Assessment of drug-related problems and their impact on blood pressure control in patients with hypertension

Rana Abu Farha,[1] Iman Basheti,[2] Hassan Abu Al Ruz,[3] Akram Alsaleh,[4] Salah AbuRuz[1,5]

[1]Department of Biopharmaceutics and Clinical Pharmacy, Faculty of Pharmacy, University of Jordan, Amman, Jordan
[2]Department of Clinical Pharmacy, Faculty of Pharmacy, Applied Science University, Amman, Jordan
[3]Orthopedic Department, Ibn Al Haytham Hospital, Amman, Jordan
[4]Department of Internal Medicine, Faculty of medicine, University of Jordan, Amman, Jordan
[5]College of Pharmacy, King Saud Bin Abdulaziz University for Health Sciences, National Guards Health Affairs, Riyadh, Saudi Arabia

Correspondence to
Professor Salah AbuRuz, Department of Biopharmaceutics and Clinical Pharmacy, Faculty of Pharmacy, University of Jordan, Amman 11942, Jordan; aburuz@ju.edu.jo

ABSTRACT

Objectives Hypertension is among the leading causes of cardiovascular disease worldwide. No previous studies have examined specifically the types of drug-related problems (DRPs) in patients with hypertension, and how these problems affect blood pressure control. So, the primary aim of this study was to investigate the prevalence and nature of DRPs in outpatients with hypertension and reveal any associations between DRPs and blood pressure control in these patients.

Methods This was a cross-sectional correlation study. A total of 200 patients who fulfilled the inclusion criteria were recruited through outpatient clinics. Patients' data were assessed to identify DRPs using a systematic evidence-based approach.

Results Two hundred participants were recruited in this cross-sectional study. About half of the participants (48.5%) had uncontrolled hypertension. The average number of DRPs was 6.31±2.63. The main identified DRPs affecting blood pressure control included patients' lack of knowledge about their medications, lack of adherence to their medications, suboptimal efficacy of medications prescribed and the need for additional monitoring. Logistic regression analysis was performed to identify the most important predictors, and significant associations were found between poor blood pressure control and the above-identified variables except for knowledge about medication ($p \leq 0.05$).

Conclusion The number of DRPs among patients with hypertension is relatively high. These DRPs were associated with poor blood pressure control. The implementation of clinical pharmacy services for all patients with hypertension is strongly recommended.

INTRODUCTION

Hypertension is among the leading causes of cardiovascular disease worldwide.[1 2] Unawareness and poor control of hypertension remain important national health concerns.[3–6] Although factors such as decreased access to medical care and financial barriers contribute to low control, blood pressure control is poor even in patients who can receive pharmacological treatment.[7] In Jordan, the prevalence of hypertension is very high approaching 32.3%.[8] Among those populations of patients with hypertension, it was found that only 39.6% of the patients had controlled blood pressure value, with the majority of patients not achieving their blood pressure goal.[8]

Many factors were found to be significantly associated with blood pressure control. Poor adherence to evidence-based guideline recommendations, adverse effects of blood pressure-lowering drugs, attitudes of patients in relation to disease and treatments, poor adherence to medications and lack of structured, efficient healthcare facilities are some reasons for the low rates of hypertension control.[9–13]

Patients with hypertension often receive multiple medications and have different comorbid chronic diseases that can lead to the occurrence of drug-related problems (DRPs).[14 15] A DRP is an event or circumstance involving medication therapy that actually or potentially interferes with an optimum outcome for a specific patient.[16] Although there are several studies that investigated the impact of pharmaceutical care on blood pressure control,[11 17–20] none explored specifically the types of DRPs in patients with hypertension, and how these problems affect blood pressure control.

The primary aim of this study was to investigate the prevalence and nature of DRPs in outpatients with hypertension and to reveal any association between DRPs and blood pressure control in these patients.

METHODS

Study design and clinical setting

This cross-sectional correlation study was approved by the Institutional Review Board at the Jordan University Hospital, and was carried out at the outpatients' cardiac clinics at Jordan University Hospital. The study was conducted over a 3-month period.

Study subjects

During the 3 months' study period, the outpatient cardiac clinic served 1300 patients eligible for inclusion who were diagnosed with primary hypertension. However, we were able to approach only 209 patients (15%), from which, 200 patients agreed to take part in the study (response rate 95.7%). Inclusion criteria included adult patients (≥18 years of age) with doctor diagnosis of primary hypertension for at least 6 months, receiving treatment for hypertension with no change in medication regimen for at least 1 month. Patients were excluded if they were diagnosed by the physician with secondary hypertension (such as renovascular disease, pheochromocytoma, Cushing's syndrome and primary aldosteronism) or if they were going through hypertensive crisis (defined as systolic blood pressure >180 mm Hg or diastolic blood pressure >120 mm Hg).

Data collection

Patients visiting outpatient clinics at the Jordan University Hospital were approached for participation in the study using convenient sampling technique. Patients who responded to the researcher were offered to participate in the study, and an information leaflet was provided on acceptance. Verbal consent was sought from the respondent before study entry.

All participants had their blood pressure measured at one arm while seated, after at least 5 min of rest. Measurements were obtained by the researcher, who is also an experienced clinical pharmacist (RAF) using an auscultatory sphygmomanometer. Three previous blood pressure readings were also obtained from the patients' files (if they were obtained within the last 3 months), and an average blood pressure reading was calculated for the patient to evaluate their blood pressure control. Hypertension is considered controlled according to Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) criteria if patient's average blood pressure was below 140/90 mm Hg or below 130/80 mm Hg in patient with diabetes or those with chronic renal failure; otherwise, patient is considered to have uncontrolled hypertension.

Patient's medical file was reviewed to collect information regarding their demographic information, clinical tests performed (fasting plasma glucose, serum creatinine, cholesterol, triglyceride, high-density lipoprotein, low-density lipoprotein and haemoglobin A1c), date of the clinical tests (whether they were taken within the last 3 months or not) and also to obtain information about the patient's diagnosed conditions, drug therapies and any other medical problems.

Patient's adherence and knowledge towards pharmacological and non-pharmacological therapies were also assessed using validated questionnaire.

Classification of DRPs

For the classification of DRPs, AbuRuz et al[21] classification system was used. DRPs were divided into six main categories: (1) indication, (2) effectiveness, (3) safety, (4) knowledge, (5) adherence and (6) miscellaneous.

Identification of DRPs

All types of DRPs were identified using a systematic approach.[22] DRPs affecting effectiveness were identified through comparing patients' treatment with current evidence-based guideline recommendations. The JNC 7 recommendation was used to determine effectiveness of treatment and appropriateness of treatment.[23] For patients suffering from other diseases, their treatment was evaluated using the appropriate updated evidence-based treatment guidelines for the documented diseases. Appropriateness of dosing regimen was checked by comparing doses with evidence-based guideline recommendations. The I-fact (Facts and Comparison, 2010) was used for identifying major drug–drug interactions.

Problems towards adherence to medications or lifestyle activities were assessed using a validated translation of the scale developed by Morisky et al.[24] Adherence scale was first translated to Arabic and then back translated to English following a worldwide recognised approach for translation and adoption of instruments. Patient's knowledge was assessed based on ability to answer correctly the questionnaire related to their medications and lifestyle activities. All the Arabic versions of questionnaires (for both adherence and knowledge) were tested for face and content validity by the authors of the study, and questions were adjusted as appropriate.

Sample size calculation

A pilot study was conducted initially on 30 patients to estimate the average number of DRPs in patients with controlled and those with uncontrolled hypertension. The mean difference in DRPs was 2.5, and SDs were 2.3 and 1.8 in patients with controlled and uncontrolled hypertension, respectively. Setting α at 0.05 and using power of 80%, the minimum required sample size to obtain a significant difference was calculated as 12 subjects per group. A sample size of 200 was decided to be involved in the study in order to have more generalisable results.

Data analysis

Data were coded and entered into Statistical Package for Social Science V.17 (SPSS Chicago, Illinois, USA). Group differences (controlled and uncontrolled hypertension) were studied using bivariate analysis that is, independent sample Student's t test for continuous independent variables and χ^2 analysis for categorical independent variables. Based on the information obtained from the bivariate analysis, a framework for the risk factors associated with uncontrolled hypertension was developed using logistic regression analysis.

RESULTS

Demographic and clinical characteristics of the study sample

The demographic and clinical characteristics of the sample are shown in table 1. The mean age of patients was around 59.7 years (SD=10.2); males accounted for 39.5% of all the patients recruited. About half of the participants (51.5%) had controlled hypertension, with a mean value of 126/77 mm Hg.

Table 1 Demographic and clinical characteristics of study sample (n=200)

Parameter	
Age (mean (SD)) years	59.7 (10.2)
Gender: male, n (%)	79 (39.5)
Marital status, n (%)	
Single	2 (1)
Married	163 (81.5)
Widowed	34 (17)
Divorced	1 (0.5)
Education, n (%)	
Not educated	27 (13.5)
Primary	89 (44.5)
Secondary	12 (6)
High school	22 (11)
Control of hypertension, n (%)	
Controlled	103 (51.5)
Uncontrolled	97 (48.5)
Blood pressure (systolic/diastolic) mm Hg (mean (SD))	
Controlled	126/77 (9.7/6.3)
Uncontrolled	150/88 (14.0/8.01)
Duration of hypertension (years) (mean (SD))	
Controlled	7.7 (6.2)
Uncontrolled	9.1 (6.5)
Number of prescribed medications (mean (SD))	
Controlled	6.1 (2.5)
Uncontrolled	6.8 (2.6)

Drug-related problems

The total number of identified DRPs was 1261 (average 6.31, SD 2.63, range 0–15). Figure 1 shows the number and percentage of the different categories of the identified DRPs. DRPs affecting effectiveness were the most frequently identified DRPs among the study sample, approximating for 29.60%. Within effectiveness DRPs, drug interactions were the most common. 'Untreated condition' was the least frequent DRPs identified, accounting for 1.59% of the total DRPs identified in the study sample.

Effect of DRPs on blood pressure control

Initial screening of data showed a significant association between number of DRPs and poor blood pressure control (independent sample t test, $p < 0.05$) (figure 2).

A bivariate analysis was applied to determine exactly which classes of DRPs significantly affect blood pressure control. Four classes of DRPs were significantly associated with poor blood pressure control ($p < 0.05$). These classes included knowledge about medications, adherence to medications, effectiveness DRPs and the need for additional monitoring (table 2).

Some of the identified variables may affect blood pressure as a consequence of their correlation and interaction with other variables. Therefore, logistic regression was performed to find out the factors which were independently and significantly associated with blood pressure control.

All variables identified above (table 2) were entered into logistic regression analysis to identify the most important predictors. Result revealed three of preidentified variables (adherence to medications, effectiveness DRPs and need for additional monitoring) were significantly associated with poor blood pressure control ($p \le 0.05$) (table 3).

A test of the final model against a constant-only model was statistically reliable, χ^2 ((degree of freedom of 8) $= 55.945$, $p < 0.0005$), indicating that the predictors, as a set, reliably distinguished between patients with controlled and
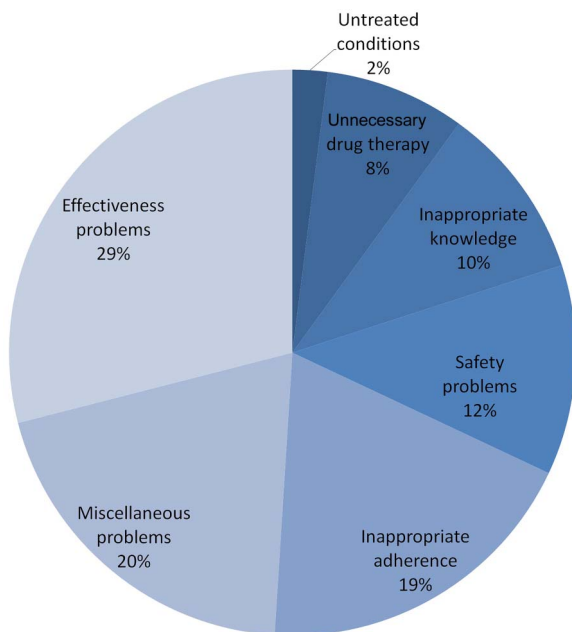

Figure 2 Differences among respondents with controlled and uncontrolled hypertension with regard to drug-related problems (DRPs) identified. SD for controlled and uncontrolled group was 2.2 and 2.4, respectively (*significant at 0.05 level).

uncontrolled hypertension. The variance in blood pressure control accounted for by the predictors was 32.5% (Nagelkerke R^2).

DISCUSSION

To our knowledge, the association between DRPs and blood pressure was not previously investigated in the literature. This is the first study to reveal the association between DRPs in patients with hypertension and its effect on their blood pressure control.

Results of this study revealed a high number of DRPs in patients with hypertension. The average number of DRPs was 6.31 per patient. To date, there has been no comparable study done specifically on DRPs in patients with hypertension both locally and globally. The number of DRPs identified was three times higher than the number detected by other study, which was conducted in patients who had diabetes mellitus with hypertension.[15]

Drug interactions, dose regimen issues and the need for additional therapy were the most frequent type of DRPs identified. These results were comparable with previous study, which found that drug choice problems and drug interactions were among the most frequent categories of DRPs in patients who had diabetes with hypertension.[15]

Non-adherence to medication was significantly associated with poor blood pressure control at both bivariate and multivariate regression. It was found that poor adherence to medication increased the risk of having uncontrolled blood pressure by 137.9% compared with adherent patients (OR 2.37). This finding was similar to previously published reports that examined the relationship of blood pressure control with an index of compliance, and found that poor blood pressure control was associated with a lower compliance index ($p > 0.05$).[25] Also another study suggested that in order to increase the effectiveness of medical care for hypertension, it is important to improve compliance with antihypertensive agents.[26] These results stresses on the importance of improving compliance with

Figure 1 Percentage of different categories of drug-related problems identified among patient with hypertension (n=200). Total number of drug-related problems was 1261.
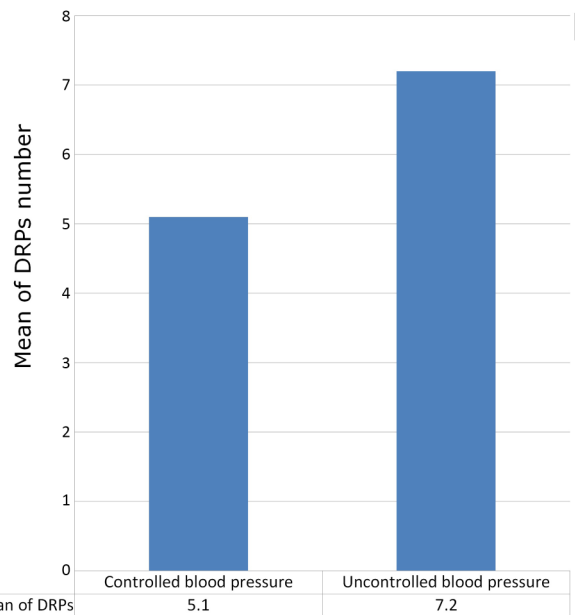
Table 2 Differences among respondents with controlled and uncontrolled hypertension with regard to specific classes of actual drug-related problems identified

| | Hypertension control | | | |
Actual drug-related problem categories	Controlled (103)	Uncontrolled (97)	p Value	OR
Indication drug-related problems (yes, n (%))	49 (47.6)	50 (51.5)	0.574	1.172
Effectiveness drug-related problems (yes, n (%))	44 (42.7)	78 (80.4)	0.000*	5.505
Safety drug-related problems (yes, n (%))	42 (40.8)	46 (47.4)	0.344	1.310
Adherence to medications (non-adherent, n (%))	36 (35.0)	49 (50.5)	0.026*	1.900
Adherence to self-care activities (non-adherent, n (%))	78 (75.7)	81 (83.5)	0.173	1.623
Knowledge about medications (poor knowledge, n (%))	38 (36.9)	56 (57.7)	0.003*	2.336
Knowledge about self-care activities (poor knowledge, n (%))	17 (16.5)	18 (18.6)	0.703	1.153
Miscellaneous drug-related problems (yes, n (%))	68 (66.0)	84 (86.6)	0.001*	3.326

*Significant at 0.05 level, χ^2 test.

Table 3 Logistic regression for actual drug-related problems identified, affecting blood pressure control

Variables	B	SE	p Value	OR	95% CI for OR
Indication drug-related problems (1: no; 2: yes)	−0.080	0.349	0.819	0.923	0.460 to 1.830
Effectiveness drug-related problems (1: no; 2: yes)	1.786	0.352	0.000*	5.966	2.990 to 11.903
Safety drug-related problems (1: no; 2: yes)	0.120	0.338	0.722	1.128	0.582 to 2.187
Adherence to medications (1: adherent; 2: non-adherent)	0.867	0.356	0.015*	2.379	1.185 to 4.777
Adherence to about self-care activities (1: adherent; 2: non-adherent)	0.724	0.427	0.090	2.062	0.893 to 4.760
Knowledge about medications (1: good; 2: poor)	0.614	0.353	0.082	1.848	0.924 to 3.693
Knowledge about self-care activities (1: good; 2: poor)	−0.647	0.483	0.180	0.523	0.203 to 1.349
Miscellaneous drug-related problems (1: no; 2: yes)	1.382	0.448	0.002*	3.982	1.655 to 9.577

*Significant at 0.05 level.

antihypertensive agents in order to increase the effectiveness of medical care for patients with hypertension.

Although the impact of poor adherence to medications is well known in the literature, the effect of both effectiveness DRPs and the need for additional monitoring on blood pressure were not covered previously in the literature. Presence of effectiveness DRPs was found to increase the risk of having uncontrolled hypertension by 496.6% compared with those without effectiveness DRPs (OR 5.966). The need for additional monitoring such as 'need for lipid profile monitoring or HBA1c monitoring' was also found to increase the odds of being with uncontrolled hypertension by 298.2% compared with those without these problems (OR 3.982).

It is worth mentioning the main limitations of this study: (1) this study was conducted only in one centre, and therefore, may not be representative of the whole patients' population; (2) the severity of DRPs, the proportion of self-medication and use of alternative and complementary medicines were not assessed; (3) since this study used a convenient sampling approach rather than random sampling, the results may not be representative of all patients with hypertension attending the Jordan University Hospital; (4) also, we did not study the impact of each DRP on other clinical outcomes or total healthcare costs and (5) we did not make suggestions for resolving the issue of the detected DRPs, and did not discuss the results of the review and possible solutions with the responsible physician.

how and how much resolving identified DRPs will impact blood pressure control. Pharmaceutical care services are strongly recommended for all patients with hypertension, even those with controlled blood pressure who suffer from several DRPs. Effectiveness, adherence and monitoring DRPs should be given the highest priority.

Key messages

What is already known on this subject?
► Unawareness and poor control of hypertension remain important national health concerns.
► Many factors were found to be significantly associated with blood pressure control.

What this study adds?
► The number of drug-related problems (DRPs) among patients with hypertension is considered relatively high and DRPS are associated with poor hypertension control.
► Pharmaceutical care services are strongly recommended for all patients with hypertension.
► Effectiveness, adherence and monitoring DRPs should be given the highest priority when providing pharmaceutical care to patients with hypertension.

CONCLUSION

The number of DRPs among patients with hypertension is relatively high in both patients with controlled and uncontrolled blood pressure. These DRPs were associated with poor blood pressure control. A more valid design is needed to investigate

Ethics approval Institutional Review Board at the Jordan University Hospital.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Kearney PM, Whelton M, Reynolds K, *et al*. Worldwide prevalence of hypertension: a systematic review. *J Hypertens* 2004;22:11–19.
2 Wong ND, Dede J, Chow VH, *et al*. Global cardiovascular risk associated with hypertension and extent of treatment and control according to risk group. *Am J Hypertens* 2012;25:561–7.
3 Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988–2000. *JAMA* 2003;290:199–206.
4 Amar J, Chamontin B, Genes N, *et al*. Why is hypertension so frequently uncontrolled in secondary prevention? *J Hypertens* 2003;21:1199–205.
5 Lang T, de Gaudemaris R, Chatellier G, *et al*. Prevalence and therapeutic control of hypertension in 30 000 subjects in the workplace. *Hypertension* 2001;38:449–54.
6 Pickering TG. Therapeutic inertia and the medicare crisis. *J Clin Hypertens* 2006;8:667–70.
7 Hyman DJ, Pavlik VN. Characteristics of patients with uncontrolled hypertension in the United States. *N Engl J Med* 2001;345:479–86.
8 Jaddou HY, Batieha AM, Khader YS, *et al*. Hypertension prevalence, awareness, treatment and control, and associated factors: results from a national survey, Jordan. *Int J Hypertens* 2011;2011:828797.
9 Neutel JM, Smith DH. Improving patient compliance: a major goal in the management of hypertension. *J Clin Hypertens (Greenwich)* 2003;5:127–32.
10 Oliveria SA, Lapuerta P, McCarthy BD, *et al*. Physician-related barriers to the effective management of uncontrolled hypertension. *Arch Intern Med* 2002;162:413–20.
11 Orozco-Beltran D, Brotons C, Moral I, *et al*. [Factors affecting the control of blood pressure and lipid levels in patients with cardiovascular disease: the PREseAP Study]. *Rev Esp Cardiol* 2008;61:317–21.
12 Ferrari P. Reasons for therapeutic inertia when managing hypertension in clinical practice in non-Western countries. *J Hum Hypertens* 2009;23:151–9.
13 Bulatova NR, Yousef A-M, AbuRuz SD, *et al*. Hypertension management and factors associated with blood pressure control in Jordanian patients attending cardiology clinic. *Trop J Pharm Res* 2013;12:827–33.
14 Munger M. Polypharmacy and combination therapy in the management of hypertension in elderly patients with co-morbid diabetes mellitus. *Drugs Aging* 2010;27:871–83.
15 Zaman Huri H, Fun Wee H. Drug related problems in type 2 diabetes patients with hypertension: a cross-sectional retrospective study. *BMC Endocr Disord* 2013;13:2.
16 Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. *Am J Hosp Pharm* 1990;47:533–43.
17 Garcao JA, Cabrita J. Evaluation of a pharmaceutical care program for hypertensive patients in rural Portugal. *J Am Pharm Assoc (Wash)* 2002;42:858–64.
18 Zhao P-X, Wang C, Qin L, *et al*. Effect of clinical pharmacist's pharmaceutical care intervention to control hypertensive outpatients in China. *Afr J Pharm Pharmacol* 2012;6:48–56.
19 de Souza WA, Yugar-Toledo JC, Bergsten-Mendes G, *et al*. Effect of pharmaceutical care on blood pressure control and health-related quality of life in patients with resistant hypertension. *Am J Health Syst Pharm* 2007;64:1955–61.
20 Robinson JD, Segal R, Lopez LM, *et al*. Impact of a pharmaceutical care intervention on blood pressure control in a chain pharmacy practice. *Ann Pharmacother* 2010;44:88–96.
21 AbuRuz SM, Bulatova NR, Yousef AM. Validation of a comprehensive classification tool for treatment-related problems. *Pharm World Sci* 2006;28:222–32.
22 Aburuz S. The case for evidence-based pharmaceutical care. *Res Social Adm Pharm* 2015;11:e146–7.
23 Chobanian AV, Bakris GL, Black HR, *et al*. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA* 2003;289:2560–72.
24 Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;24:67–74.
25 Caldwell JR, Theisen V, Kaunisto CA, *et al*. Psychosocial factors influence control of moderate and severe hypertension. *Soc Sci Med* 1983;17:773–82.
26 Ren XS, Kazis LE, Lee A, *et al*. Identifying patient and physician characteristics that affect compliance with antihypertensive medications. *J Clin Pharm Ther* 2002;27:47–56.