Characterization of Adverse Drug Reaction Reports from Healthcare Staff in a Tertiary Healthcare Facility in Saudi Arabia

Khalid Mohsen Alotaibi[1]*, Naif Saud Alosaimi[2], Majed Hamad Almutairi[3], Fahad Fehaid Alotaibi[4], Abdullah Abdulaziz Alhowidi[5], Rahayef Nayef Alotaibi[6], Turki Abdullah Alotaibi[7], Basil Naser Alamri[8], Muhammed Nasser Alwehaibi[9]

1 Clinical Pharmacist, Ministry of Defense, Riyadh, Saudi Arabia

phkmotb@gmail.com

2 Ministry of Interior (General administration of Medical Services), Bisha, Saudi Arabia

3 Family Medicine, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

4 Social Service, Ministry of Defense, Riyadh, Saudi Arabia

5 Emergency Assistant Consultant, Imam Abdularhman Alfaisal Hospital, Riyadh, Saudi Arabia

6 Department of Pharmacy Practice, King Faisal University, Al Ahsa, Saudi Arabia

7 Clinical Pharmacist, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

8 Pharmacists, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

9 Pharmacist, Ministry of Defence, Military Medical Services, Riyadh, Saudi Arabia

Abstract : According to the World Health Organization (WHO), adverse drug reactions (ADRs) are harmful and unintended effects that occur when medications are administered at doses commonly used for disease prevention, diagnosis, treatment, or for altering physiological functions. These reactions constitute a major global public health concern due to their impact on patient safety and healthcare systems worldwide [1].

ADRs are a major cause of morbidity and mortality, particularly in hospitalized patients [2]. Varying patterns of ADRs with non-uniform reporting have been observed in previous studies. The most reported ADRs in Saudi Arabia were in systemic anti-infective agents (22.27%) followed by antineoplastic and immunomodulating agents (21.49%). Specifically, serious ADRs were reported in vancomycin (2.7%), ceftriaxone (1.8 %), fingolimod (1.4 %), and paracetamol (1.4%) [9]. Males have been reported to have more ADRs with the reactions predominantly being cardiovascular (9.9%), followed by dermatological (9.5%) [10]. We aim to investigate ADRs reports at PSMMC we expect greater number of ADRs compared to previous local studies which will give us a clear look at drugs safety and efficacy at our population.

Keywords – Adverse Drug Reactions (ADR), ADR reporting, Pharmacovigilance

1. INTRODUCTION

Adverse drug reactions represent a major public health concern due to their direct impact on mortality, morbidity, longer hospital stays, and cost burden. Vigilant monitoring is essential to mitigate these risks and minimize avoidable public health burden.

According to the World Health Organization (WHO), adverse drug reactions (ADRs) are harmful and unintended effects that occur when medications are administered at doses commonly used for disease prevention, diagnosis, treatment, or for altering physiological functions. These reactions constitute a major global public health concern due to their impact on patient safety and healthcare systems worldwide [1]. ADRs are a major cause of morbidity and mortality, particularly in hospitalized patients [2]. Moreover, there is an associated increase in hospitalizations, increased healthcare costs due to prolonged hospital stays, additional testing and a consequent increase in the public health burden [3][4]. Monitoring ADR reports considered as an effective tool for assessing drug therapy safety and efficacy [5]. Despite advances in drug development and approval processes, the real-world safety of medications often becomes evident only after widespread clinical use, underscoring the critical role of pharmacovigilance. The World Health Organization (WHO) describes pharmacovigilance as the scientific discipline and associated activities focused on identifying, evaluating, comprehending, and preventing adverse effects of medicines as well as other potential issues related to drug use [6].It serves as a bridge between theoretical and clinical research on drugs and actual patient outcomes. Reporting of these ADRs by both patients and healthcare practitioners is considered the foundation of pharmacovigilance because this information allows for the completion of a drug profile, monitoring of medication risks, and implementation of corrective strategies [7].

In Saudi Arabia, like in many countries, adverse drug reaction reporting is a growing area of focus. A similar approach of reporting by patients and healthcare professionals is employed by the Saudi Food and Drug Authority. Varying patterns of ADRs with non-uniform reporting have been observed in previous studies. The most reported ADRs in Saudi Arabia were in systemic anti-infective agents (22.27%) followed by antineoplastic and immunomodulating agents (21.49%). Specifically, serious ADRs were reported in vancomycin (2.7%), ceftriaxone (1.8 %), fingolimod (1.4 %), and paracetamol (1.4%) [9]. Previous studies have indicated a higher occurrence of adverse drug reactions (ADRs) among male patients, with cardiovascular

reactions being the most commonly reported (9.9%), followed closely by dermatological manifestations (9.5%) [10]. Similarly, Lobo et al. (2023) reported an overall ADR incidence of 3.1% among hospitalized patients, with a greater proportion observed in males (55.7%) compared to females (44.3%). In this study, cutaneous reactions were the most frequently affected system (34.5%), followed by metabolic (16.5%) and gastrointestinal (14.2%) systems [11].

Prince Sultan Military Medical City (PSMMC) is one of the largest tertiary care centers in Saudi Arabia, offering advanced medical services to a diverse population. The complex cases managed at PSMMC require polypharmacy and the use of high reaction risk medications. The gap in literature hinders improvements in drug safety and ADR related patient outcomes. The application of institution specific approach aims to reflect local prescribing habits, genetic predispositions, or environmental factors unique to Saudi Arabia in general and the institutional practices at PSMMC.

This study aims to add to the already present literature regarding ADRs and associated factors while also bridging the existing gap. Patient demographics, affected organ systems, drug classes involved, and factors affecting safety have all been evaluated in the context of ADRs. The determination of these patterns can guide clinicians and policymakers in the development of educated changes in protocols for ADR prevention, recognition, reporting and management. The study is also expected to contribute to regional pharmacovigilance literature by providing a comprehensive overview of ADR trends in one of Saudi Arabia's major healthcare institutions.

The aim of this study is:

- To identify the ADRs reported at Prince Sultan Military Medical City in Saudi Arabia over a one-year period

To analyze trends of reported ADRs with respect to demographic trends, drug classes involved, system organ classes affected, severity levels.

2. METHODS

This study employed a retrospective observational design for the analysis of ADR reports submitted by healthcare professionals at PSMMC, a large tertiary care center located in Riyadh, Saudi Arabia.

A retrospective review was conducted on all adverse drug reaction (ADR) reports submitted by healthcare professionals within a tertiary healthcare system in Saudi Arabia over the period from January 2023 to December 2023.The inclusion criteria for this study are:

- ADR reports submitted during the defined study period (January 1, 2023, to December 31, 2023)
- Any patient who experienced a reported ADR in an inpatient or outpatient setting at PSMMC
- Complete ADR reports with the information on patient demographics, drug group, organ system involved, severity of reaction, and patient outcome

Exclusion Criteria:

- Duplicate reports entered in the system
- Non reported ADRs in an inpatient or outpatient setting at PSMMC
- Reports with incomplete or missing essential data
- ADRs resulting from medication errors or intentional overdose

The following data variables were analyzed:

- Patient demographics: age (classified into pediatric, adult and geriatric groups) and sex (male versus female)
- System Organ Class (SOC): the physiological system affected, based on the Medical Dictionary for Regulatory Activities (MedDRA)
- ADR classification: immunologically mediated vs. non-immunological ADRs.
- Severity level: assessed using Hartwig's Severity Assessment Scale, which stratifies ADRs into seven levels, ranging from mild to fatal

Results

Following data extraction, descriptive statistics were employed to summaries and organize the information on demographics, frequency of ADRs and categorical variables. To analyze ADR patterns, cross tabulations were used. Pie charts and histograms were mapped out for visual analysis of ADR patterns across categories.

Chi-square analyses were performed to evaluate the statistical significance of associations between categorical variables, including age categories and specific adverse drug reactions (ADRs). Odds ratios (ORs) along with 95% confidence intervals (CIs) were computed to examine the relationship between drug classes and immunologically mediated reactions. Data entry and statistical analyses were carried out using Microsoft Excel and SPSS software (version 26.0). Statistical significance was defined as a p-value of less than 0.05.

The results cover key aspects, including patient demographics, the classification of ADRs by system organ class and drug category, severity assessment, and associated risk factors. Additionally, the impact of immunologically mediated reactions and the pharmacovigilance measures implemented to enhance ADR monitoring are discussed. These findings provide valuable insights into ADR patterns, highlighting trends in drug safety and the effectiveness of current reporting.

Demographics

Table 1: Demographic data

Category	Count	Percentage
Male	10,962	42.30%
Female	14,966	57.70%
Pediatrics ≤ 18	6,244	24.10%
Adults (19-64)	15,088	58.20%
Elderly< 65	4,596	17.70%
Total ADR Reports	25,928	100%

Table 1 presents the demographic distribution of ADR reports. Among the total 25,928 reports, females account for a higher proportion (57.7%) compared to males (42.3 %).

Age-wise, adults constitute the largest group (58.2%), followed by pediatrics (24.1%) and the elderly (17.7%). These figures highlight the variations in ADR reporting across different demographic groups.

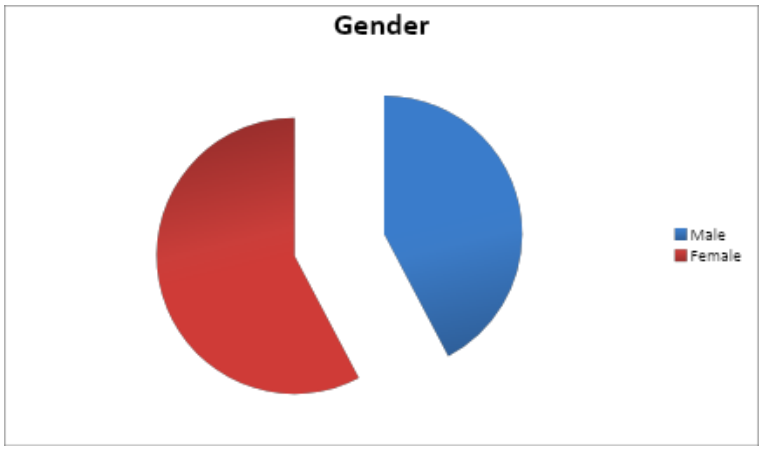

Figure 1: Gender Distribution of ADRs

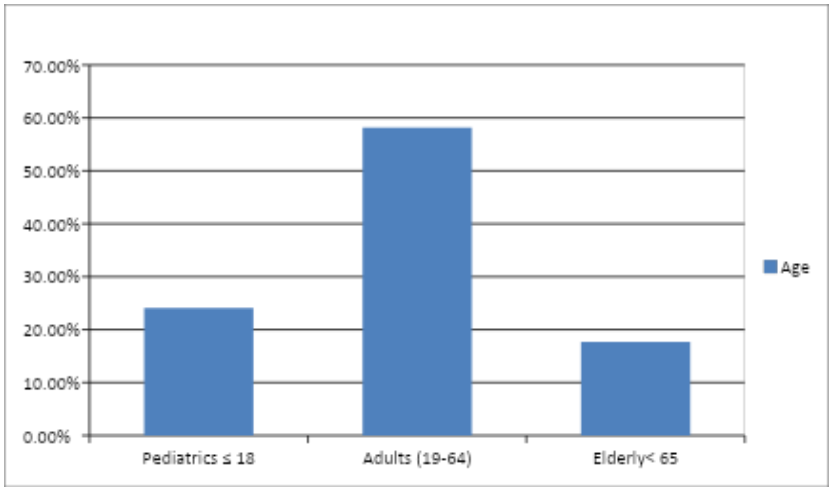

Figure 2: Age Distribution of ADRs

Table 2: Classification by System Organ Class (SOC), Frequency, and Age Distribution (with Percentages)

System Organ Class (SOC)	Pediatrics (≤18)		Adults (19-64)		Elderly (≥65)		Total
	F	%	F	%	F	%	
Diarrhea	652	36.5%	905	50.7%	228	12.8%	1,785
Constipation	312	19.4%	987	61.3%	313	19.4%	1,612

System Organ Class (SOC)	Pediatrics (≤18)		Adults (19-64)		Elderly (≥65)		Total
	F	%	F	%	F	%	
Headache	419	31.8%	701	53.2%	198	15.0%	1,318
Vomiting	498	39.3%	612	48.4%	156	12.3%	1,266
Injection Site Reaction	389	34.1%	578	50.6%	175	15.3%	1,142
Fatigue and Drowsiness	256	22.6%	659	58.3%	217	19.2%	1,132
Abdominal Pain	277	31.5%	459	52.2%	143	16.3%	879
Hypotension	82	12.2%	412	61.0%	181	26.8%	675
Gastric Ulcer (NSAID Use)	45	7.5%	356	59.2%	200	33.3%	601
Anemia	78	14.7%	301	56.9%	150	28.4%	529

Table 2 classifies ADR cases by System Organ Class (SOC), frequency, and age distribution. Diarrhea is the most frequently reported ADR (1,785 cases), with adults (50.7%) being the most affected, followed by pediatrics (36.5%) and the elderly (12.8%). Constipation is also common, predominantly affecting adults (61.3 %), while pediatric and elderly cases are nearly equal (19.4% each). Headache, vomiting, and injection site reactions are more frequent in adults but still significantly reported in pediatrics. Hypotension and gastric ulcers (associated with NSAID use) are more prevalent among the elderly, with 26.8 % and 33.3 % of cases, respectively. Overall, adults account for the highest percentage of ADRs across most categories.

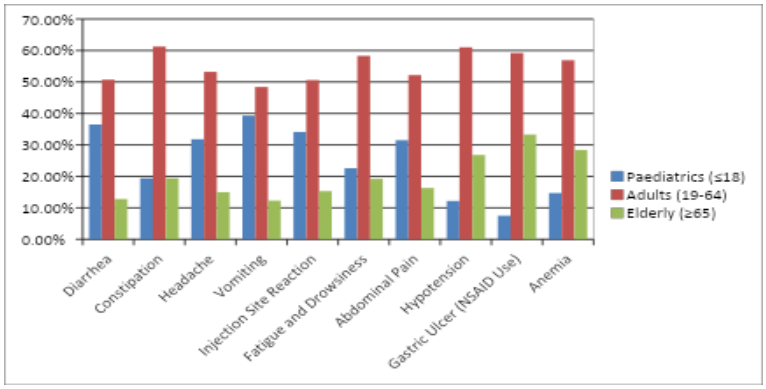

Figure 3. Classification by System Organ Class (SOC), Frequency, and Age Distribution (with Percentages)

Table 3: Frequencies of ADRs by Drug Class and Age Distribution

Drug Class	Pediatrics (≤18)		Adults (19-64)		Elderly (≥65)		Total Cases
	F	%	F	%	F	%	
Metformin	5	0.4%	908	74.8%	301	24.8%	1,214
Enoxaparin	9	0.9%	972	97.3%	18	1.8%	999
Atorvastatin	2	0.2%	579	65.5%	303	34.3%	884
Augmentin	34	7.4%	407	88.1%	21	4.5%	462
Diclofenac	1	0.2%	416	98.8%	4	0.95%	421
Amlodipine	2	0.5%	237	60.3%	154	39.2%	393
Morphine	51	14.0%	290	79.9%	22	6.1%	363
Tramadol	31	9.9%	264	84.6%	17	5.4%	312
Perindopril	0	0.0%	212	70.2%	90	29.8%	302
Escitalopram	0	0.0%	247	84.9%	44	15.1%	291

Table 3 presents the frequencies of ADRs by drug class and age distribution. Metformin, primarily used for diabetes management, shows the highest number of ADR cases (1,214), with adults (74.8%) being the most affected, followed by the elderly (24.8%). Enoxaparin and diclofenac display an overwhelming majority of ADR cases in adults (97.3 % and 98.8 %, respectively), with minimal reports in pediatrics and the elderly. Atorvastatin and amlodipine show a relatively higher ADR proportion in the elderly (34.3% and 39.2 %, respectively). Morphine and tramadol, both analgesics, are more frequently associated with ADRs in adults, with some pediatric cases (14.0% and 9.9%, respectively). Notably, escitalopram and perindopril report no ADRs in pediatrics, with most cases occurring in adults.

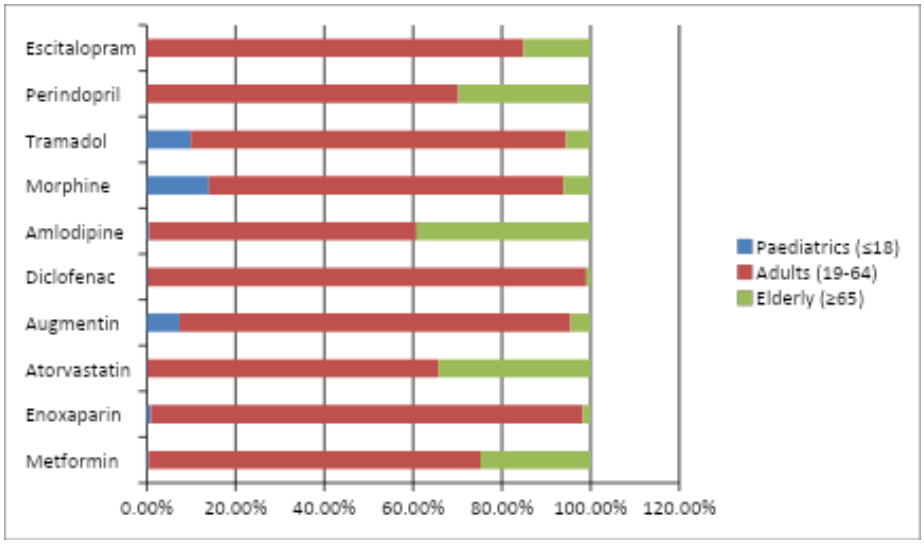

Figure 4: Frequencies of ADRs by Drug Class and Age Distribution

Table 4: Associated Drug Class with Immunologically Mediated Reactions Compared to Other ADRs

Drug Class	**OR (95% CI)**	**p-value**
Antimicrobials	1.25 (1.18, 1.33)	<0.001
Analgesics	1.15 (1.06, 1.24)	<0.001
Cardiovascular Drugs	0.68 (0.60, 0.76)	<0.001
Antidiabetics	0.96 (0.85, 1.08)	0.49
CNS Drugs	0.59 (0.50, 0.68)	<0.001
Respiratory Drugs	0.67 (0.57, 0.79)	<0.001

Table 4 compares the association of different drug classes with immunologically mediated reactions versus other ADRs using odds ratios (OR) and confidence intervals (CI). Antimicrobials show the highest association (OR = 1.25, 95% CI: 1.18–1.33, $p < 0.001$), followed by analgesics (OR = 1.15, 95% CI: 1.06–1.24, $p < 0.001$), indicating a significantly increased risk of immunologically mediated reactions. Conversely, cardiovascular drugs (OR = 0.68), CNS drugs (OR = 0.59), and respiratory drugs (OR = 0.67) show a lower likelihood of causing such reactions ($p < 0.001$). Antidiabetics have no significant association ($p = 0.490$). These findings highlight notable differences in immunogenic potential across drug classes.

Table 5: Hartwig's Severity Assessment Scale

Severity Level	Description
Level 1	An adverse drug reaction (ADR) occurred but did not require any change in therapy with the suspected medication.
Level 2	The adverse drug reaction led to the temporary withholding, discontinuation, or adjustment of the suspected medication. No antidotal or additional therapeutic intervention was required, and the hospital length of stay was not extended.
Level 3	The adverse drug reaction necessitated withholding, discontinuation, or modification of the suspected medication, and/or required the administration of an antidote or supportive therapy. However, the reaction did not result in an extended length of hospital stay (LOS).
Level 4	A Level 3 ADR that resulted in an increased hospital stay of at least one day, or the ADR was the primary reason for hospital admission.
Level 5	A Level 4 ADR that required intensive medical care or monitoring.
Level 6	The ADR caused permanent harm or disability to the patient.
Level 7	The ADR directly or indirectly resulted in the death of the patient.

Table 6: ADRs by Severity

Severity Level	Cases	Percentage
Mild (Levels 1-2)	25,859	99.70%
Moderate (Levels 3-4)	4	0.02%
Severe (Levels 5-7)	65	0.25%

Table 5 categorizes ADRs by severity based on Hartwig's Severity Assessment Scale. Most cases (99.7%) are classified as mild (Levels 1-2), indicating that most ADRs required minimal or no intervention. Only 0.02% of cases were moderate (Levels 3-4), involving treatment modifications or hospital stays. Severe ADRs (Levels 5-7), which include cases requiring intensive medical care, permanent harm, or death, accounted for 0.25 % of reports. These findings suggest that while ADRs are common, serious reactions remain rare.

This study examines the reporting patterns of adverse drug reactions (ADRs) documented by healthcare professionals at Prince Sultan Military Medical City (PSMMC) in Saudi Arabia. A retrospective review of ADR reports submitted between January and December 2023 was undertaken to evaluate patient demographic characteristics, implicated drug classes, affected organ systems, and the severity of reported reactions.

The results indicate that ADRs were more frequently reported in females (57.7%) than males (42.3%), with adults (58.2%) being the most affected age group. Gastrointestinal disorders were the most reported ADRs (27.3%), followed by nervous system disorders and general disorders. Among drug classes, antimicrobials, analgesics, and cardiovascular drugs accounted for a significant proportion of ADRs. The severity assessment, based on Hartwig's scale, revealed that the majority of ADRs were mild (99.7%), with only 0.02 % classified as moderate and % percent as severe.

Further analysis showed that antimicrobials and analgesics had a higher association with immunologically mediated reactions, while cardiovascular and CNS drugs had a lower likelihood.

These findings highlight the importance of continuous ADR monitoring, improved reporting systems, and proactive risk mitigation strategies to ensure drug safety and efficacy in the local population.

DISCUSSION

This study has conducted a comprehensive retrospective analysis of ADRs at PSMMC during the year 2023. The findings provide crucial insights into the demographic patterns, gender distribution, organ systems affected, drug groups involved, reaction severity. These results add to the local body of knowledge, enhance the importance of institution-based studies and provide similar as well as diverging trends in comparison with the global ADR reporting.

There is a higher frequency of ADRs reported in females (57.7%) compared to males (42.3%). This is one of the most prominent observations in this study because it aligns with the global literature. This difference is due to varying pharmacokinetics. With a standard drug dose, females are exposed to higher concentrations of drug and longer elimination times [13]. These reaction differences are highest among anticoagulants and diuretics [14]. However, on a local level, these findings contradict earlier studies, in which higher rates of ADRs were reported among males. This discrepancy might be due to differences in varying pharmaceutical companies in drug dispensing, differences in prescription patterns or varying documentation of reactions. Further research is needed to assess the reason behind these discrepancies and evaluate homogenizing trends. Moreover, it also highlights the need for sex-disaggregated pharmacovigilance data to ensure equitable and effective drug safety measures.

In the context of ADRs with respect to age related distribution, adults categorized as ages 19 to 64 years, accounted for the majority of reported ADRs (58.2%), followed by pediatrics (24.1%) and the elderly (17.7%). These statistics might be due to the highest exposure to pharmacological treatments for chronic diseases and conditions. Moreover, the presentation of adults in healthcare facilities is also the highest. The notable rate of ADRs in the pediatric population highlights the need for cautious prescribing and vigilant monitoring in this vulnerable group. Moreover, it is also important to keep in mind weight related dosages used in the pediatric population to avoid overdosing.

The most frequently reported ADR category in terms of organ system involved was gastrointestinal system, in the form of diarrhea, constipation, vomiting, and abdominal pain. These findings were also most observed in the adult population. These findings align with both local and international trends which suggest that dermatological and gastrointestinal reactions are the most common types of ADRs [15]. Although this group of ADRs is rarely life threatening, they do impact adherence and quality of life [16].

Among different drug classes, microbials, analgesics, and cardiovascular acting drugs are the most frequently involved in ADRs. Specifically, the most common drugs involved were found to be metformin, enoxaparin, and atorvastatin. The trend of increasing ADRs with metformin and atorvastatin may reflect the high prevalence of type 2 diabetes mellitus and hyperlipidemia in the adult population of Saudi Arabia. Moreover, enoxaparin is an anticoagulant routinely used in surgical and critically ill patients. Therefore, the ADR patterns not only reflect the

drugs itself but also the patterns of disease and morbidity of a certain population. Moreover, these findings highlight the need for an extensive medication review when prescribing polypharmacy in chronic conditions.

A particularly noteworthy aspect of this study was the assessment of immunologically mediated reactions. Immune mediated reactions including rashes, hypersensitivity syndromes, and anaphylactic reactions, were mostly related to antimicrobials (OR = 1.25) and analgesics (OR = 1.15). These findings are consistent with the previous reports with cephalosporins and penicillin's being responsible for most allergic reactions [12].

The severity of the ADRs has been assessed using the Hartwig's scale which demonstrates that the majority (99.7%) of the reported reactions are mild and do not require intensive management. The moderate and severe reactions, despite being rare (0.02 % and 0.25 %, respectively) are clinically significant because they require discontinuation of the culprit drug along with extended hospitalization and intensive care. The low rate of severe reactions may demonstrate the safety profile of the drugs approved for use clinically as well as the utility of early detection.

CONCLUSION

To conclude, this study has provided a detailed analysis of ADRs reported at PSMMC over a one-year period and assessed the trends of these reactions with respect to different variables. ADRs were reported to be more common in females than males. Moreover, the drug classes mainly involved in these reactions included antimicrobials and analgesics. Immunologic reactions were also reported to be due to the formerly mentioned classes of drugs. ADRs mainly involve the gastrointestinal system in the form of gastrointestinal distress (vomiting, diarrhea). In Saudi Arabia, the most reported drugs were found to be metformin, atorvastatin and enoxaparin. Importantly, the majority of ADRs were classified as mild according to Hartwig's Severity Assessment Scale, indicating that while ADRs are common, most do not result in significant clinical complications. The presence of moderate and severe cases is still significant. These findings emphasize that an identification of trends and patterns could help in the aim for prevention of future reactions, mindful prescribing practices and overall, improvement of public health burden due to ADRs.

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