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Original Article

Burden and predictors of drug-related hospital admissions in Saudi Arabia: a prospective study

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ABSTRACT

Drug-related problems (DRPs) significantly contribute to hospitalization, increase healthcare costs, and adversely affect patient outcomes. This study aimed to determine the prevalence and preventability of drug-related hospital admissions (DRHAs) in medical wards at King Fahad University Hospital, Saudi Arabia. A prospective study was conducted among adult patients admitted to the medical unit. DRHAs were assessed using the validated AT-HARM 10 tool. Data were analyzed using SPSS version 23, with statistical significance set at $p<0.05$. A total of 200 patients were included, of whom 26.0% experienced DRHAs. Among these admissions, 86.5% were considered definitely preventable, and 51.9% were of moderate severity. Non-compliance was the most common contributing factor (71.2%), followed by untreated conditions (7.7%) and improper drug selection (5.8%). Cardiovascular medications accounted for the largest proportion of DRHAs (69.2%), followed by immunosuppressants, antianemic agents, and antibiotics (5.8% each). Multivariate logistic regression showed that patients with chronic diseases were significantly more likely to experience DRHAs than those without chronic diseases (OR=11.4; 95% CI: 1.752–73.789; p=0.011). Patients with chronic kidney disease were also more likely to experience DRHAs than those without chronic kidney disease or end-stage renal disease (OR=2.8; 95% CI: 1.055–7.553; p=0.039). DRHAs accounted for a substantial proportion of medical admissions, with most considered preventable. Early identification and management of DRPs, particularly among patients with chronic diseases, may reduce avoidable hospitalizations and improve therapeutic outcomes.

Keywords: Drug-related problems, Drug-related hospital admissions, AT-HARM 10, Naranjo algorithm, Hepler-Strand classification.

Introduction

Medications are crucial in the prevention and treatment of various illnesses and serve as the most common intervention in primary care [1]. However, medications bear a dual nature and act as a double-edged sword, capable of saving lives on one hand and being a potential source of harm on the other hand. Adverse drug reactions (ADRs) and adverse drug events (ADEs) are widely recognized as leading causes of avoidable harm, iatrogenic injury, and increased healthcare expenses [2-4]

Medications profoundly improve the patient's quality of life (QoL), yet they lead to a higher incidence of Drug-Related Problems (DRPs) in both inpatients and outpatients. DRPs, as defined by the Pharmaceutical Care Network, are "an event or circumstance involving drug therapy that actually or potentially interferes with the desired health outcomes" [5-7]. Currently, there are more than 20 different classifications of DRPs [8-11]; however, Hepler and Strand categorized them into eight main categories: untreated indications, incorrect drug selection,

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subtherapeutic dosage, failure to receive drugs, overdosage, ADRs, drug interactions, and drug use without a clear indication [12-15].

The presence of DRPs is strongly associated with the failure to achieve the desired health outcomes, resulting in heightened risks of morbidity and mortality, prolonged hospital stay, increased healthcare costs, compromised patient QoL, and poor patient satisfaction with treatment [2, 16-18]. Several factors may significantly increase the risk of suffering a DRP, such as polypharmacy (the use of more than four or five drugs), affecting 40% and 90% of adults aged >65, and 75 years, respectively. Moreover, the type of disease and the specific study setting can also contribute to an increased risk of DRPs [19-23].

It is worth noting that DRPs significantly increase the risk of emergency department visits and Drug-Related Hospital Admissions (DRHAs); however, in most cases, these DRPs are preventable [20, 24-26]. Studies have indicated that ADRs and ADEs account for up to 30% of hospital admissions and emergency department visits [27-32]. According to one study, DRPs were responsible for 40% of DRHAs, of which 58% were deemed preventable [23, 32, 33]. A recently conducted systematic review reported ADR-related hospital admissions ranging from 4.2% to 30% (with 8.3% pooled prevalence), while ADE-related hospital admissions ranged from 4.9% to 30.7% (with 13.9% pooled prevalence). Of these DRHAs, 24% to 97.6% (with a pooled preventability rate of 44.7%) were preventable ADR-related admissions, and 65.3% to 73.7% (with a pooled preventability rate of 71%) ADE-related admissions were preventable [1]. Another systematic review reported that DRHAs ranged from 3% to 64% (with a median of 21%), of which 5% to 87% (with a median of 69%) were deemed preventable readmissions [34].

Regarding DRHAs in Saudi Arabia, a study indicated 13.9% of medication-related hospital admissions [35], whereas another similar study conducted in 2014 revealed 92.9% DRHAs, of which 85.7% were deemed preventable [36]. Similarly, a study conducted in 2015 reported that 26.5% of hospital admissions in the emergency department were attributed to DRPs, of which 70% were deemed preventable [37]. Furthermore, another study in Saudi Arabia reported 41.5% DRHAs among adult patients with cardiovascular diseases and diabetes mellitus [38].

Considering the significant occurrence of DRHAs in Saudi Arabia, ranging from 13.9% to 92.9%, with a noteworthy proportion of preventable DRHAs (ranging from 70% to 85.7%), it is necessary to expand upon the existing literature in this area. Therefore, the current study aimed to ascertain the prevalence, preventability, and associated risk factors of DRHAs at the medical unit of King Fahad Hospital of the University (KFHU), Khobar, Saudi Arabia.

Materials and Methods

Study design

A prospective study was performed among the adult patients who were admitted to the medical unit at King Fahad Hospital of the University (KFHU), Khobar, Saudi Arabia. The duration of the study was five months from May to September 2023.

Inclusion/exclusion criteria

Patients of either gender, both male and female, aged 18 years and above, admitted to the internal medical wards of the hospital were included in this study. The following patients were excluded from this study: patients with intentional medication poisoning, patients with scheduled admission in the internal medical ward, pediatric patients, and patients who visited the emergency department.

Sample size

The sample size for this study was determined using a recommended proportion formula, i.e., $n=Z^2 (P)(1-P)/d^2$, where "n" refers to sample size, "p" is the anticipated prevalence, "d" is the margin of error (5%), and "Z" is the Z-statistic (1.96). Based on the anticipated prevalence of 13.9%, a total of 184 samples were calculated using the above-mentioned formula; however, we included 200 patients in this study to make the findings more accurate.

Assessment tool

AT-HARM 10 [39], a validated assessment tool, was utilized for measuring the prevalence of drug-related hospital admissions (DRHAs). The tool comprised ten "YES" or "NO" questions; the first three help in identifying admissions that are unlikely to be drug-related (U), while the remaining help in identifying drug-related admissions (P). In contrast, Hepler-Strand classification was employed for categorizing DRPs.

Data collection and procedure

Patients' sociodemographic and clinical data were collected by one clinical pharmacist from the electronic records of patients meeting the inclusion criteria, using a data collection form. Once a patient's admission was confirmed as a Drug-Related Hospital Admission (DRHA) using the AT-HARM 10 tool, the Helper-Strand classification method was applied to categorize drug-related problems (DRPs). The preventability of DRPs was determined based on previous studies that employed best practices [40, 41]. DRP severity was classified as mild (symptoms or lab abnormalities not requiring treatment), moderate (requiring treatment or hospital admission, or causing non-permanent disability), or severe (life-threatening, causing permanent disability, or fatal) [42, 43]. For ADR-related hospital admissions, the Naranjo algorithm was used to assess the drug-event relationship, while non-compliance was also evaluated separately.

Statistical analysis

The collected data were analyzed using SPSS version 23 for all types of statistical analysis, and for statistical significance, a p-value <0.05 was considered statistically significant. Patients' demographic characteristics and clinical variables were presented in the form of frequencies and percentages. For ascertaining risk factors for DRHAs, binary logistic regression analysis was performed, and odds ratios (ORs) with 95% confidence intervals were calculated. For crude OR (COR), univariate logistic regression was performed, while for adjusted OR (AOR), multivariate logistic regression was performed by considering only those variables having a p-value <0.20.

Results and Discussion

A total of n=200 patients' data is included in the result section; among them, the majority of the participants were female (75.9%) and male (27.4%) in the NDRHAs and DRHAs group. Regarding age, the highest percentage of NDRHAs falls within the age group of 29-38 years (87.5%), while DHRAs have the highest percentage in the 59-68 years age group (38.5%). Regarding education status, most of the patients in the NDRHAs group (79.7%) had a bachelor's level of education, while in the DRHAs group (30.8%) had had an elementary level of education. Regarding employment status, (79.5%) of the patients in the NDRHAs group were employed, while in the DRHAs group, the majority (38.5%) were self-employed **(Table 1)**.

Table 1. Sociodemographic Characteristics of Patients (n=200)

Gender	NDRHAs		DHRAs	
	Frequency	Percentage	Frequency	Percentage
Male	85	72.6%	32	27.4%
Female	63	75.9%	20	24.1%
Age				
18-28 years	26	86.7%	4	13.3%
29-38 years	28	87.5%	4	12.5%
39-48 years	16	69.6%	7	30.4%
49-58 years	23	63.9%	13	36.1%
59-68 years	24	61.5%	15	38.5%
69-78 years	18	81.8%	4	18.2%
79 years and above	13	72.2%	5	27.8%
Education status				
Illiterate	21	72.4%	8	27.6%
Elementary school	9	69.2%	4	30.8%
High school	67	71.3%	27	28.7%
Bachelor's	51	79.7%	13	20.3%
Employment status				
Employed	58	79.5%	15	20.5%
Unemployed	54	77.1%	16	22.9%
Self-employee	16	61.5%	10	38.5%
Retired	20	64.5%	11	35.5%

The patients admitted to the hospital had different co-morbid conditions, among which most of the patients (16.0%) had hypertension, followed by (14.8%) diabetes mellitus. A higher number of patients (78.0%) were on drug therapy for chronic diseases, and a higher number of patients (42.7%) were using ≥6 drugs **(Table 2)**.

Table 2. Clinical characteristics of patients admitted (n=200)

	Frequency	Percentage
Co-morbid conditions		
Hypertension	70	16.0
Diabetes mellitus	65	14.8
Dyslipidemia	45	10.3
Chronic kidney disease	37	8.4
Heart failure	18	4.1
Coronary artery disease	14	3.2
Hypothyroidism	10	2.3
Atrial fibrillation	7	1.6
Ischemic heart disease	6	1.4
Asthma	6	1.4
Stroke	5	1.1
Others	155	35.4
Patients on drug therapy for chronic diseases		
Yes	156	78.0
No	44	22.0
Drugs		
1-2 drugs	32	22.4
3-5 drugs	50	35.0
≥6 drugs	61	42.7

Among n=200 patients admitted to the hospital, (26.0%) were related to DRHAs, of which (25.5%) were preventable. Regarding preventability (86.5%) were preventable, while most of them (51.9%) were of moderate severity **(Table 3)**. The most common DRHAs that contributed to hospital admission of the patients include non-compliance (71.2%), followed by untreated conditions (7.7%), improper drug selection (5.8%), sub-therapeutic dosage (5.8%), and adverse drug reactions (5.8%), respectively **(Figure 1)**. The assessment of ADRs was performed by using the Naranjo algorithm, and 66.3% of the adverse drug reactions were definite, and 33.3% were probable.

Table 3. Patterns of DRHAs among patients' admission

	Drug-related hospital admissions	Frequency	Percentage
Admission (n=200)	NDRHAs	148	74.0
	DRHAs	52	26.0
Severity (n= 52)	Moderate	27	51.9
	Severe	25	48.1
Preventability (n=52)	Definitely preventable	45	86.5
	Potentially preventable	6	11.5
	Not preventable	1	1.9

NDRHAs: Non-drug related hospital admission; DRHAs: Drug-related hospital admission; ADRs: Adverse drug reactions

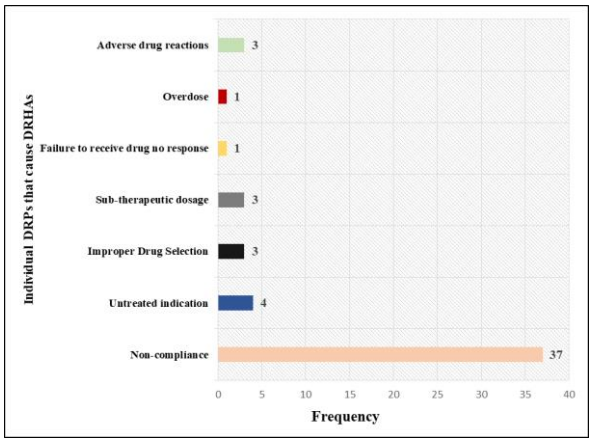

Figure 1. Individual DRPs that cause DRHAs (n=52)

Cardiovascular drugs accounted for 69.2% of the DRHAs, followed by immune suppressants, anemia medication, and antibiotics with 5.8% each **(Table 4)**. The most common drugs that accounted for ADR-related admission were atorvastatin, Prednisolone, and perindopril **(Table 4)**.

Table 4. Class of drugs and ADRs responsible for DRHAs among patients' admission

	Frequency	Percentage
Class of drugs		
Cardiovascular	36	69.2
Immune suppressants	3	5.8
Anemia medication	3	5.8
Antibiotics	3	5.8
NSAIDs	2	3.8
Anti-convulsant	1	1.9
Anti-diabetic	1	1.9
Anti-hyperlipidemic	2	3.8
Antihistamine	1	1.9
ADRs-related admissions		
Atorvastatin	1	-
Prednisolone	1	-
Perindopril	1	-

Univariate logistic regression was performed while taking admission to hospitals (NDRHAs/DRHAs) as a dependent variable and gender, age, education status, chronic diseases, chronic kidney disease, and number of drugs as independent variables. The findings of univariate regression revealed age, chronic diseases, chronic kidney disease, and the number of drugs that were independently associated with the admission of patients to hospitals related to DRHAs. These four variables were subjected to multivariate logistic regression to identify the predictors contributing to DRHAs and NDRHAs among the patients, and the results showed a statistically significant association with chronic disease and patients with chronic kidney disease. Patients with chronic disease were 11.4 times more likely to have DRHAs as compared to patients without chronic diseases (95% CI=1.752; 73.789 and p-value=0.011), and chronic kidney disease patients were 2.8 times more likely to have DRHAs as compared to patients with no chronic kidney disease and ESRD (95% CI=1.055; 7.553 and p-value=0.039) **(Table 5)**.

Table 5. Associated factors with DRHAs among patients

	Univariate regression			Multivariate regression		
	COR	CI 95%		AOR	CI 95%	
Age						
18-28 years	**Reference**			**Reference**		
29-38 years	0.9	0.210	4.100	0.4	0.072	1.892
39-48 years	2.8	0.717	11.273	0.4	0.081	2.036
49-58 years	3.7	1.049	12.865	1.1	0.234	4.892
59-68 years	4.1	1.182	13.963	1.7	0.436	6.287
69-78 years	1.4	0.319	6.542	1.5	0.425	5.550
79 years and above	2.5	0.573	10.914	0.4	0.087	1.982
Gender						
Male	**Reference**			-	-	-
Female	0.8	0.442	1.610	-	-	-
Education status						
Illiterate	Ref			-	-	-
Elementary school (1–8)	1.2	0.279	4.884	-	-	-
High school (9–12)	1.1	0.418	2.678	-	-	-
Bachelor's	0.7	0.242	1.850	-	-	-
Chronic diseases						
No	Ref			**Reference**		
Yes	9.9	2.305	42.561	11.4*	1.752	73.789
Chronic kidney disease (CKD)						
No CKD	**Reference**			Ref		
CKD	3.4	1.412	8.211	2.8*	1.055	7.553
ESRD	1.0	0.267	3.906	0.6	0.146	2.570
Number of drugs						
No drugs	**Reference**			**Reference**		
1-2 drugs	3.8	1.302	11.185	0.9	0.214	3.788
3-5 drugs	3.9	1.445	10.364	0.8	0.217	3.331
≥6 drugs	2.8	1.069	7.412	0.4	0.106	1.702

Multivariate logistic regression was used; NDRHAs/DRHAs were taken as the dependent variable; COR: crude odds ratio; AOR: adjusted odds ratio; CI: confidence interval; * p-value <0.05 was considered statistically significant.

The burden of DRPs contributing to hospitalization is significantly increasing not only in developing countries but also in developed countries. It exerts a substantial burden on healthcare systems in terms of higher healthcare costs and affects the patient's prognosis. Our results seem to be more accurate compared to other studies, as we used the validated AT-HARM 10 tool, while previous studies relied on expert opinions and trigger tools, which are used for medication safety purposes rather than for assessing the reasons for hospital admission. Various epidemiological studies demonstrated a higher prevalence of patient admission to hospitals resulting from DRPs [44-48]. Hence, timely identification and resolution of DRPs is

very crucial to avoid any morbidity and mortality to the patients and also assist in the reduction of the burden exerted on patients, the community, and the healthcare system [43]. Previous studies performed in Saudi Arabia reported a higher number of patient visits to the emergency department, and hospitalizations were related to DRPs [35-38, 49, 50]. However, this study focuses on identifying the latest trends in DRHAs and identifying the factors that lead to hospitalization in Saudi patients at King Fahad Hospital of the University (KFHU), Khobar, Saudi Arabia.

The findings of our study revealed that 26.0% of the hospital admissions were attributed to DRPs. Other studies performed in different countries reported 31.9% of DRHAs in Ethiopia [43], 30.6% in Malaysia [41], 36.0% in Sweden [51], 37.9% in France [52], 50.2% in the United States [53], and 82% in Uganda [54]. The variation of DRHAs in our study and other reported studies may be due to variations in study design, study setting, study population, and definition for categorization of DRPs and DRHAs. Regarding preventability, our study findings showed that 98.0% of these DRPs were preventable, of which 86.5% were definitely preventable. Our study findings are supported by other studies, which also reported considerably higher preventability rates of DRPs, such as 97.6% [1], 87% [34], 51.3% [55], 60.9% [56], 42.9% [57], 53.5% [58], 46% [59], 76.4% [60], and 69% [61]. In our study, 51.9% of these DRPs were of moderate severity, while a study reported 7.12% of moderate severity, and 6.78% were severe [42].

The DHRAs in our study accounted for different factors; the most common were non-compliance (71.2%), followed by untreated conditions (7.7%), improper drug selection (5.8%), sub-therapeutic dosage (5.8%), and ADRs (5.8%). The majority of the DRHAs in our study resulted from non-compliance and untreated conditions, which can be easily addressed. These findings are consistent with a similar study, which also reported non-compliance, untreated conditions, and ADRs as the most common reasons for DRHAs [43]. Similarly, studies conducted in India and Hawaii regarded untreated conditions as the reason for DRHAs [42, 62]. Another latest study in India reported non-compliance (46.6%) as the most common reason for DRHAs, followed by ADRs (22%), and sub-therapeutic dosage (7.6%) [42]. In our study, the DRHAs resulting from ADRs are very low compared to other studies; the possible reason for this can be due to different populations and assessment criteria for ADRs. Another possibility for the variation in the findings of our study and other studies can be due to illiteracy, polypharmacy, poor health care setups, and misconceptions. In our study, cardiovascular drugs (69.2%) were on top among other drugs for DRHAs, which is aligned with findings of other studies with 51.1% [43], 21.5% [36], and 27.0% [56] of DRHAs resulting from cardiovascular medications. In our study, the majority of the patients were using ≥6 drugs, which is consistent with previous literature that polypharmacy can contribute to DRPs and consequently lead to DRHAs [63]. Our findings also indicate that patients who had polypharmacy were approximately three times more likely to experience DRPs.

Our study findings revealed that patients who have chronic diseases have an 11.4 times higher likelihood of having DRHAs as compared to patients without chronic diseases. Chronic diseases have a higher prevalence of DRPs due to comorbidities, polypharmacy, and medication non-adherence [64]. Another study reported that patients with co-morbid conditions, such as chronic disease, were three times more likely to have DRPs compared to those without comorbidity [63]. Similarly, patients with chronic kidney disease (CKD) in our study were approximately three times more prone to DRPs, which is evident from previous literature [65, 66]. CKD patients due to compromised renal function tend to be at a higher risk for DRPs, of which medication dosing errors are among the top [67, 68], thereby these patients are more prone to DRHAs [69-71].

Taken together, the current study revealed a higher prevalence of DRHAs (26%) compared to a previous study performed in 2017 in Saudi Arabia (13.9%) [35]. Interestingly, the prevalence of preventable DHRAs was also notably higher in the current study (98%) compared to previous studies, which reported preventable rates ranging from 70% to 85.7% preventable DHRAs, respectively. Therefore, based on these findings, it is highly recommended that future research focusing on identifying strategies to reduce the prevalence of DRHAs, specifically preventable DRHAs, be conducted. The following areas need to be focused on in future research, such as ensuring appropriate dosing guidelines, improving medication management systems, and enhancing communication and education for healthcare professionals and patients. In addition, monitoring for high-risk populations, i.e., CKD patients and those on polypharmacy, and targeted interventions may be beneficial in decreasing the prevalence of DRHAs.

Limitations and strengths of the study

The study was performed in one center only, and the findings cannot be generalized to the whole population of Saudi Arabia. Patients reported to an emergency department or intensive care unit were not included in this study, which can be a limitation of this study. Another possible limitation is that the study was performed for only 3 months' duration, and the duration of hospital stay was not recorded at the time of data collection. To cover these possible limitations, a large multi-centered study with a longer duration needs to be conducted to identify further the risk factors contributing to DRHAs. The strength of this study is that it helped to identify the factors and predictors that lead to DRHAs in Saudi Arabia, and these findings will help to design a road map for the healthcare professionals and also create a need for the implementation of a clinical pharmacy setup to identify drug-related problems at their initial stage to prevent DRHAs.

Conclusion

The incidence of DRHAs within the study population was notably elevated, predominantly attributed to factors such as non-compliance, untreated conditions, and improper drug administration. A significant proportion of DRPs were found to

be preventable and exhibited moderate severity levels. Early detection during its initial phases by clinical pharmacists is crucial to mitigate such DRHAs, thereby optimizing patient therapy and reducing the financial burden on patients, their families, and the healthcare system. Integration of clinical pharmacists into the healthcare team, primarily through medication review and reconciliation practices, stands as a pivotal strategy to effectively address these challenges.

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