## PRIMARY CARE EPIDEMIOLOGY

# Control of Arterial Hypertension among Type 2 Diabetics 

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#### Abstract

Arterial hypertension (AH) frequently coexists with diabetes mellitus, occurring twice as frequently in diabetics as in the nondiabetic subjects. AH in diabetic patients is a well-recognized cardiovascular risk factor, accounting for up to $75 \%$ of additional cardiovascular disease risks, contributing significantly to the overall morbidity and mortality in this high-risk population. Patients with both disorders are prone to a markedly higher risk for premature microvascular and macrovascular complications. According to the intervention studies, the benefits that accrue after treatment is evidence based. Aggressive blood pressure (BP) control reduces both macrovascular and microvascular complications. A report of the Joint National Committee (JNC 7) on prevention, detection, evaluation and treatment of high blood pressure concluded that the blood pressure measurement in diabetic patients, should be less than $130 / 80 \mathrm{mmHg}$. Blood pressure is poorly controlled in most European countries and the control rate is even lower in high-risk patients, particularly in diabetic patients. Primary healthcare physicians play a very important role in treating hypertensive patients, as most of them are being followed up at the primary healthcare clinics.

The objective of this study was to determine the degree of BP control in hypertensive diabetics, according to the evidence and current guidelines, in a cohort of hypertensive diabetics, who were under general practitioner care.

Material and Methods: The study was conducted at outpatient in the health care clinics. Data was collected by 12 physicians, on 600 patients with type 2 diabetes mellitus (T2DM) and AH, seen in the clinics, during the period of study between March 2012 and March 2013. Patient demographic, clinical, and laboratory characteristics and drug usage were obtained. Patients were classified under four groups based on the degree of systolic and diastolic blood pressure control.

Results: A total of 600 patients ( $45.6 \%$ females and $54.3 \%$ males; mean age: $62 \pm 5.8$ years) were included in the study. The mean duration of the diabetes was $5.2 \pm 2.0$ years. Poor control of AH was observed among $71.4 \%$ of the cases. Only $28.6 \%$ of the diabetic patients were found to have controlled blood pressure, and the difference was found to be statistically significant ( $\mathrm{p}<0.001$ ). Angiotensin-converting enzyme (ACE) inhibitors were used in $55 \%$ of the subjects, while angiotensin receptor blockers (ARB) were used in $34 \%$; beta-blockers were given in $37.6 \%$ of cases, whereas calcium channels blockers (CCB) were given to $30.3 \%$, and diuretics were administered in $22.6 \%$ of the cases.

Conclusion: Only $28.3 \%$ of the hypertensive diabetics met the recommended BP values for diabetes. More efforts are required, addressed particularly to control the BP in diabetics. More aggressive therapy by the physicians concerned could improve blood pressure control and thus reduce the cardiovascular morbidity and mortality. As the adequate control of the BP usually warrants more than one medication, physicians should be careful when selecting hypertensive medications, because some combinations are not beneficial.


Keywords: arterial hypertension; type 2 diabetes mellitus; blood pressure control.

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## Abbreviations

$\mathbf{B W}$, body weight; $\mathbf{B H}$, body height; BMI, body mass index; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; Glyc, glycemia; Cre, creatinemia; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride.

## Introduction

AH and T2DM are both common, chronic conditions that frequently coexist. Patients with both disorders face markedly higher risks for premature microvascular and macrovascular complications. The occurrence of hypertension in diabetics substantially increases the risk for coronary heart disease, stroke, nephropathy and retinopathy [1-3]. According to intervention studies, the benefits accruing from the treatment of hypertension in diabetics, is evidence based [4]. A major determinant of risk reduction is the blood pressure level achieved. Aggressive control of BP reduces both macrovascular and microvascular complications. Recently, the European Society of Hypertension, European Society of Cardiology and Report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure (JNC7) concluded that the BP measurement in diabetic patients should be less than $130 / 80 \mathrm{mmHg}$ [5-7]. However, BP is poorly controlled in most European countries and the control rate is even lower in the high-risk patient categories such as diabetic patients. However, studies show that 60-69\% of the hypertensive diabetics treated in general practice, do not achieve the targets recommended. The discrepancy between the blood pressure targets recommended and the actual lower control rate and the reasons for it have been broadly debated [8-11]. Nevertheless, appropriate management of AH patients with T2DM remains controversial [12]. Therefore, treated but uncontrolled hypertension remains a major problem in preventive health care. Primary healthcare physicians, therefore, play a very important role in treating hypertension in diabetic patients, as most of them are being followed up at primary healthcare clinics. Hence, it would be worthwhile to investigate blood pressure control and the pursuit of targets recommended, in a cohort of hypertensive diabetics, who are under general practitioner care.

The objective of this study was to determine the degree of BP control in hypertensive diabetics, according to the evidence and current guidelines, in a cohort of hypertensive diabetics, who were under general practitioner care.

## Material and Methods

In all 300 participants ( 137 women and 163 men) were prospectively tested. The study was conducted at an outpatient clinic. The participants in the study were selected from among the primary care patients, who were receiving ongoing care for diabetes mellitus and hypertension, between March 1, 2012 and March 1, 2013.

Inclusion criteria: Patients were eligible for inclusion in the study if they were between 45 and 79 years of age, were undergoing treatment for diabetes mellitus and hypertension, diagnosed by use-validated criteria [6]. We recorded information from all the healthcare encounters during one calendar year.

Exclusion criteria: These include a diagnosis of dementia senilis, secondary hypertension, serum creatinine level $>2 \mathrm{mg} / \mathrm{dl}$, and age below 45 and above 79 .

## Clinical and demographic characteristic

The survey obtained data on the age, gender, calculated body
mass index, educational level, marital status, health habits, duration of hypertension and diabetes, as well as knowledge of the side effects of the target BP drugs, compliance and adherence to the drug treatment. All participants in the study were subjected to an external electrocardiogram (ECG with lab version 3.0). From the blood samples the values of glycemia, lipid status (total cholesterol, LDL-C, HDL-C, triglycerides), and creatinine, in the morning, post 12-hour fasting period were determined.

BP was measured according to standard protocol. The mean systolic and diastolic blood pressures recorded during the study period, were calculated.

Patients were classified based on the degree of their systolic and diastolic blood pressure control under 4 groups [6].

## Systolic BP groups

I: ( $<120 \mathrm{mmHg}$ ); II: (120-129 mmHg); III: (130-139 $\mathrm{mmHg})$; IV: ( $>140 \mathrm{mmHg}$ ).

## Diastolic BP groups

I: ( $<80 \mathrm{mmHg}$ ); II: ( $80-84 \mathrm{mmHg}$ ); III: ( $85-89 \mathrm{mmHg}$ ); IV: (>90 mmHg).

Controlled BP was defined as $\mathrm{SBP}<130 \mathrm{mmHg}$ and DBP $<80 \mathrm{mmHg}$. Uncontrolled BP was defined as $\mathrm{SBP}>130 \mathrm{mmHg}$ and $\mathrm{DBP}>80 \mathrm{mmHg}$. (On the other hand, blood pressure was considered to be controlled if the current reading was less than $130 / 80 \mathrm{mmHg}$.)

Statistical analyses: The continuous data acquired from the examinations for each group are shown as the middle value +/- for standard deviation (SD). In the series with attributive marks, the percentage of the structure is determined (percentage). The differences in the series with attributive marks are tested with the difference test (p). In the series with numerical marks descriptive statistics are employed (Mean, $95 \%$ CI, Min, Max and SD). In the series with numerical marks with no deviation from the normal distribution, the difference is tested with t -test for independent samples $(\mathrm{t})$. Logistical regressive analysis is used to test the association between the categorized variables and a $p$-value of 0.05 or less is considered the indication for statistical significance. These data are shown in the Tables and graphs. Statistical processing of the data is done by using the statistical programs STATISTICA 7.1 and SPSS 19.0.

## Results

A total of 600 patients ( $45.6 \%$ females and $54.3 \%$ males; mean age: $62 \pm 5.8$ years) completed the survey and provided data for a one-year medical record review. Tables (1 and 1a) present the basic demographic, clinical and laboratory characteristics of studied population.

A small percentage of the patients $(28.3 \%)$ were seen to have had their BP under control based on the evidence and current guidelines, in a cohort of hypertensive diabetics, while a high percentage of patients ( $71.7 \%$ ) continued to have uncontrolled BP, despite undergoing medical treatment. The difference was found to be statistically significant ( $\mathrm{p}<0.001$ ) (Tables 2 and 3). Based on the mean SBP during the study
year, $37.17 \%$ patients had high normal blood pressure, whereas $27.67 \%$ of the patients had stage I hypertension and $6.83 \%$ patients had stage II or higher BP. Whereas, based on the mean DBP during the study year, $25.83 \%$ of the patients had high normal blood pressure, $12.33 \%$ of the patients had stage I hypertension, and $1.67 \%$ had stage II or higher BP (Tables 3a and 3b).

Table 1.
Basic demographic, clinical and laboratory characteristics of study population

| Variable | $\mathbf{N}$ | Mean $\pm \mathbf{S D}$ | $\mathbf{9 5 \%} \mathbf{~ C I}$ |
| :--- | :---: | :---: | :---: |
| Age(yr) | 600 | $61.97 \pm 5.8$ | $61.5-62.4$ |
| BW $(\mathrm{kg})$ | 600 | $76.28 \pm 11.8$ | $75.3-77.2$ |
| BH(cm) | 600 | $168.88 \pm 6.5$ | $168.3-169.4$ |
| $\mathrm{BMI}(\mathrm{kg} / \mathrm{m})$ | 600 | $27.3 \pm 3.9$ | $26.9-27.6$ |
| BP-d(yr) | 600 | $6.3 \pm 1.7$ | $6.2-6.5$ |
| DM-d(yr) | 600 | $5.2 \pm 2.0$ | $5.0-5.3$ |
| No | 600 | $4.4 \pm 0.6$ | $4.3-4.4$ |
| Glic | 600 | $6.4 \pm 0.5$ | $6.1-6.5$ |
| TC | 600 | $5.9 \pm 0.3$ | $5.86-5.92$ |
| LDL-C. | 600 | $3.4 \pm 0.3$ | $3.42-3.49$ |
| HDL-C. | 600 | $1.3 \pm 1.4$ | $0.76-1.9$ |
| TG | 600 | $1.96 \pm 0.24$ | $1.94-1.97$ |
| Serum creatinine | 600 | $80.9 \pm 7.5$ | $80.4-81.6$ |

Abbreviations: No- number of measures of BP during 1 year; $D M d$ diabetes mellitus duration.

## Table 1a.

Basic demographic and clinical characteristics of study population

| Variable |  | N | \% |
| :---: | :---: | :---: | :---: |
| Gender | Females | 275 | 45.8 |
|  | Males | 325 | 54.2 |
| Marital status | M | 255 | 42.5 |
|  | UnM | 49 | 8,1 |
|  | D | 15 | 2.5 |
|  | W | 97 | 16.1 |
| Atherosclerotic disease | AP | 27 | 4,5 |
|  | IM | 24 | 8 |
|  | HF | 118 | 19.6 |
|  | IC | 13 | 2,1 |
| Educational level | E | 151 | 25.1 |
|  | H | 164 | 44.0 |
|  | C | 183 | 30.5 |
| Knowledge of goal BP | Yes | 280 | 46.6 |
|  | No | 320 | 53.4 |
| Exercise to lower BP | No | 291 | 48.5 |
|  | Yes(2-3d/w) | 180 | 30.0 |
|  | Yes(5d/w) | 129 | 21.5 |
| Heredity of BP | Yes | 245 | 40.8 |
|  | No | 355 | 59.2 |
| Heredity of DM | Yes | 301 | 50.1 |
|  | No | 299 | 49.9 |
| Medication Compliance | Yes | 529 | 88.2 |
|  | No | 71 | 11.8 |
| Medication Adherence | Yes | 540 | 90.0 |
|  | No | 60 | 10.0 |
| Side effect to medication | Yes | 58 | 9.4 |
|  | No | 542 | 90.3 |

Abbreviations: M- married; Un- unmarried; $D$ - divorced; $W$ widowed; AP- history of angina pectoris;IM- history of myocardial infarction;HF- history of heart failure; IC- history of stroke; Eelementary school; H- high school; C-college.

Table 2.
SBP and DBP in the patient group

| SBP | $<\mathbf{1 2 0}$ <br> $\mathbf{m m H g}$ | $(\mathbf{1 2 0 - 1 2 9 )}$ <br> $\mathbf{m m H g}$ | $\mathbf{( 1 3 0 - 1 3 9 )}$ <br> $\mathbf{m m H g}$ | $\mathbf{( 1 4 0 - 1 5 9 )}$ <br> $\mathbf{m m H g}$ | $>\mathbf{1 6 0}$ <br> $\mathbf{m m H g}$ | Total |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: |
| N | 55 | 115 | 223 | 166 | 41 | 600 |
| $\%$ | $9.17 \%$ | $19.17 \%$ | $37.17 \%$ | $27.67 \%$ | $6.83 \%$ | $100 \%$ |
| DBP | $<80$ <br> $\mathbf{m m H g}$ | $\mathbf{( 8 0 - 8 4 )}$ <br> $\mathbf{m m H g}$ | $\mathbf{( 8 5 - 8 9})$ <br> $\mathbf{m m H g}$ | $\mathbf{9 0 - 9 9})$ <br> $\mathbf{m m H g}$ | $>\mathbf{1 0 0}$ <br> $\mathbf{m m H g}$ | Total |
| N | 358 | 78 | 77 | 74 | 10 | 600 |
| $\%$ | $59.6 \%$ | $13 \%$ | $12.83 \%$ | $12.33 \%$ | $1.67 \%$ | $100 \%$ |

Table 3.
Degree of BP control in the patient group

| Pearson Chi-square: 11.85, df=1, $\mathbf{p}=\mathbf{0 . 0 0 0}$ |  |  |  |
| :---: | :---: | :---: | :---: |
| Blood Pressure control |  |  |  |
|  | Controlled BP <br> $(<130 / 80 \mathrm{mmHg})$ | Uncontrolled BP <br> $(>130 / 80 \mathrm{mmHg})$ | Total |
| N | 170 | 430 | 600 |
| $\%$ | $28.33 \%$ | $71.67 \%$ | $100 \%$ |

## Table 3a.

SBP category

| Blood pressure category | N | \% |
| :--- | :---: | :---: |
| Controlled | 170 | $28.33 \%$ |
| High Normal | 223 | $37.17 \%$ |
| Stage I hypertension | 166 | $27.67 \%$ |
| Stage II hypertension or greater | 41 | $6.83 \%$ |

Table 3 b.
DBP category

| Blood pressure category | N | \% |
| :--- | :---: | :---: |
| Controlled | 358 | $59.6 \%$ |
| High Normal | 155 | $25.83 \%$ |
| Stage I hypertension | 74 | $12.33 \%$ |
| Stage II hypertension or greater | 10 | $1.67 \%$ |

The most frequently used agents were the ACE inhibitors, which were used by $55 \%$ of the patients, followed by ARB, which were used by $34 \%$ of the patients, while beta-blockers were used in $37.6 \%$ patients, CCB were used in $30.3 \%$ of the patients and diuretics were used in $22.6 \%$ patients (Table 4).
Table 4.
Used antihypertensive agents among hypertensive patients

| Antihypertensives | $\mathbf{N}$ | \% |
| :--- | :---: | :---: |
| ACE inhibitors | 330 | $55 \%$ |
| ARB | 204 | $34 \%$ |
| Beta-blockers | 226 | $38 \%$ |
| CCB | 182 | $30 \%$ |
| Diuretics | 137 | $23 \%$ |
| Prazosin | 5 | $8 \%$ |

In the study groups, more than half of the patients (56.4\%) were using antihypertensives as a dual therapy for BP control. Monotherapy was used in $31.1 \%$ of the patients, triple therapy was used in $11.9 \%$ of patients and quadruple therapy was used in $0.6 \%$ of the patients (Table 5).
Table 5.
Antihypertensives used as one or more agents among hypertensive patients

| Character of therapy | Study group <br> (n=600) |  |
| :--- | :---: | :---: |
|  | $\mathbf{N}$ | \% |
| Monotherapy | 187 | $31.1 \%$ |
| Dual therapy | 339 | $56.4 \%$ |
| Triple therapy | 72 | $11.9 \%$ |
| Quadruple therapy | 2 | $0.6 \%$ |

Among the patients with controlled SBP $(<130 \mathrm{mmHg})$, ACE inhibitors were used in $88.2 \%$ of the patients, ARB in $15.9 \%$ of the patients, beta blockers in $27.6 \%$ of the patients, CCB in $28.2 \%$ of the patients and diuretics in $9.4 \%$ of the patients (Table 6). Monotherapy was used in 48.2\% of the patients, of whom $82.35 \%$ used ACE inhibitors as monotherapy. Dual therapy was used in $47.05 \%$ and triple therapy in $0.5 \%$ of patients (Table 7).
Table 6.
Used antihypertensives among patients with controlled SBP

| Antihypertensives | Patients with controlled SBP <br> (n=170) |  |
| :--- | :---: | :---: |
|  | N | \% |
| ACE inhibitors | 150 | $88.2 \%$ |
| ARB | 27 | $15.8 \%$ |
| Beta-blockers | 47 | $27.6 \%$ |
| CCB | 48 | $28.2 \%$ |
| Diuretics | 16 | $9.4 \%$ |

Table 7.
Antihypertensives used as one or more agents in patients with controlled SBP

| Number of <br> antihypertensives$\|$Patients with controlled SBP <br> $(n=170)$  <br>  N <br> Monotherapy 82 <br> Dual therapy 80 <br> Triple therapy 8 | $48.2 \%$ |
| :--- | :---: | :---: |

From among the patients with controlled DBP, ACE inhibitors were used in $92.1 \%$ of the patients, whereas ARB was used in $7.5 \%$ of the patients, beta-blockers in $13.1 \%$ of the patients, CCB in $13.4 \%$ of the patients and diuretics in $4.4 \%$ of the patients (Table 8). Monotherapy was used in $31.1 \%$ of the patients, of whom $56.41 \%$ used ACE inhibitors as monotherapy. Dual therapy was used in $56.4 \%$ and triple therapy was used in $11.9 \%$ of patients (Table 8).

## Table 8.

Used antihypertensives among patients with controlled DBP

| Antihypertensives | Patients with controlled DBP <br> (n=358) |  |
| :--- | :---: | :---: |
|  | $\mathbf{N}$ | \% |
| ACE inhibitors | 330 | $92.1 \%$ |
| ARB | 27 | $7.5 \%$ |
| Beta-blockers | 47 | $13.1 \%$ |
| CCB | 48 | $13.4 \%$ |
| Diuretics | 16 | $4.4 \%$ |

Table 8 a.
Antihypertensives used as one or more agents among hypertensive patients

| Number of <br> antihypertensives | Patients with controlled DBP <br> $(\mathbf{n = 3 5 8 )}$ |  |
| :--- | :---: | :---: |
|  | N | \% |
| Monotherapy | 131 | $31.1 \%$ |
| Dual therapy | 202 | $56.4 \%$ |
| Triple therapy | 33 | $11.9 \%$ |

Multivariate analysis was used to identify the association of blood pressure control and the demographic, clinical and laboratory characteristics.

We found the following factors to be significantly associated with poor BP control: age, gender, BMI, low literacy rates, poor adherence to and noncompliance with the prescribed treatment, lack of awareness and knowledge of appropriate target BP, low physical activity, presence of atherosclerotic disease, experience of specific side effects attributed to the antihypertensive medication and uncontrolled glycemia. All the parameters are given in the Tables 9 and $9 \mathrm{a}-9 \mathrm{~g}$.

Table 9.
Association of Age/BW/BMI with poor BP control

|  | B | S.E. | Wald | df | Sig. | Exp(B) | 95.0\% CI for <br> EXP(B) |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | Lower Upper |  |
| StepGender(1) | -.059 | .314 | .035 | 1 | .851 | .943 | .510 | 1.744 |
| $1(\mathrm{a})$ Age | -.205 | .034 | 36.079 | 1 | .000 | .814 | .761 | .871 |
| BW | -.008 | .025 | .115 | 1 | .735 | .992 | .945 | 1.041 |
| BMI | -.351 | .101 | 12.204 | 1 | .000 | .704 | .578 | .857 |
| Constant | 12.6624 .721 | 7.192 | 1 | .007 | $315,441.82$ |  |  |  |

Variable(s) entered on step 1: Age; Body weight;BMI.
Table 9a.
Association of educational level with poor BP control

|  | B | S.E. | Wald | df | Sig. | $\operatorname{Exp}(\mathrm{B})$ | $\begin{gathered} \hline 95.0 \% \text { CI for } \\ \text { EXP(B) } \\ \hline \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | Lower | Upper |
| StepHigh 1(a) school(1) | . 533 | . 539 | . 975 | 1 | . 323 | 1.703 | . 592 | 4.902 |
| ${ }^{1(a)}$ College(1) | 3.044 | . 511 | 35.542 | 1 | . 000 | 20.985 | 7.715 | 57.083 |
| Constant | -2.762 | . 465 | 35.256 |  | . 000 | . 063 |  |  |

Variable(s) entered on step 1: (a) 1: High school(1); College(1)

Table 9b.
Association between knowledge of goal BP and poor BP control

|  | B | S.E. | Wald | df | Sig. | $\boldsymbol{E x p}(\mathrm{B})$ | $\begin{gathered} \text { 95.0\% CI for } \\ \text { EXP(B) } \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | Lower | Upper |
| Step Knowl. of 1(a) goal BP | . 959 | . 292 | 10.768 | 1 | . 001 | 2.610 | 1.472 | 4.629 |
| Constant | -1.570 | . 218 | 51.703 | 1 | . 000 | . 208 |  |  |

Variable(s) entered on step 1: (a) knowledge of goal BP.

## Table 9c.

Association of atherosclerotic disease with poor BP control


Variable(s) entered on step 1a; AP- angina pectoris; IM-myocardial infarction; HF- heart failure.
Table 9d.
Association of exercise with BP control

|  | B | S.E. | Wald | df | Sig. | Exp(B) | 95.0\% CI for <br> EXP(B) |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Exercise to <br> lower BP |  |  |  |  |  |  | Lower | Upper |
| Step 2-3 <br> 1(a) d/w(1) <br> $5 \mathrm{~d} / \mathrm{w}(1)$ <br> Constant | -.359 | -1.927 | .483 | .551 | 1 | .458 | .699 | .271 |

Variable(s) entered on step 1a: Exercise to lower BP (2-3 days in week and 5 days in week).

Table 9e.
Association between medication compliance, adherence and poor BP control

|  | B | S.E. | Wald | df | Sig. | Exp(B) | 95.0\% CI for <br> EXP(B) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | Lower | Upper |
| Step adherence <br> (a) <br> compliance <br> (1) <br> Constant | 2.133 | 1.029 | 4.297 | 1 | .038 | 8.441 | 1.123 | 63.42 |

Variable(s) entered on step la: medication compliance, and adherence.

## Table 9f.

Association of side effect attributed to medication with poor BP control

|  | B | S.E. | Wald | df | Sig. | Exp(B) | 95.0\% CI for <br> EXP(B) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | Lower | Upper |
| Step Side effect <br> 1(a) (1) <br> Constant | -2.257 | 1.026 | 4.837 | 1 | .028 | .105 | .014 | .782 |

Variable(s) entered on step 1a: Side effect attributed to medication.

Table 9 g.
Association between Glyc / TC / TG and poor BP control

|  | B | S.E. | Wald | df | Sig. | $\operatorname{Exp}(\mathrm{B})$ | $\begin{gathered} \text { 95.0\% CI for } \\ \text { EXP(B) } \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | Lower | Upper |
| Step Glycemia 1(a) | -4.173 | 1.285 | 10.543 | 1 | . 001 | . 015 | . 001 | . 191 |
| TC | -2.400 | . 949 | 6.394 | 1 | . 011 | . 091 | . 014 | . 583 |
| TG | -11.388 | 2.627 | 18.797 | 1 | . 000 | . 0002 | . 000 | . 002 |
| Constant | 58.222 | 10.480 | 30.867 | 1 | . 000 |  |  |  |

Variable(s) entered on step 1a: Glycemia, TC, TG.

## Discussion

Hypertension is known to contribute to diabetic microvascular and macrovascular complications [13]. To reduce the risk, hypertension must be diagnosed accurately and promptly, and the patient should receive adequate treatment. However, new guidelines have been published to emphasize the importance of aggressive BP in diabetics [57]. Only $28.3 \%$ of the 600 hypertensive diabetics, in this study, met the currently recommended BP value for diabetes ( $<130 / 80 \mathrm{mmHg}$ ) based on the evidence and current guidelines [5-7], despite ongoing medical treatment. This indicated that even greater efforts are required to control BP in diabetics. In this study, it was observed that the predominant part of the BP which was poorly controlled was the SBP $(>130 \mathrm{mmHg})$ which accounted for $71.4 \%$ of cases (Table 1). Results from the Systolic Hypertension in Elderly Program (SHEP) and Systolic Hypertension in Europe (Sys-Eur) trial favored the aggressive treatment of diabetics with isolated systolic hypertension $[14,15]$. Therefore, greater efforts are required to address this aspect of BP. Older age was associated with poorer BP control, relative to that seen in the younger treated patients. It was found that SBP increases with age, but the DBP tends to level off between 55 to 60 years. This increase in the SBP is a strong predictor of cardiovascular disease with advancing age [16]. The clinical benefits of treating systolic hypertension in older patients have now been demonstrated in several randomized, placebo-controlled trials; however, the implications of these trials may not be fully accepted in routine practice. Even the oldest patient, age $>80$ years, appears to benefit from antihypertensive therapy. It is possible that despite the proven benefits of antihypertensive therapy in this age group, the older patients are still treated less aggressively compared with the younger ones [17]. Increased BMI was associated with poorer BP control. The present finding is consistent with a few prior studies that have identified the correlations between poor BP control and BMI [5,6]. A minimum of 20-40 minutes of aerobic exercise performed less than five times a week was associated with poorer BP control. Studies show that exercise and weight reduction, help independently, in reducing the BP, while combining both have additive benefits in diabetic hypertensives [19,20]. The lack of knowledge of appropriate SBP and the low literacy rate were also found to be risk factors for poor BP control. Patients who indicated, during the interview, their lack of awareness that
their target SBP should be $<130 / 80 \mathrm{mmHg}$, were significantly more likely to have a higher mean blood pressure documented in their medical records. Such patients may have been less likely to take their medication, adopt healthy lifestyle changes or see their physician if their blood pressure was outside the ideal range. Educational interventions have also been shown to improve compliance with BP medication. However, not all trials concerned with patient education resulted in improved compliance or BP control. The same authors did find some improvement in both compliance and BP control when the patients were taught to check their own BP and chart it, along with their pill-taking schedule. The important difference between these two approaches may lie in the relevance of the educational message to the patient's specific BP levels (as opposed to general concepts about hypertension and the associated risks) [8, 21]. Other factors against BP control with combined medication are noncompliance and non-adherence. The Canadian Coalition for Blood Pressure Control reported a non-compliance rate of $50 \%$. Non-adherence is the major cause of treatment failure [22, 23]. Patients seen in the clinic may get tired of taking long-term medication for their BP and blood glucose control. The impact of co-morbidity on hypertension control has not been examined extensively in large sized studies. We found angina to be associated with better blood pressure control. This may be due to the improved compliance in these patients, more aggressive treatment or the direct effect of cardiovascular disease. A trend was also observed for patients with congestive heart failure or a history of myocardial infarction to have better blood pressure control. Although the study sample included a large number of diabetic patients, diabetes was not associated with better control despite the published recommendations suggesting that these patients, in particular, should be well controlled with a target of $<130 / 80 \mathrm{mmHg}$ [24, 25]. Another potentially important observation was the relationship between poor BP control and adverse events attributed to antihypertensive medications. Patients who report adverse effects may also differ in terms of unmeasured factors, which are also associated with uncontrolled hypertension. It was observed that most patients with uncontrolled hypertension had poorly controlled blood glucose and lipids. The results from both ACCORD and ADVANCE trials indicate that near-normal glycemic control for a median of 3.5 to 5 years does not reduce the cardiovascular events within that time frame [26, 27]. Physicians' educational input with respect to the importance of BP control in diabetics and the better selection of drugs for combination therapy should be considered promptly and efficiently.

In this study, ACE inhibitors were found to be the most frequently utilized antihypertensive agents (used by $55 \%$ of the patients), followed by ARB, which were used by $34 \%$ of the patients. Recent trials have suggested that for the prevention of cardiovascular events, ACE inhibitors may be superior to alternative antihypertensive agents [28, 29]. Results from the Heart Outcome Prevention Evaluation (HOPE) study showed that a reduction in the cardiovascular events with ACE inhibitors was much greater than that expected for BP reduction alone, compared with the placebo
[30, 31]. The ACE inhibitors favorably affected not only the cardiovascular events, but also the renal ones as well as the quality of life when compared with other regimens [32, 33]. In this study, $31 \%$ of the patients with controlled BP used an antihypertensive as the agent in monotherapy, and $56.5 \%$ of the patients with controlled BP used an antihypertensive as the agent of dual therapy. It appears to be advisable to combine the ACE inhibitors with other medications in order to have a more potent effect. The JNC 7 favors the combination of drugs for a more potent BP reduction. However, it does not favor the combination of ACE inhibitors with B blockers or the combination diuretics with calcium channel blockers. Therefore, for patients with uncontrolled BP, it is advisable to observe the type of drugs used in combination before deciding to add on another drug to the existing regimen [6].

## Study Limitations

Several limitations in this study deserve mention. As the study design was observational, each patient was managed at the discretion of his or her physician. Study design limited the ability to make causal inferences regarding the associations between the predictor variables and hypertension control.

## Clinical Implications

These data provide further evidence that poor BP control is common and that patients at particular risk of poor control can be identified. Targeted interventions to improve the management in such patients could make a substantial difference in stemming the epidemic of poorly controlled hypertension. This study provides a framework for identifying hypertensive patients who are at high risk for poor control, and many of the factors identified may be amenable to improvement. Older patients can be targeted for greater attention to BP control, particularly in light of the evidence for improvement in the clinical outcomes with hypertension therapy in this population. Patients with poor knowledge of the goal of their hypertension therapy should be informed about their target BP, to enable them to participate more fully in their own management. Finally, clinicians should discuss with patients, the potential adverse effects of their hypertension therapy, look out for the presence of such symptoms in routine follow-up history taking, and when they occur, make relevant modifications to the therapy.

## Conclusion

Only $28.3 \%$ of the hypertensive diabetics met the recommended BP values for diabetes. More efforts are required, addressed particularly to control the BP in diabetics. More aggressive therapy by the physicians concerned could improve blood pressure control and thus reduce the cardiovascular morbidity and mortality. As the adequate control of the BP usually warrants more than one medication, physicians should be careful when selecting hypertensive medications, because some combinations are not beneficial.

## References

1. Sowers JR, Epstein M, Frohlich ED. Diabetes, hypertension, and cardiovascular disease: an update. Hypertension 2001; 37(4):1053-9.
2. Sowers JR, Haffner S. Treatment of cardiovascular and renal risk factors in diabetic hypertensive. Hypertension 2002; 40(6):781-8.
3. Bakris GL, Williams M, Dworkin L, Elliott WJ, Epstein M, Toto R, et al. Preserving renal function in adult with hypertension and diabetes: a consensus approach. National Kidney Foundation Hypertension and Diabetes Executive Committees Working Group. Am J Kidney Dis 2000; 36(3):646-61.
4. Tight blood pressure control and risk of macrovascular and microvascular complication in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. BMJ 1998; 317(7160):703-13.
5. Erdine S, Ari O, Zanchetti A, Cifkova R, Fagard R, Kjeldsen S, Mancia G, et al. ESH-ESC guidelines for management of hypertension. Herz 2006; 31(4):331-8.
6. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. The Seventh Report of the Join National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289(19):2550-72.
7. Arauz-Pacheco C, Parrott MA, Raskin P; American Diabetes Association. Hypertension management in adult with diabetes. Diabetes Care 2004; 27:S65-67.
8. Knight EL, Bohn R1, Wangs PS, Glynn RJ, Mogun H, Avorn J. Predictors of uncontrolled hypertension in ambulatory patients. Hypertension 2001; 38(4):809-14.
9. Douglas JG, Ferdinand KC, Bakris GL, Sowers JR. Barriers to blood pressure control in African Americans. Overcoming obstacles is challenging, but target goal can be attained. Postgrad Med 2002; 112(4):51-62.
10. Hart PD, Bakris GL. Hypertension control rates: time for translation of guidelines into clinical practise.AM J Med 2004; 117(1):62-4.
11. Gaede P,Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med 2003; 348(5):383-93.
12. Anwer Z, Shaman RK, Garg VK, Kumar N, Kumari A. Eur Rev Med Pharmacol Sci 2011; 15(11):1256-63.
13. Gress TW, Nieto FJ, Shahar E, Wofford MR, Brancati FL. Hypertension and antihypertensive therapy as risk factors for type-2 diabetes mellitus. Atherosclerosis Risk in Communities Studi. N Engl J Med 2000; 342(13):905-12.
14. Curb JD, Pressel SL, Cutler JA, Savage PJ, Applegate WB, Black H, et al. Effect of diuretic- based antihypertensive treatment on cardiovascular disease risk in older diabetic patient with isolated systolic hypertension. Systolic Hypertension in the Elderly Program Cooperative Research Group. JAMA 1996; 276(23):1886-92.
15. Tuomilehto J, Rastenyte D, Birkenhäger WH, Thijs L, Antikainen R, Bulpitt CJ, et al. Effect of calciumchannel blockade in older patients with diabetes and systolic hypertension. Systolic Hypertension in Europe Trial Investigators, N Engl J Med 1999; 340(9):677-84.
16. Kannel WB, Gordon T. Evaluation of cardiovascular risk in the elderly: the Framingham study. Bull NY Acad Med 1978; 54(6):573-91.
17. Giannattasio CR, Cairo M, Cesana F, Alloni M, Sormani P, Colombo G, et al. Blood pressure control in Italian essential hypertensive treated by general practitioners. Am J Hypertens 2012; 25(11):1182-7.
18. Naik AD, Kallen MA, Walder A, Street RL Jr. Improving hypertension control in diabetes mellitus: the effect of collaborative and proactive health communication. Circulation 2008; 117(11):1361-8.
19. Halbert JA, Silagy CA, Finucane P, Withers RT, Hamdorf PA, Andrews GR. The effectiveness of exercise training in lowering blood pressure: a meta-analysis of randomized controlled trials of 4 -weeks or longer. J Hum Hypertens 1997;11(10):641-9.
20. Hagberg JM, Park JJ, Bown MD. The role of exercise straining in the treatment of hypertension: an update. Sports Med 2000; 30(3):193-206.
21. Sampanis C, Zamboulis C. Arterial hypertension in diabetes melitus: from theory to clinical practice. Hippokratia 2008; 12(2):74-80.
22. Chockalingam A, Bacher M, Campbell N, Cutler H, Drover A, Feldman R, et al. Adherence to management of high blood pressure: recommendations of the Canadian Coalition for High Blood Pressure Prevention and Control. Can J Public Health 1998; 89(5):15-111.
23. Glynn RJ, Field TS, Rosner B, Hebert PR, Taylor JO, Hennekens CH. Evidence for a positive linear relation between blood pressure and mortality in elderly people. Lancet 1995; 345(8953):825-9.
24. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. The effect of initial drug choice and comorbidity on antihypertensive therapy compliance: results from a population-based study in the elderly. Am J Hypertens 1997; 10(7 Pt 1):697-704.
25. Di Bari M, Salti F, Nardi M, Pahor M, De Fusco C, Tonon E, et al. Undertreatment of hypertension in communitydwelling older adults: a drug-utilization study in Dicomano, Italy. J Hypertens1999; 17(11):1633-40.
26. Patel A; ADVANCE Collaborative Group, MacMahon S, Chalmers J, Neal B, Woodward M, Billot L, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patient with type 2 diabetes mellitus (the ADVANCE trial): a randomized controlled trial. Lancet 2007; 370(9590):829-40.
27. ACCORD Study Group, Cushman WC, Evans GW, Byington RP, Goff DC Jr, Grimm RH Jr, Cutler JA, et al. Effects of intensive blood-pressure control in type 2 dibates mellitus. N Engl J Med 2010; 362(17):1575-85.
28. Pahor M, Psaty BM, Furberg CD. Treatment ofhypertensive patients with diabetes. Lancet 1998; 351(9104):689-90.
29. Pahor M, Psaty BM, Furberg CD. New evidence on the prevention of cardiovascular event in hypertensive patients with type 2 diabetes. J Cardiovasc Pharmacol 1998; 32(Suppl 2):S18-23.
30. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Education Study Investigators. N Eng J Med 2000; 342(3):145-53.
31. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000; 355(9200):353-9.
32. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting enzyme inhibition on diabetic nephropathy. N Eng J Med 1993; 329(20):1456-62.
33. Croog SH, Levine S, Testa MA, Brown B, Bulpitt CJ, Jenkins CD, et al. The effects of antihypertensive therapy on the quality of life. N Eng J Med 1986; 314(26):1655-64.

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