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Drug-related problems in a sample of outpatients with chronic diseases: a cross-sectional study from Jordan

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Abstract: Optimization of drug therapy and preventing drug-related problems (DRPs) are major factors to improve health care, reduce expenditure, and potentially save lives. This study aimed at describing the types, numbers, and frequencies of DRPs in the outpatient settings of a group of hospitals in Jordan. The study was set in the cardiology, endocrine, and respiratory outpatient clinics of five major hospitals in Jordan. Patients who visited the above clinics during the period from September 2012 to December 2013, were candidates for this study. Each included subject was fully assessed for DRPs by clinical pharmacists according to a specially designed and validated pharmaceutical care manual. The main outcome measures were the number and types of DRPs. Data were collected from 2,898 patients (mean age ± standard deviation: 56.59±13.5 years). The total number of identified DRPs was 32,348, with an average of 11.2 DRPs per patient. The most common DRPs were a need for additional or more frequent monitoring, a problem in patients' adherence to self-care activities or nonpharmacological therapy, and that the patient was not given instruction in or did not understand nonpharmacological therapy or self-care advice. The numbers of DRPs per patient in our sample were associated with older age (>57 years), being unmarried, having an education level of high school or less, not having health insurance, and the presence of certain clinical conditions, including hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, cardiac catheterization, heart failure, and gout. In conclusion, implementation of clinical pharmacy services is a strategy to limit DRPs. Certain patient populations are more vulnerable to DRPs.

Keywords: drug-related problems, outpatient, hospital, Jordan

Introduction

For most diseases, drug therapy enhances health-related quality of life.[1] However, inappropriate use of drugs may be harmful and could evoke side effects.[2] Drug therapy is growing more complex, thus making appropriate patient management increasingly challenging.[3] A drug-related problem (DRP), defined as a drug therapy problem, is any undesirable event experienced by a patient that involves, or is suspected to involve, drug therapy and that interferes with achieving the desired goals of therapy.[4] Accordingly, in clinical medicine, a wide range of DRPs may arise.[5] Optimization of drug therapy and preventing DRPs may save some of the health care expenditure, potentially save lives, and enhance patient's quality of life.[6–8] Previous studies have largely addressed DRPs as a cause of hospitalization,[6,9,10] and in elderly,[7,11] ambulatory care,[11–14] nursing homes,[15] and hospitalized patients.[16]

DRPs have been identified as contributing to negative clinical and economic outcomes in several international health care systems such as the Netherlands,[17] Denmark,[18]

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New Zealand,[19] Qatar,[12] and Saudi Arabia.[20] In Jordan, a study aimed at describing DRPs of hospitalized patients in the internal medicine department of one hospital showed a mean DRP rate of 9.4 per patient.[16] Another recently published study assessed DRPs in patients with chronic diseases who visited community pharmacies and reported a mean DRP rate of 4.1 per patient.[21] However, there are no published large-scale studies describing DRPs in outpatient settings in Jordan. Such data could feed into decision making pertaining to reducing DRPs. This study aimed at describing DRPs in the outpatient settings of a group of hospitals that represent different sectors of the health care system in Jordan.

Methods

In this cross-sectional observational study, a sample of patients from five hospitals representing all sectors of health services, including public, private, and military hospitals, were assessed for DRPs. These hospitals were King Abdullah University Hospital and Princess Basma Teaching Hospital in Irbid, University of Jordan Hospital, Prince Hamzeh Hospital, and Al Bashir Hospital in Amman and Al-Karak Hospital at Al Karak city. These hospitals were chosen based on several criteria, including geographic location, being a major hospital in its area, and the type of health sector represented.

Ethical approval

The study protocol was approved by the institutional review boards of King Abdullah University Hospital, University of Jordan Hospital, and the Ministry of Health, Jordan, which oversees all the other three hospitals.

Sample size

Previous literature related to inappropriate drug use in Jordan indicated that the standard deviation (SD) for the number of identified DRPs was five.[16,22] Based on this, the minimum required sample size to estimate the average number of DRPs within a confidence of 99% was calculated to be 94/hospital/setting. The following equation was used: sample size = (1.96× SD/desired error ratio).[2]

Study subjects

Patients who visited the cardiology, endocrine, and respiratory outpatient clinics during the period from September 2012 to December 2013 were invited to participate, and if they fitted the inclusion criteria, they were given a brief explanation about the study and asked to sign the informed consent form. Thus, informed written consent was obtained from all participants. The inclusion criteria were patients aged >18 years old, had at least one chronic medical condition, and received at least two medications, including all routes of administration, topical, inhaled, as needed, over the counter, etc. Patients with mental diseases and patients who did not speak Arabic or English language were excluded from the study.

Definition and classification of DRPs

The tool described in AbuRuz et al was used for the classification of DRPs.[16,22] This classification system was previously evaluated for reproducibility, inter-rater agreement, content validity, and internal and external validities and was tested on >200 patients.[16,22] All DRPs were identified by pharmacists (n=5) who held a Doctor of Pharmacy degree and who were trained on the study protocol in a special workshop that was held by the principal investigator of the study. DRPs were evaluated to ensure uniformity of classification in Table 1 by

Table 1 Classification of DRPs among studied patients (n=2,898)

DRP type	n (%)
A need for additional or more frequent monitoring	13,498 (41.73)
A problem in patients' adherence to self-care activities or nonpharmacological therapy	4,351 (13.45)
The patient was not given instruction in or did not understand nonpharmacological therapy or self-care advice	4,002 (12.37)
The patient was not given instruction in or did not understand important information regarding his medications	3,373 (10.43)
The patient requires additional combination therapy or stepping up	2,456 (7.59)
Drug use without an indication	799 (2.47)
A need for consultation	621 (1.92)
Untreated conditions that require pharmacological or nonpharmacological therapy	595 (1.84)
Dosage regimen issue	515 (1.59)
More effective drug is available	444 (1.37)
A need for additional diagnostic test	392 (1.21)
A problem in patients' adherence to medications	344 (1.06)
The patient treatment should be stepped down	316 (0.98)
Drug product not available	133 (0.41)
Duplication	97 (0.30)
Safety interactions issues	81 (0.25)
A current drug is contraindicated/unsafe for patient condition and should be stopped, monitored, or replaced	74 (0.23)
Safety dosage regimen issues	54 (0.17)
A safer drug is recommended	51 (0.16)
The patient is at high risk of developing ADR and needs monitoring or prophylaxis	48 (0.15)
Efficacy interaction issue	40 (0.12)
Allergic reaction or an undesirable effect: are there symptoms or medical problems that may be drug induced	27 (0.08)
Addiction or recreational drug use	22 (0.07)
The chosen medication(s) is not (are not) cost-effective	12 (0.04)
Avoidable adverse reaction	3 (0.01)

Abbreviations: DRPs, drug-related problems; ADR, adverse drug reaction.

a panel of clinical pharmacists that included the study's main author and coauthors and other five clinical pharmacists. According to AbuRuz et al,[22] DRPs were pooled under six main categories: indication, effectiveness, safety, knowledge, adherence, and miscellaneous. The indication category included the following two subcategories: unnecessary drug therapy (ie, the patient is receiving a medication for no valid medical indication) and untreated condition (ie, the patient has a medical problem that requires medication therapy but he/she is not receiving it). The efficacy category included four subcategories. First, more effective drug is available or recommended: the patient has a medication indication but he is not being treated properly with the most effective therapy. Second, the patient requires additional or combination therapy or stepping up because of actual or potential therapy failure or because of guidelines recommendation. Third, efficacy issues of dosage regimen: the patient has a medical problem that is being treated with too little of the correct medication because of a wrong dose, frequency, or duration. The patient may also have inappropriate dose regimen because of inappropriate timing or wrong dosage form. Finally, efficacy interactions issues: the patient has or is at risk of developing a medical problem or symptom that is the result of a drug–drug, drug–food, or drug–laboratory test interaction that reduces the efficacy of the drugs. The safety category included six subcategories. First, a current drug is contraindicated or unsafe for patient condition and should be stopped and monitored. Second, safer drug therapy is recommended. Third, the patient is at high risk of developing adverse drug reaction and needs monitoring or prophylaxis. Fourth, allergic reaction or undesirable effects: presence of symptoms or medical problems that may be drug induced. Fifth, safety dosage regimen issues: the patient has a medical problem that is being treated with too much of the correct medication because of a wrong dose, frequency, or duration. The patient may also have an inappropriate dose regimen because of inappropriate timing or wrong dosage form. Sixth, safety interactions issues: the patient has or is at risk of developing a medical problem or symptom that is the result of a drug–drug, drug–food, or drug–laboratory test interaction. The knowledge category included two subcategories. The patient was not given instruction in or did not understand important information regarding his or her medications (the purpose of his or her medication(s), how much, how and when to take it, what to avoid, how to prevent the side effect, and how to monitor his or her treatment). The patient was not given instruction in or did not understand nonpharmacological therapy or self-care advice (avoidance of risk factors, smoking, alcohol, diet, exercise, etc). The adherence category included two subcategories: problem in patient's adherence to medications (forget, skip, cannot afford, cannot swallow/administer drug, etc) and a problem in patients' adherence to self-care activities or nonpharmacological therapy. The miscellaneous category included four subcategories: a need for additional or more frequent monitoring, a need for additional diagnostic test, a need for consultation, and the chosen medication is not cost-effective.

Procedure

Patients were recruited by pharmacists who were involved in the study. Patients were approached at the physician office right after they finished their dialogue with the physician. Once a patient was recruited, he or she was fully assessed for DRPs by clinical pharmacists according to the following procedure: collecting patient's information using a specially designed and validated pharmaceutical care manual.[22] Patient's information was collected from patient's medical file and patient interviewing to obtain information on patient's knowledge and adherence and by participating in medical rounds. Collected information was recorded on special paper-based forms that were prepared based on the pharmaceutical care manual.[22] Patient's information was analyzed to identify DRPs utilizing an evidence-based approach[23] and by investigating laboratory data, assessing the achievement of treatment outcomes, and interviewing patients.

Identifying DRPs

A systematic approach was utilized in identifying DRPs.[4] Effectiveness-related problems were identified through comparing patients' treatment with the most updated clinical practice evidence-based guideline recommendations. Appropriateness of dosing regimen was checked by comparing doses with evidence-based guidelines recommendations or using drug information references such as Lexicomp's *Drug Information Handbook*.[4] Patients' clinical characteristics were taken into account when deciding about the appropriateness of dosage regimen. Adverse drug reactions were identified by conducting review of symptoms and by investigating patients' data for any possible adverse reaction related to patients' medications.[4] Potential adverse drug reactions were also checked by identifying patients who were at risk but were not receiving prophylaxis (eg, patients' not receiving prophylaxis for non-steroidal anti-inflammatory drugs-induced ulcer). I-Facts (Facts and Comparisons Drug

Interactions Facts) were used for identifying clinically important drug–drug interactions.[4]

Data analysis

Data were coded and entered into SPSS Version 19 (IBM Corporation, Armonk, NY, USA). Categorical data were expressed as numbers and percentage. Age and continuous data were expressed as mean ± SD. Unpaired *t*-test was used to compare the mean number of DRPs among patients according to demographic and health conditions (eg, hypertension and diabetes mellitus).

Results

Out of 3,112 patients, we collected data from 2,898 patients. Demographic data are shown in Table 2. The mean ± SD of patients' age was 56.59±13.5, and ~40.1% of them were males. More than 90% of patients had health insurance. Additionally, 9.1% of patients suffered from drug allergy. Table 3 shows the clinical or disease characteristics of patients. Notably, ~74% of the patients suffered from hypertension, 52.2% were diabetic, and 38.0% had dyslipidemia. Laboratory parameters of the studied sample are shown in Table 4.

The total number of identified DRPs was 32,348 with a mean ± SD of 11.2±6.2 DRPs per patient. DRPs were classified into standard categories as shown in Table 1.

Table 2 Patient's demographic data (n=2,898)

Variable	n (%) or mean ± SD
Age	56.59±13.5
Sex	
Male	1,162 (40.1%)
Female	1,724 (59.5%)
Clinic type	
Cardiology	1,523 (52.5%)
Endocrine	725 (25.0%)
Respiratory	650 (22.5%)
Hospital	
King Abdulla University Hospital (KAUH)	549 (19.0%)
Princess Basma Teaching Hospital	575 (19.8%)
University of Jordan Hospital	650 (22.4%)
Prince Hamzeh Hospital	501 (17.3%)
Al Bashir Hospital	218 (7.5%)
Al-Karak Hospital	402 (13.9%)
Health insurance	
Yes	2,652 (91.5%)
No	90 (3.1%)
Allergy	
Yes	264 (9.1%)
No	2,478 (85.5%)

Note: Due to missing values, some numbers do not add up to 100%.
Abbreviation: SD, standard deviation.

Table 3 Clinical characteristics of patients (n=2,898)

Clinical variable	n (%)
Hypertension	2,146 (74.1)
Diabetes mellitus	1,510 (52.2)
Dyslipidemia	1,100 (38.0)
Ischemic heart disease	846 (29.2)
Cardiac catheterization	801 (27.6)
Asthma	608 (21.0)
Heart failure	261 (9.0)
Cholecystectomy	248 (8.6)
Hypothyroidism	178 (6.1)
Gout	144 (5.0)
Chronic obstructive pulmonary disease	117 (4.0)
Renal impairment	101 (3.5)
Coronary artery bypass graft	76 (2.6)
Rheumatoid arthritis	64 (2.2)

The most common DRPs were a need for additional or more frequent monitoring, a problem in patients' adherence to self-care activities or nonpharmacological therapy, and the patient was not given instruction in or did not understand nonpharmacological therapy or self-care advice. Other DRPs are also shown in Table 1. Associations of numbers of DRPs per patient with patient demographic and clinical conditions are shown in Tables 5 and 6. Older patients (>57 years), not married, having education of high school or less, and not having health insurance were associated with significantly more DRPs/patient. Hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, cardiac catheterization, heart failure, and gout were associated with significantly higher numbers of DRPs, whereas asthma and chronic

Table 4 Laboratory parameters of patients (n=2,898)

Parameter	Mean ± standard deviation (SD)	Normal range
Low density lipoprotein (LDL; mmol/L)	3.05±1.09	2.6–4.8
High density lipoprotein (HDL; mmol/L)	1.20±0.39	0.9–1.5
Cholesterol (mmol/L)	4.94±1.28	0.0–5.2
Triglycerides (TG; mmol/L)	2.07±1.43	0.0–1.7
Glucose (mmol/L)	10.08±13.23	4.1–5.9
Glycosylated hemoglobin (AIC; %)	7.49±2.09	4.0–6.2
Creatinine (Cr; mg/dL)	1.36±8.41	0.5–1.2
Creatinine clearance (CrCl; mL/min)	117.97±522.23	88–137
Aspartate transaminase (AST; U/L)	23.23±21.80	0.0–50.0
Alanine transaminase (ALT; mIU/mL)	21.71±20.14	0.0–50.0
Hemoglobin (g/dL)	13.22±7.54	11.0–16.5
Thyroid-stimulating hormone (TSH, mIU/mL)	2.58±3.01	4.0–0.22

Table 5 Number of DRPs according to clinical characteristics of patients

Clinical variable	DRPs (mean ± SD)	*P*-value[a]
Age[b]		
≤57	10.17±6.2	<0.001
>57	11.76±6.1	
Sex		
Male	11.02±6.0	0.690
Female	10.92±6.3	
Social status		
Single (never married, divorced, and widowed)	10.33±6.1	0.007
Married	11.11±6.2	
Educational level		
High school or less	11.45±6.3	<0.001
More than high school	9.58±5.8	
Occupation		
Nonmedical	10.96±6.2	0.820
Medical	11.20±6.0	
Health insurance		
Yes	11.19±6.3	<0.001
No	8.16±5.5	

Notes: [a]Unpaired *t*-test was used to compare the mean of DRPs. [b]Median age of the study sample =57 years.
Abbreviations: DRPs, drug-related problems; SD, standard deviation.

Table 6 Number of DRPs according to clinical characteristics of patients

Clinical variable	DRPs (mean ± SD)	*P*-value[a]
Hypertension		
Yes	11.86±6.0	<0.001
No	8.40±6.0	
DM		
Yes	14.52±5.6	<0.001
No	7.08±4.1	
Dyslipidemia		
Yes	13.34±6.1	<0.001
No	9.51±5.8	
Ischemic heart disease		
Yes	13.06±6.1	<0.001
No	10.10±6.0	
Cardiac catheterization		
Yes	12.80±6.3	<0.001
No	10.40±6.2	
Asthma		
Yes	7.58±5.86	<0.001
No	11.57±5.98	
Heart failure		
Yes	12.54±6.3	<0.001
No	10.81±6.2	
Cholecystectomy		
Yes	11.78±5.8	0.071
No	11.03±6.3	
Hypothyroidism		
Yes	11.90±5.4	0.056
No	10.90±6.3	
Gout		
Yes	12.22±5.1	0.013
No	10.90±6.2	
COPD		
Yes	8.35±3.4	<0.001
No	11.07±6.2	

Note: [a]Unpaired *t*-test was used to compare the mean of DRPs in patients who have the clinical condition (eg, hypertension and DM) versus those who do not.
Abbreviations: COPD, chronic obstructive pulmonary disease; DRPs, drug-related problems; SD, standard deviation; DM, diabetes mellitus.

obstructive pulmonary disease were associated with lower numbers of DRPs.

Discussion

This study is the first to evaluate DRPs in outpatient clinics in Jordan and the Middle East and North African regions. Current results indicated an average of eleven DRPs per outpatient with chronic disease in Jordanian hospitals. The most commonly identified DRPs were a need for additional or more frequent monitoring, a problem in patients' adherence to self-care activities or nonpharmacological therapy, and the patient was not given instruction in or did not understand nonpharmacological therapy or self-care advice.

The need for additional or more frequent monitoring was found to be the most commonly encountered DRPs in a study about implementing collaborative medication management services in Australia.[24] This is in agreement with the results of the current study. Additionally, results of the current study showed that DRPs related to adherence to self-care activities represent 13.45% of total encountered DRPs. This is consistent with a study done among patients with heart failure in Spain, where nonadherence rate to self-care activities of ~14% was reported.[25] Additionally, in a study evaluating hospitalized patients in Jordan, the rate of DRPs due to need for consultation and need for additional diagnostic tests was similar to the ones reported in the current study.[16] Finally, the rate of DRPs related to patients not given instruction in or do not understand important information about their medication or nonpharmacological intervention was found to be similar to a Malaysian study that evaluated DRPs in inpatients with diabetes.[26] Other not common DRPs in this current study, such as more effective drug is available, current drug is contraindicated, dosage regimen issue, and drug use without indication, were also found to be least common in other studies.[16,26]

The current results indicated the association between the presence of DRPs and certain medical conditions such as hypertension, diabetes mellitus, dyslipidemia, ischemic heart

disease, cardiac catheterization, heart failure, and gout. This is consistent with the results of a previous study that found the medications used in the management of mentioned conditions (eg, diuretics, digoxin, insulin, and oral antidiabetics.) as risk factors for DRPs among patients.[27] On the other hand, the presence of asthma and chronic obstructive pulmonary disease was associated with significantly fewer numbers of DRPs. This could be related to multiple local campaigns related to the assessment of DRPs among respiratory patients, especially those pertaining to inhaler device techniques, which is the major source of DRPs among these patients.[28]

This study has certain strengths such as its large sample size, its coverage of several hospitals representing different aspects of health care in Jordan, and its coverage of outpatient settings, which is an area that has limited literature compared to inpatient settings. Yet, this study has some weaknesses such as aiming to only describe the current situation of DRPs without doing actual interventions, assessing the acceptance rate of other health care providers to these interventions, and assessing the extent of implementation of interventions and their impact on patient health outcomes. These points were not attempted because clinical pharmacy services are not implemented in most of the governmental hospitals in Jordan, and this study is expected to provide corner stone evidence for decision makers to show the need for implementing clinical pharmacy services. Future work is suggested to cover the above points and to fully evaluate clinical pharmacy model services, which will provide more evidence to ensure the success and benefits of implementation of clinical pharmacy services in reducing DRPs and improving patient health outcomes.

Conclusion

Implementation of clinical pharmacy services is a recommended strategy to identify DRPs in Jordanian health settings.

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Disclosure

The authors report no conflicts of interest in this work.

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