female patients (n = 13,292, 55.9%). Patients were divided into four age groups, with the majority being under 21 years old (n = 17,000, 71.5%), followed by patients over 60 years (n = 3,104, 13.1%). The majority of ADR reports were submitted by pharmacists (n = 18,306, 77.0%), followed by technology functions (n = 5,201, 21.9%) and nurses (n = 269, 1.1%). When considering pharmacists, the highest rate of ADR reporting came from outpatient pharmacists (n = 14,076,

76.89%), followed by clinical pharmacy (n = 2,825, 15.43%), and inpatient pharmacists (n = 1,405, 7.67%) **(Table 1).**

Table 1: Shows the demographics and general characteristics of patients and study participants

Characteristics	Frequency (%)
Gender	
Male	10,486 (44.1%)
Female	13,292 (55.9%)
Age Categories (Years)	
<21	17,000 (71.5%)
21 to 40	1,520 (6.4%)
41 to 60	2,152 (9.1%)
>60	3,104 (13.1%)
Job Disposition	
Nurse	269 (1.1%)
Pharmacist	18,306 (77.0%)
Technology Function	5,201 (21.9%)
Pharmacist	
Clinical Pharmacist	2,825 (15.43%)
Inpatient Pharmacist	1,405 (7.67%)
Outpatient Pharmacist	14,076 (76.89%)

Table 2 illustrates and compares the ADR reporting rates before and after the intervention based on continuous training and education, technology function (trigger tool), patient interview, and annual performance evaluation with weekly feedback reports. The results demonstrate significant increases in ADR reporting levels after implementing continuous training and education (34.6% to 65.4%, P < 0.0001), technology function (trigger tool) (38.3% to 61.7%, P < 0.0001), patient interview (35.5% to 64.5%, P < 0.0001), and annual performance evaluation with weekly feedback reports (9.0% to 91.0%, P < 0.0001).

Table 2: Interventions and Differences in Rate of ADR Reporting (Before and After Intervention)

Time Series	Frequency	Mean	Reporting Rate	Difference	*P* value
Continuous Training and Education					
From January to May 2022 (Before)	93	18.6	34.6%	-83.0	**<0.0001**
From June to December 2022 (After)	176	25.1	65.4%		
Technology Function (Trigger Tool)					
From January to May 2022 (Before)	1,990	398.0	38.3%	-60.7	**<0.0001**
From June to December 2022 (After)	3,211	458.7	61.7%		
Patient Interview					
From January to May 2022 (Before)	3,279	655.8	35.5%	-2680.0	**<0.0001**
From June to December 2022 (After)	5,959	851.3	64.5%		
Annual Performance Evaluation with weekly feedback reports					
From January to May 2022 (Before)	820	164.0	9.0%	-7428.0	**<0.0001**
From June to December 2022 (After)	8,248	1178.3	91.0%		

When all interventions were assessed, the effect size was 35.8%, and a statistically significant difference was observed in the ADR reporting rate before and after interventions (30.4% versus 59.6%, *P* < 0.0001) (Table 3).

Table 3: Total Interventions and Differences in Rate of ADR Reporting (Before and After Intervention)

Time series	Freq	Mean	Reporting rate%	difference	F-Test	P-value	Eta Squared
From January to May (Before)	6387	188.15	30.4%	8168	6.783	0.000**	35.8%
From June to December (After)	14555	710.10	59.6%				
Total	20942	491.79					

The most effective interventions were annual performance evaluations with weekly feedback reports, and the least effective interventions were technology functions (trigger tool). The percentage change for each intervention is as follows: continuous training and education (30.8%), technology function (trigger tool)

(23.4%), patient interview (29.0%), and annual performance evaluation with weekly feedback reports (90.0%) (Table 4).

Table 4: Percentage Changes in ADR Interventions between the first half and the second half of 2022

Interventions	Mean	Std	Percentage of change
Continuous training and -education	22.42	14.00	30.8%
technology function [trigger tool]	433.42	110.90	23.4%
patient interview	769.83	409.36	29%
Annual Performance Evaluation (APE) with weekly feedback reports	755.67	963.63	90%

In terms of location, compared with the first half of the 2022, there was about 6% increase in ADR reporting by clinical pharmacy in the second half of the 2022. There were about 22% improvement in reporting by outpatient pharmacy, and approximately 1% and 5% for nurses and inpatient pharmacy respectively, during the same period. No significant increase in the percentage of change adverse drug reaction reporting was noted for technology (Table 5).

Table 5: Change in ADR Reporting between the First and Second Half of 2022 based on Location

	From January to May 2022 (Before)	From June to December 2022 (After)	Percentage Change
Nurse	0.7%	1.3%	0.6%
clinical Pharmacy	0.7%	6.6%	5.9%
Inpatient Pharmacy	1.2%	6.6%	5.4%
Outpatient Pharmacy	19.6%	41.5%	21.9%
Technology	10.0%	11.9%	1.8%
Total	32.2%	67.8%	35.6%

The majority of the ADRs reported in 2022 were by pharmacists (77.0%). Compared with the first half of 2022, pharmacists reported a 33.2% increase in the second half of 2022 (Table 6).

Table 6: Change in ADR Reporting between the First and Second Half of 2022 based on Job Disposition

	From January to May 2022 (Before) (*n* = 6,387)	From June to December 2022 (After) (*n* = 14,555)	Percentage Change
Nurse	0.7%	1.3%	0.6%
Pharmacist	21.5%	54.6%	33.2%
Technology	10.0%	11.9%	1.8%
Total	32.2%	67.8%	35.6%

There was a significant association between location and type of profession and serious ADR reporting in the second half of 2022 (Table 7).

Table 7: Location and Type of Profession and Serious ADR Reporting (Cochrane-Orcutt Regression

Variables	Coefficient	Standard Error	*P* Value
Location	511.9	25.9	**<0.0001**
Job	327.9	8.4	
Nurse	303.4	16.5	
Pharmacist	687.3	17.1	
Technology	463.5	20.5	

DISCUSSION

ADR is an unintended hazardous response to a therapeutic compound and primarily reflects the direct pharmacological action of the drug itself ((*Australian Government, Department of Health, Therapeutic Goods Administration (2019). Reporting Adverse Events*, 2021). ADRs are prevalent in healthcare environments, accounting for approximately 7% of hospitalizations in adult patients (Al Hamid *et al.*, 2014). It has also been reported that around 10% to 17% of hospitalized patients encounter ADR (Bouvy *et al.*, 2015; Miguel *et al.*, 2012). A systematic review recently reported that patients with ADR associated with hospital admissions are at a 5-fold increased risk of having another ADR episode within the first 90 days after discharge.

In fact, the odds of having yet another ADR episode remained significantly high for about five years (Schmid *et al*., 2022).

Notwithstanding the evidence, pharmacovigilance remains an enigmatic entity among healthcare personnel (AlShammari & Almoslem, 2018; Moinuddin *et al*., 2018). However, a handful of research studies have shown improvement in pharmacovigilance, i.e., ADR reporting with appropriate interventions (Khalili *et al*., 2020; Moinuddin *et al.*, 2018; Paudyal *et al.*, 2020). With this backdrop, this study sought to evaluate the impact of diverse interventions (continuous training and education, technology function (trigger tool), patient interviews, and introduction of ADR reporting in annual performance evaluation with weekly feedback reports) in improving ADR reporting in PSMMC, Riyadh, Saudi Arabia.

In the present study, we found that the number of ADR significantly increased after implementation of interventions (continuous training and education, technology function (trigger tool), patient interviews, and introduction of ADR reporting in annual performance evaluation with weekly feedback reports). A number of research studies, including systematic reviews and meta-analyses, have communicated encouraging outcomes of several interventions on ADR reporting among healthcare professionals (Cervantes-Arellano *et al*., 2024; Chang *et al*., 2017; Menat *et al.*, 2021; Moinuddin *et al*., 2018; Paudyal *et al.*, 2020). The following interventions to improve pharmacovigilance have been reported in the literature: instructive activities, trigger tools, public-wide appraisals, awards and honors, and monetary remunerations.

Research investigations have confirmed the positive role of instruction-based interventions, either with other interventions or standalone, in enhancing ADR reporting (Paudyal *et al*., 2020; Tang *et al.*, 2020). A systematic review study by Li *et al.*, (2020) demonstrated 9.26 times higher ADR reporting rates with a blend of interventions compared to 7.19 times improvement with standalone interventions. They integrated education awareness, automated ADR reporting instruments, prompts, financial remunerations, telephonic interventions, and feedback reports (Tang *et al.*, 2020). Another systematic review and meta-analysis by Paudyal *et al*., (2020) reported that on-site educational interventions coupled with monetary benefits manage to improve ADR reporting among healthcare providers. Overall, their pooled analysis revealed 3.5 times improved ADR reporting (Relative Risk 3.53; 95% CI 1.77 – 7.06) in the interventional cohort in contrast to controls (Paudyal *et al*., 2020). Our study findings align with earlier reports, as we witnessed a significant 30.8% change in ADR reporting following continuous training and education intervention. Furthermore, a multifaceted combination of interventions in our study also led to a substantial increase in the number of ADR reports.

The financial aspect is yet another feature that has emerged in the hospital system to improve ADR reporting. Our study found the addition of ADR reporting in annual performance evaluation with weekly feedback reports as the ideal intervention in motivating nurses and pharmacists to report ADR (90.0% change) actively. A study from Saudi Arabia by Ali *et al*., (2018) documented a 40.6% increase in monthly reporting of ADR reports with incentives, which comprised monthly nomination, appreciation certificate, leave, and potential one-month extra salary (Moinuddin *et al*., 2018). A study from China also experienced an improvement in ADR reporting after introducing financial motivations and ADR regulations, i.e., a median number of reports/year improved from 29 (before intervention) to 277 (1st intervention period) and 666 (2nd intervention period) (Chang *et al*., 2017).

The present study found that pharmacists were significant contributors to ADR reporting. Pharmacists were more likely to report serious ADR reports. This pattern of high ADR reporting has also been observed earlier in Saudi Arabia, where pharmacists were proactive. Significant improvement in reporting was witnessed for pharmacists (% change: 660), followed by nurses (% change: 257) and doctors (% change: 210) (Moinuddin *et al*., 2018). Studies have also found that serious ADR were mainly notified by physicians (Alvarez-Requejo *et al*., 1998; Moinuddin *et al*., 2018); however, we did not evaluate physicians in the current study. The plausible reason for the high reporting of ADR by pharmacists could be working knowledge, field expertise, exposure, work responsibilities associated with ADR reporting, and subject interest.

This interventional study had few limitations that merit documentation and cautious interpretation of the findings. First, it was a single-center study carried out in Riyadh, and therefore, findings may not be representative of other hospital settings in other regions of Saudi Arabia. Second, the present study only enrolled nurses and pharmacists. Hence, we could not assess how physicians and consultants would have responded to the interventions introduced and how this might have affected the pharmacovigilance landscape (ADR reporting) in PSMMC. Finally, our study spanned from January 2022 to December 2022, indicating that the time duration of the evaluation was approximately six months after the intervention. Therefore, we could not assess these interventions' yearly differences, long-term impact, and sustainability. Based on these limitations, we emphasize replicating this research study on a broader scale with an improved hospital sample size to extend the study's generalizability.

To the best of our literature review, this is the first-ever study to incorporate four diverse interventions together towards pharmacovigilance and investigate its impact on ADR reporting in the region. Furthermore, our study is among the few that used interrupted time series analysis to examine the before and after interventional effects on ADR reporting (Chang *et al*., 2017;

Moinuddin *et al*., 2018). Lastly, the accuracy of ADR reports was not an issue as these were systematically evaluated by authorized pharmacists of the *Medication Safety officer and Drug Posing Information Centre of the hospital.*

CONCLUSION

To conclude, pharmacovigilance is an important facet in the healthcare setting. Our study findings revealed that all the interventions improved the dynamics of pharmacovigilance in PSMMC by enhancing ADR reporting among nurses and pharmacists, with introduction of ADR reporting in annual performance evaluation with weekly feedback reports being the ideal intervention. These interventions must be permanently instituted into the hospital ecosystem to endorse pharmacovigilance with ongoing yearly evaluation.

Abbreviations

SPSS, Statistical Package for Social Sciences (SPSS)
Adverse drug reactions (ADR)
Prince Sultan Medical Military City (PSMMC)

Author's Contributions

Author HA conceived of the idea of the research study and methodology. Author HA and WA collected the data, while Author HA, BA and YB performed appropriate statistical anlysis. HA, YB and MA Authors reviewed research literature, discussed the results, and contributed to the final veriosn of the manuscript.

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