Predictors of Uncontrolled Blood Pressure in Treated Hypertensive Individuals: First Population-Based Study in Lebanon

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Arterial hypertension is a leading risk factor for cardiovascular disease and stroke. This study aimed to assess the predictors of uncontrolled systolic and diastolic blood pressure (BP) in Lebanon among treated hypertensive individuals. The authors included 562 participants 40 years and older. The potential predictors included sociodemographic characteristics, self-reported health information, and medication adherence. Prevalence of uncontrolled systolic and diastolic BP reached 43.1% and 24.9%, respectively. Independent predictors of uncontrolled systolic BP were older age, male sex, and low and medium medication adherence level. Predictors of uncontrolled diastolic BP were younger age, obesity, and low medication adherence level. Married individuals and patients taking statins had better diastolic BP control. Uncontrolled BP is a major public health problem in Lebanon. The authors identified low adherence as a major modifiable risk factor for systolic and diastolic BP control and obesity as a major modifiable risk factor for diastolic BP control. *J Clin Hypertens (Greenwich)*. 2016;18:871–877. © 2016 Wiley Periodicals, Inc.

Arterial hypertension (AH) is a leading risk factor for cardiovascular disease (CVD) and stroke.[1] Approximately 30% of the general population has AH, and this proportion increases to two thirds in older individuals.[2]

A meta-analysis of 61 prospective studies including one million adults showed that the cardiovascular risk increases continuously and consistently without evidence of a threshold, down to blood pressures (BPs) as low as 115/75 mm Hg.[3]

Audits conducted in patients with AH showed insufficient BP control, despite availability of effective antihypertensive treatments and guidelines.[4] The prevalence of uncontrolled AH varies between countries.[5] In the United States, analysis of data from the National Health and Nutrition Examination Survey (NHANES) 2003–2010 indicated that more than 45% of treated individuals did not have their BP controlled at the 140/90 mm Hg threshold.[6] Meanwhile, within Europe, BP control reached 40%, 30%, 28%, 19%, and 21% among treated patients in England, Germany, Italy, Spain, and Sweden, respectively.[5] Similarly, within the Middle East, BP control reached 34.4% and 37% among treated patients in Jordan and Saudi Arabia, respectively.[7,8]

Two recent studies evaluated BP control in the Lebanese population. On one hand, Matar and colleagues[9] reported a prevalence of 46% of uncontrolled BP in treated individuals; however, their study population was not representative of the whole population and they could not identify any predictor of uncontrolled BP. On the other hand, the I-PREDICT[10] study found that diabetes was associated with uncontrolled BP while predictors of good BP control were the early control of BP and the prescription of combination therapy at baseline; however, participants in this study were outpatients from hospitals and private clinics, thus they are not representative of the Lebanese population.

Both studies conducted in Lebanon[9,10] did not tackle the relationship between advancing age and uncontrolled BP and did not assess medication adherence in treated hypertensive individuals. Furthermore, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)[11] suggests that systolic BP (SBP) is the main risk factor for CVD and stroke after 50 years of age and accounts for most cases of uncontrolled AH in individuals 60 years and older. In contrast, diastolic BP (DBP) is a more potent CVD risk factor than SBP until age 50.[11]

Thus, the aim of our study was to assess sociodemographic, self-reported, and clinical predictors of uncontrolled SBP and DBP among treated hypertensive individuals in a nationally representative sample of the Lebanese population.

METHODS

Study Design and Population

In the framework of the study assessing the prevalence of CVDs and their risk factors among Lebanese

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residents, we carried out a cross-sectional study between September 2013 and October 2014 using a multistage cluster sample across Lebanon. We randomly selected 100 circumscriptions from the list of circumscriptions in Lebanon (villages, towns, and cities). Then, using a software program, we randomly selected residents aged 40 years and older from the list of dwellers provided by the local authority. After providing oral and written consent, participants underwent a face-to-face interview. A total of 1515 individuals were enrolled. Analysis in this study was limited to 562 participants who had been diagnosed with AH by a physician and were taking antihypertensive medications.

Data Collection

The following self-reported data were collected: sociodemographic characteristics (eg, age, sex, educational level, marital status), history of heart disease, smoking status, frequency and duration of physical activity, medication use for BP and glucose control, and lipid-lowering medication.

Medication Adherence

We measured medication adherence using the eight-item Morisky Medication Adherence Scale (MMAS-8). The MMAS-8 was designed to facilitate identification of barriers and behaviors associated with adherence to hypertensive medication.[12] MMAS-8 is a self-report questionnaire with eight questions (items). Response choices are yes/no for items 1 through 7 and a five-point Likert response scale for the last item. The total score on the MMAS-8 can range from 0 to 8, with scores of <6, 6 to <8, and 8 reflecting low, medium, and high adherence, respectively.

Following the method recommended by the World Health Organization, we translated the MMAS-8 into Arabic, and independently back-translated it into English by two translators to verify and solve any translation inconsistencies. We then tested the translated version in a group of 20 patients with AH to check for understanding of the questions in accordance with its original meaning and no inconsistencies were revealed.

Measurements

Trained medical students performed the measurements. Anthropometric measurements included weight (kg) and height (m). Body mass index (BMI) was calculated by dividing weight in kilograms by height in square meters. BMI was categorized into three classes: normal weight (BMI <25 kg/m^2), overweight (25 kg/m^2≤BMI<30 kg/m^2), and obese (BMI ≥30 kg/m^2). We measured SBP and DBP twice following a standardized protocol using an electronic automatic validated device (Omron M6 Comfort; Omron, Kyoto, Japan).[13] Individuals underwent random capillary blood glucose (RCBG)[14] using Accu-Check Performa (Roche Diagnostics GmbH, Mannheim, Germany).

BP Control Cut-Points

All cut-points for uncontrolled BP, SBP, and DBP were based on the Eighth Joint National Committee (JNC 8).[15] Patients with mean SBP ≥140 mm Hg were considered to have uncontrolled SBP and patients with mean DBP ≥90 mm Hg were considered to have uncontrolled DBP. Uncontrolled BP was defined as SBP ≥140 mm Hg and/or DBP ≥90 mm Hg.

Clinical and Self-Reported Predictors Definitions

Diabetes was defined as RCBG >200 mg/dL or self-reported medication use for glucose control.[16] We defined current smokers as individuals who smoked tobacco in the previous 12 months, and we included those who had quit within the past year. We defined history of heart disease as any self-reported history of myocardial infarction, stenting, angioplasty, or coronary artery bypass graft. We considered individuals as physically active if they were regularly involved in moderate-intensity physical activity for at least 150 minutes per week or vigorous-intensity physical activity for 75 minutes at least per week.[17]

Statistical Analysis

Before statistical analysis, two independent observers double-checked the quality control of the questionnaires; we performed an additional audit on a random selection of 5% of the questionnaires. We analyzed data using SPSS version 20.0 (IBM Corporation, Armonk, NY). We tested for the internal consistency of the MMAS-8 by calculating Cronbach's alpha.[18] The item-total correlation values ranged from 0.42 to 0.62 for the eight items composing the MMAS-8. The internal consistency (Cronbach's alpha reliability) was 0.77. We used means with standard deviations to describe normally distributed variables, medians with interquartile ranges to describe non-normally distributed variables, and percentages with counts to describe categorical variables. The outcome variables were uncontrolled SBP and DBP. We tested univariate associations using the Pearson chi-square (χ^2) test for categorical variables. We performed multivariable analyses using logistic regression models in backward likelihood ratio methods to evaluate potential predictors of systolic and diastolic uncontrolled BP, taking into account potential confounding variables. We assessed the predictors of uncontrolled SBP and DBP in the whole sample and then by sex to account for a potential modifier effect. The potential predictive factors included sociodemographic characteristics, known cardiovascular risk factors, and medication adherence. A P value <.05 was considered statistically significant.

RESULTS

Sample Description

Table I shows the basic characteristics of the study population. The median age of the participants was

63.7 years (interquartile range, 55–74; minimum, 40; maximum, 91), half were female, and 19.5% had a university degree. Slightly more than one third of participants were obese, 37.3% had diabetes mellitus, and 40.4% were taking statins. The mean SBP for the study population was 135±19 mm Hg (minimum, 70; maximum, 200), and the mean DBP was 80±14 mm Hg (minimum, 50; maximum, 130). The prevalence of uncontrolled BP was 51.1% (95% confidence interval [CI], 47.7%–54.5%). SBP and DBP prevalence reached 43.1% (95% CI, 39.7%–46.5%) and 24.9% (95% CI, 21.9%–27.9%), respectively. Approximately one in five participants were considered poorly adherent, with 47% (n=52) of poorly adherent participants having uncontrolled SBP and 35% (n=39) having uncontrolled DBP.

Regarding the number of antihypertensive drugs used, 48.6% of individuals were taking monotherapy, 25.8% were taking dual therapy, and 9.8% were taking three or more antihypertensive medications (Table I).

Multivariable Analyses of the Total Sample

Multivariable logistic regression indicated that age 55 years and older, male sex (adjusted odds ratio [adjOR], 1.96; 95% CI, 1.22–3.13), low (adjOR, 2.22; 95% CI, 1.20–4.10) and medium (adjOR, 2.41; 95% CI, 1.44–4.03) medication adherence level, and treatment with three or more antihypertensive drugs were significantly and independently associated with uncontrolled SBP (Table II). We also found that age younger than 55 years, obesity (adjOR, 2.44; 95% CI, 1.20–4.94), and low medication adherence (adjOR, 1.93; 95% CI, 1.03–3.61) were significantly and independently associated with uncontrolled DBP, whereas being married (adjOR, 0.58; 95% CI, 0.34–0.99) and taking statins (adjOR, 0.61; 95% CI, 0.37–0.99) were associated with better DBP control (Table II).

Multivariable Analyses by Sex

Older age was associated with uncontrolled SBP and controlled DBP in both men and women (Table III and Table IV). Low medication adherence was associated with uncontrolled DBP in men, while in women, low and medium levels of adherence were associated with uncontrolled SBP and DBP. Furthermore, in women, obesity was associated with uncontrolled DBP and diabetes with better DBP control (Table III and Table IV).

DISCUSSION

Our study has shown that half of treated hypertensive patients have uncontrolled AH, one in four has uncontrolled DBP, and 43% have uncontrolled SBP.

Older age, male sex, lower medication adherence level, and a combination of three or more antihypertensive drugs were independent and positive predictors of uncontrolled SBP. Predictors of uncontrolled DBP were younger age, living alone, obesity, lower medication adherence level, and use of statins (protective).

TABLE I. Characteristics of Study Participants[a]

Characteristics	Study Participants (n=562)
Sex	
Female, No. (%)	282 (50.2)
Age, median (IQR), y	63.7 (55–74)
Educational level, No. (%)	
High school or less	444 (79.0)
University degree	110 (19.5)
Missing data	8 (1.5)
Marital status, No. (%)	
Married	423 (75.2)
Single/divorced/widowed	138 (24.6)
Missing data	1 (0.02)
History of heart disease	138 (24.5)
History of stroke/TIA	45 (8.0)
Diabetes mellitus	210 (37.3)
Current smoking	247 (43.9)
BMI class, No. (%)	
Normal weight	113 (20.0)
Overweight	231 (41.1)
Obese	201 (35.8)
Missing data	17 (3.1)
Regular physical activity	120 (21.3)
Antihypertensive drugs, No. (%)	
1	273 (48.6)
2	145 (25.8)
≥3	55 (9.8)
Missing data	89 (15.8)
Lipid-lowering medication (statins)	227 (40.4)
Medication adherence level, No. (%)	
Low	111 (19.8)
Medium	208 (36.9)
High	201 (35.7)
Missing data	42 (7.6)
Uncontrolled SBP	242 (43.1)
Uncontrolled DBP	140 (24.9)

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; IQR, interquartile range; SBP, systolic blood pressure; TIA, transient ischemic attack. [a]Totals do not sum to the sample size as a result of missing data.

Comparison With Other Countries

Comparison of our results with other studies assessing the prevalence of uncontrolled BP is difficult because of differences in methodology and sampling. Matar and colleagues[9] reported that uncontrolled BP reached 46% in treated hypertensive Lebanese adults (21 years and older). In neighboring countries, uncontrolled BP prevalence was higher and reached 60% in Jordan, 63% in Saudi Arabia, and 93.5% in Turkey.[7,8,19] Treated AH remains insufficiently controlled, even in high-income countries such as the United States (60%)[20] and Japan (40%).[21]

Predictors of Uncontrolled SBP and DBP of Either Sex

Our findings suggest that individuals 55 years and older are at increased risk for uncontrolled SBP levels,

TABLE II. Logistic Regression: Predictors of Uncontrolled SBP, DBP, and BP

Variables	Uncontrolled SBP AdjOR (95% CI)	Uncontrolled DBP AdjOR (95% CI)	Uncontrolled BP AdjOR (95% CI)
Age (quartile), y			
55–64 vs <55	**1.88 (1.01–3.55)**	0.66 (0.35–1.23)	
65–73 vs <55	**1.85 (1.04–3.32)**	**0.50 (0.26–0.98)**	
≥74 vs <55	**2.43 (1.19–4.92)**	**0.23 (0.11–0.51)**	
Sex			
Male vs female	**1.96 (1.22–3.12)**		**1.61 (1.08–2.44)**
Marital status			
Married vs single/widowed/divorced		**0.58 (0.34–0.99)**	
Medication adherence level			
Low vs high	**2.22 (1.20–4.10)**	**1.93 (1.03–3.61)**	**2.09 (1.23–3.56)**
Medium vs high	**2.41 (1.44–4.03)**	1.06 (0.61–1.86)	**1.60 (1.02–2.49)**
Antihypertensive drugs, No.			
One vs three or four	0.63 (0.31–1.27)		**0.52 (0.28–0.97)**
Two vs three or four	**0.45 (0.21–0.93)**		**0.41 (0.21–0.80)**
BMI class			
Overweight vs normal weight		1.27 (0.62–2.61)	
Obese vs normal weight		**2.44 (1.20–4.94)**	
Diabetes		0.62 (0.36–1.06)	
Lipid-lowering medication (statins)	–	**0.61 (0.37–0.99)**	

Abbreviations: AdjOR, adjusted odds ratio; BMI, body mass index; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure. Estimates in bold indicate significance ($P<.05$).

TABLE III. Logistic Regression: Predictors of Uncontrolled SBP, DBP, and BP Among Men

Variables	Uncontrolled SBP AdjOR (95% CI)	Uncontrolled DBP AdjOR (95% CI)	Uncontrolled BP AdjOR (95% CI)
Age (quartile), y			
55–64 vs <55	**2.48 (1.45–4.24)**	0.51 (0.21–1.23)	
65–73 vs <55	**2.03 (1.13–3.65)**	**0.24 (0.09–0.66)**	
≥74 vs <55	1.49 (0.80–2.80)	**0.22 (0.08–0.62)**	
Marital status			
Married vs single/widowed/divorced	1.74 (0.98–3.10)	2. 23 (0.93–5.63)	**3.66 (1.52–8.81)**
Medication adherence level			
Low vs high		**1.41 (1.24–3.21)**	
Medium vs high		0.50 (0.23–1.09)	
Antihypertensive drugs, No.			
One vs three or four			**0.57 (0.44–0.97)**
Two vs three or four			**0.44 (0.24–0.82)**
BMI classes			
Overweight vs normal weight	–		
Obese vs normal weight	–		
Diabetes	–		**0.36 (0.20–0.66)**

Abbreviations: AdjOR, adjusted odds ratio; BMI, body mass index; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure. Estimates in bold indicate significance ($P<.05$).

whereas younger individuals are more likely to experience uncontrolled DBP levels. Similar findings have been reported in other studies that investigated the predictors of uncontrolled AH and the relationship between SBP and DBP control and the risk of coronary heart disease.[22] The hemodynamic patterns of age-related changes in BP have been explored by Franklin and colleagues.[23] They attributed the continuous rise in SBP throughout life, coupled with an early rise and late fall (after the age of 50) in DBP, to large artery stiffness.[23]

We found that male sex was an independent predictor of uncontrolled SBP after adjusting for age, medication adherence, and cardiovascular risk factors. Our finding is consistent with several studies of ambulatory practices.[24,25] Nevertheless, data on the association of sex with BP control have been conflicting. In fact, other

TABLE IV. Logistic Regression: Predictors of Uncontrolled SBP, DBP, and BP Among Women

Variables	Uncontrolled SBP AdjOR (95% CI)	Uncontrolled DBP AdjOR (95% CI)	Uncontrolled BP AdjOR (95% CI)
Age (quartile), y			
55–64 vs <55	**3.47 (1.95–6.19)**	0.80 (0.40–2.10)	
65–73 vs <55	**2.07 (1.06–4.05)**	1.47 (0.54–4.04)	
≥74 vs <55	**4.95 (2.68–9.12)**	**0.22 (0.05–0.92)**	
Marital status			
Married vs single/widowed/divorced			
Medication adherence level			
Low vs high	**1.78 (1.07–2.95)**	**2.14 (1.10–3.95)**	**5.6 (2.51–12.52)**
Medium vs high	**1.88 (1.17–3.05)**	1.25 (0.87–1.81)	**2.98 (1.48–6.02)**
Antihypertensive drugs, No.			
One vs three or four			**0.52 (0.13–0.81)**
Two vs three or four			**0.41 (0.21–0.80)**
BMI classes			
Overweight vs normal weight	–	0.56 (0.17–1.79)	
Obese vs normal weight	–	2.27 (0.72–7.21)	
Diabetes	–	**0.20 (0.08–0.50)**	**0.34 (0.18–0.65)**

Abbreviations: AdjOR, adjusted odds ratio; BMI, body mass index; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure. Estimates in bold indicate significance ($P<.05$).

studies have reported either no difference[26] or better control in men.[27]

Being married was a predictor of good DBP control. A similar study conducted by Morgado and colleagues[28] reported a positive association between married status and good BP control.

In the present study, low medication adherence was associated with uncontrolled SBP and DBP. This is in agreement with most of the existing evidence.[22] The Combination Pill of Losartan Potassium and Hydrochlorothiazide for Improvement of Medication Compliance Trial (COMFORT)[29] demonstrated that patients with a relatively low adherence rate (<90%) showed significantly higher systolic and diastolic BP compared with those with a perfect adherence rate (100%) over a 6-month treatment period.

Results from the national US population-based Reasons for Geographic and Racial Disparities in Stroke (REGARDS) cohort study[30] showed that each level of worsening medication adherence was associated with significant and increasing odds of uncontrolled BP (≥140/90 mm Hg). Furthermore, studies demonstrated that low adherence to antihypertensive therapy is associated with increased risk of stroke and other cardiovascular events.[31,32] Given the high prevalence of AH in Lebanon, the increased risk of stroke and cardiovascular events resulting from uncontrolled BP could have important public health implications.

While several studies have demonstrated the association of obesity with uncontrolled BP,[33,34] others have not found a significant association.[22,28] We found obesity to be associated with uncontrolled DBP but not uncontrolled SBP.

We also found that individuals treated with three or more antihypertensive drugs were more likely to have uncontrolled SBP compared with those taking dual combination therapy. Although this measure has some intrinsic limitation caused by the study design, the observed relationship could be explained by the fact that individuals whose BP is more difficult to control are likely to be treated with multiple antihypertensive drugs.[26]

Moreover, we observed a gap between guideline recommendations and practice, since 58% of participants with uncontrolled hypertension were receiving monotherapy. Guidelines promote early dual combination treatment.[2] This gap might partially explain our results. Furthermore, the I-PREDICT study[10] demonstrated poor agreement between Lebanese doctors' perceptions on BP control status and the guidelines.

We found a trend for diabetes to be associated with better DBP control. Although it did not reach statistical significance, this positive relationship could be explained by the more aggressive treatment for diabetic patients. Furthermore, we defined BP control based on the JNC 8 report (SBP <140 mm Hg; DBP <90 mm Hg). In fact, JNC 7 guidelines set a lower BP goal for diabetic hypertensive patients (<130/80 mm Hg),[12] and these low BP goals are difficult to achieve, especially in patients with diabetes. This explains the positive association between diabetes and poor BP control in studies using a lower cutoff value for diabetic patients.[11]

Our study findings showed that the use of statins was negatively associated with uncontrolled DBP.[34] This could be explained by the ability of statins to activate endothelial nitric oxide synthase and improve endothelial function and flow-mediated vasodilation.[35]

Predictors of Uncontrolled SBP and DBP by Sex

We sought to further assess the potential sex modification effect on the predictors of uncontrolled SBP and

DBP. After adjusting for age, being married, nonobesity, and taking statins were no longer predictors of DBP control in both men and women. The latter findings might be explained by a lack of the study power. The number of hypertensive drugs and presence of diabetes were not kept in the final predictive model of uncontrolled SBP and DBP, respectively. Nevertheless, they were kept in the final predictive model of uncontrolled BP in both men and women. Low adherence was associated with low SBP and DBP control in women, while low adherence was associated with only low DBP control in men.

STUDY STRENGTHS AND LIMITATIONS

Our study has several strengths, such as the population-based approach, the nationally representative sample, and the random selection of participants. To our knowledge, this is the first study to identify, in real-life settings, the predictors of SBP and DBP control in treated hypertensive Lebanese residents. It is known, that in clinical trials, BP control in treated hypertensive patients is not always reflected in the real-life setting of clinical practice.[36] Therefore, we think our study reflects an adequate BP control rate in treated hypertensive patients in Lebanon.

Furthermore, all BP measurements were conducted at the study patients' homes, which is associated with minimal white-coat AH effect.

This study also has limitations. A potential information bias is expected as a result of several reasons. We assessed medication adherence using a self-report instrument because assessing medication adherence by pharmacy fill/refill data or electronically monitored prescription is not available in Lebanon. Furthermore, patients might have provided socially desirable responses resulting in a classification bias regarding the true prevalence of low medication adherence. This might have underestimated the association with poor BP control. However, the Morisky scale is a well-validated instrument that has been extensively used in assessing antihypertensive medication adherence, and a recent study demonstrated its high concordance with antihypertensive medication pharmacy fill/refill data.[37] We met the participants on one occasion and collected two BP readings. However, many major studies aiming to assess determinants of uncontrolled AH based their conclusions on BP measurements at one occasion,[5,22,26] and it was demonstrated that measurements made within a single session have strong predictive power for CVD.[3]

Although our study showed interesting results, there are still other factors that could be responsible of residual confounding. We did not collect data on patients' use of nonsteroidal anti-inflammatory drugs, salt intake, patients' access to healthcare, therapeutic inertia, patient-physician relationship, and patients' knowledge of their target BP. We suggest future studies to take these factors into account.

CONCLUSIONS

AH control can be challenging to achieve, with barriers attributed to patients and healthcare providers. Our findings from a national sample of treated hypertensive individuals provide further evidence that uncontrolled BP is a major problem in Lebanon. Older patients should be targeted for greater attention to SBP control. Our study identified low medication adherence as a major modifiable risk factor associated with poor SBP and DBP control. Furthermore, obesity was associated with poor DBP control. Future studies assessing the determinants of medication adherence as well as the patient-physician relationship are warranted to better understand the predictors of uncontrolled AH in the Lebanese population.

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Author Contributions: RF and RKZ performed the study in 40/100 circumscriptions, participated in designing the questionnaire, performed data cleaning, and equally participated in the statistical analysis, drafting, and correcting the manuscript according to other authors suggestions. PS participated in designing the questionnaire and performed the sampling strategy and sample size calculation. PS also supervised and corrected the study analysis plan, the statistical analysis, and the manuscript writing. RC supervised the data collection in 40 circumscriptions and corrected the manuscript. MNC and RA contributed to finalizing the design of the study, performing the study in 60/100 circumscriptions, entering the data, and reviewing the statistical analysis report and manuscript. HH participated in designing the questionnaire, supervised the study analysis plan, and corrected the manuscript.

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