

Blood pressure control and its associated factors in patients with hypertension and type 2 diabetes

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ABSTRACT

In this retrospective study, the medical records of hypertensive patients with type 2 diabetes attending two major hospitals were reviewed to find the factors associated with poor blood pressure control in patients who have diabetes as a comorbid disease with hypertension. Binary regression analysis was conducted to find the factors independently associated with BP control. A total of 522 participants were included in the study. Most of the participants had uncontrolled hypertension (63.4%) and uncontrolled type 2 diabetes (51.3%). Regression results revealed that having retinopathy (OR=1.468 (95% CI: 1.020-2.113), $p<0.05$), and not receiving dipeptidyl-peptidase 4 (DPP4) inhibitors were independently associated with uncontrolled BP (OR=0.633 (95%CI 0.423-0.946), $p<0.05$). Therefore, greater efforts should be exerted to improve BP control in hypertensive patients with type 2 diabetes, particularly in those suffering from retinopathy.

Keywords: hypertension, type 2 diabetes, blood pressure, blood glucose, factors

INTRODUCTION

Hypertension and diabetes mellitus are two of the most common cardiovascular risk factors with over two thirds of the diabetic population having high blood pressure (BP) [1]. The underlying pathophysiological mechanism behind the development of hypertension in patients with type 2 diabetes is thought to be related to the effect of insulin resistance on the nitric-oxide pathway, the stimulatory effect of hyperinsulinemia on the sympathetic drive, smooth muscle growth, sodium-fluid retention, and the excitatory effect of hyperglycemia on the renin-angiotensin-aldosterone system [1]. On the other hand, carbohydrates metabolism disturbance in hypertensive patients may predispose them to diabetes development [2, 3], suggesting a bidirectional pathogenic relationship between hypertension and type 2 diabetes. The risk for microvascular and macrovascular complications is greatly increased when diabetes and hypertension coexist. Additionally, it has other unfavorable effects including higher healthcare expenses and more challenging treatment plans [2, 4]. Despite the fact that lowering BP significantly reduce cardiovascular morbidity and mortality, a large proportion of diabetic patients are still having poorly controlled BP [5, 6], highlighting the need for exploring the variables that significantly impact BP control in hypertensive patients with type 2 diabetes.

Inconsistent findings were reported in the literature regarding the factors that are associated with uncontrolled BP in hypertensive patients comorbid with type 2 diabetes. A study conducted in Ethiopia reported that the main predictors of poor BP control in hypertensive diabetic patients were advanced age, longer duration of hypertension, cigarette smoking, medication non-adherence, and poor glycemic control [7], while older age, living in urban area, longer duration of type 2 diabetes, higher body mass index (BMI), poor glycemic control, and cigarette smoking were claimed as the independent predictors of uncontrolled BP in diabetic patients enrolled in another Ethiopian study [8]. A study conducted in Iran found that uncontrolled BP in hypertensive patients with type 2 diabetes was significantly correlated with higher BMI and dyslipidemia [9]. Furthermore, older age, male gender, employment status, duration of type 2 diabetes, having a diabetic foot, underweight, and obesity were found to be significantly associated with hypertension among diabetic patients participated in a study conducted in Sudan [10]. A side from the scarcity of research on the predictors of uncontrolled BP in hypertensive diabetic patients, the predictors of poor BP control in such cases reported in the existing literature are inconsistent, necessitating further research to help narrow the diversity of these findings and reveal the true predictors of poor BP control in these patients, which was the main objective of the current study.

MATERIALS AND METHODS

Study Design and Participants

The present retrospective research explored the factors associated with poor BP control in patients older than 18 years old who had hypertension and type 2 diabetes and received treatment at King Abdullah University Hospital and the Royal Medical Services Hospital between November 2021 and May 2022. The diagnosis of hypertension and type 2 diabetes was established based on the 2017 ACC/AHA [11] and the 2020 American Diabetes Association guidelines [12] respectively. Similar to the impact of antihypertensive medications on blood glucose (BG) control, it has been postulated that there is an association between antidiabetic agents and BP control. Therefore, patients were included in the study if they received drug therapy for BP and BG control. Moreover, BP control was estimated according to the last two readings of systolic and diastolic BP, and therefore, patients who had at least one hospital visit within the past six months were included in the study.

As the study targeted patients with type 2 diabetes and in order to control the confounding variables which might affect BP control, which represents the current study outcome, patients who had type 1 diabetes, had hypertension urgency or emergency, patients who received medications which might worsen BP control and pregnant women were excluded from the study. The authors declared in the ethical approval application form that the collected data will only be used for research purposes and will be kept in the principal investigator's office to ensure confidentiality.

Data Collection

Medical records and hospital data were utilized to obtain information about socio-demographic variables including age, gender, employment status, educational level, marital status, obesity, smoking, area of residency, physical activity, family history of cardiac problems, and family history of type 2 diabetes. The biomedical information included glycosylated hemoglobin (HbA1c), fasting serum glucose level, total cholesterol level, triglycerides (TG) level, high-density lipoprotein (HDL), low-density lipoprotein (LDL), glomerular filtration rate (GFR), and systolic and diastolic BP). The collected information also included the presence of comorbid diseases such as dyslipidemia, microvascular complications (retinopathy, neuropathy, and nephropathy), peripheral artery disease, heart failure, cerebrovascular disease, ischemic heart disease, renal failure, foot damage, anxiety, depression, asthma, COPD, the presence of proteinuria, and the prescribed medications. Based on the last two readings of systolic and diastolic BP, the patient was considered to have uncontrolled BP if one of the readings was above 130/80 [11], whereas those with HbA1c >7% were deemed to have uncontrolled diabetes based on ADA guidelines [12].

Statistical Analysis

Data was analyzed using the latest version of statistical package for the social sciences (SPSS). Continuous variables were presented as means and standard deviations, while categorical variables were presented as frequencies and percentages. Univariate analysis was performed using Chi-square and Mann Whitney U tests to determine the variables associated with BP control. Variables with $p < 0.2$ in the

Table 1. Socio-demographic characteristics and the study participants (n=522)

		Frequency (%) or mean (±SD)
Age		62 (±10)
Gender	Female	255 (48.8%)
	Male	267 (51.2%)
Marital status	Married	408 (78.2%)
	Other	114 (21.8%)
Educational level	High	143 (27.4%)
	Low	379 (72.6%)
Employment status	Employees	172 (32.9%)
	Retired/non-employees	350 (67.1%)
Area of residency	Rural area	159 (30.4%)
	Urban area	363 (69.6%)
Smoking	Current smoker	167 (32.0%)
	Former/non-smoking	355 (68.0%)
Physical activity	No	316 (60.5%)
	Yes	206 (39.5%)
Obesity	Non-obese	358 (68.6%)
	Obese/overweight	164 (31.4%)
Family history of cardiac problems	No	463 (88.7%)
	Yes	59 (11.3%)
Family history of type 2 diabetes	No	438 (83.9%)
	Yes	84 (16.1%)

univariate analysis were included in the multivariate analysis model. Multivariate analysis was conducted using Binary regression model to find the variables that are significantly and independently associated with BP control. A $p < 0.05$ was considered statistically significant.

RESULTS

A total of 522 participants were included in the study. The mean age of the participants was 62 (±10). Most of the participants were males (51.2%), retired/non-employed (67.1%), had low educational level (72.6%), married (78.2%), non-obese (68.6%), formerly smokers or non-smokers (68.0%), living in urban areas (69.6%), were not physically active (60.5%), had no family history of cardiac problems or type 2 diabetes (88.7% and 83.9%, respectively). Socio-demographic characteristics of study participants are included in **Table 1**.

Metformin (87.0%) and angiotensin receptor blockers (ARBs) (57.1%) were the most commonly prescribed medications, followed by beta-blockers (BB) (54.4%), while sodium-glucose cotransporter-2 (SGLT2) inhibitors (6.1%) and meglitinides (0.6%) were the least commonly given drugs. Many patients had abnormally high fasting BG level and elevated HbA1c, with a total sample mean of 170.14 mg/dl (±74.40) and 10.31 (±49.32), respectively. The sample had a low GFR as well, with a mean of 69.85 (±26.58). The means of the systolic and diastolic BP were 134 (±17) and 79 (±9), respectively.

Table 2 contains more information about laboratory testing and medications.

As shown in **Table 3**, the most frequent comorbidity was dyslipidemia (72.0%). Nearly half of the participants had microvascular complications (50.6%), with retinopathy being the most commonly recognized microvascular complication (45.2%). Most of the participants had uncontrolled hypertension (63.4%) and more than half of them had uncontrolled type 2 diabetes (51.3%).

Table 2. Medication history and lab tests

	Frequency (%) or mean (\pm SD)	
	No	Yes
Medications		
ACEI	391 (74.9%)	131 (25.1%)
BB	238 (45.6%)	284 (54.4%)
CCB	303 (58.0%)	219 (42.0%)
ARBs	224 (42.9%)	298 (57.1%)
Thiazide diuretics	330 (63.2%)	192 (36.8%)
DPP4 inhibitors	359 (68.8%)	163 (31.2%)
Insulin	237 (45.4%)	285 (54.6%)
Metformin	68 (13.0%)	454 (87.0%)
GLP1 receptor agonist	269 (51.5%)	253 (48.5%)
Meglitinides	519 (99.4%)	3 (0.6%)
SU	328 (62.8%)	194 (37.2%)
SGLT2_INH	490 (93.9%)	32 (6.1%)
Lab tests		
HbA1c	10.31 (\pm 49.32)	
Fasting serum glucose	170.14 (\pm 74.40)	
HDL	1.13 (\pm 1.83)	
LDL	2.58 (\pm 2.82)	
Total cholesterol	4.76 (\pm 8.21)	
TG	3.46 (\pm 25.64)	
GFR	69.85 (\pm 26.58)	
Systolic BP	134 (\pm 17)	
Diastolic BP	79 (\pm 9)	

Note. ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; BB: Beta-blocker; CCB: Calcium channel blocker; DPP4: Dipeptidyl-peptidase 4; GLP1: Glucagon-like peptide 1; SU: Sulfonylurea; SGLT2: Sodium-glucose cotransporter-2; TG: Triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; & GFR: Glomerular filtration rate

Univariate analysis was conducted using Chi-square and Mann Whitney U tests to determine the variables associated with BP control (all tested variables are included in **Table 4**).

Table 3. Medical characteristics of the study participants

Variable	Frequency (%)	
Dyslipidemia	No	146 (28.0%)
	Yes	376 (72.0%)
Heart failure	No	490 (93.9%)
	Yes	32 (6.1%)
cerebrovascular disease	No	454 (87.0%)
	Yes	68 (13.0%)
Ischemic heart disease	No	308 (59.0%)
	Yes	214 (41.0%)
Renal failure	No	460 (88.1%)
	Yes	62 (11.9%)
Peripheral artery disease	No	504 (96.6%)
	Yes	18 (3.4%)
Microvascular complications	No	258 (49.4%)
	Yes	264 (50.6%)
Retinopathy	No	286 (54.8%)
	Yes	236 (45.2%)
Neuropathy	No	428 (82.0%)
	Yes	94 (18.0%)
Foot damage	No	455 (87.2%)
	Yes	67 (12.8%)
Anxiety	No	407 (78.0%)
	Yes	115 (22.0%)
Presence of proteinuria on UA	No	375 (71.8%)
	Yes	147 (28.2%)
Depression	No	466 (89.3%)
	Yes	56 (10.7%)
Asthma	No	499 (95.6%)
	Yes	23 (4.4%)
COPD	No	510 (97.7%)
	Yes	12 (2.3%)
Type 2 diabetes control	Controlled	254 (48.7%)
	Uncontrolled	268 (51.3%)
BP control	Controlled	191 (36.6%)
	Uncontrolled	331 (63.4%)

Table 4. Univariate analysis of the variables associated with blood pressure control

		BP control	
		Frequency (%) or Mean (\pm SD)	
		Controlled	Uncontrolled
Age		63 (\pm 10)	62 (\pm 10)
Gender	Female	100 (52.9%)	154 (47.2%)
	Male	89 (47.1%)	172 (52.8%)
Material status	Married	148 (79.1%)	249 (97.6%)
	Other	39 (20.9%)	72 (22.4%)
Educational level	High	47 (24.9%)	94 (28.9%)
	Low	142 (75.1%)	231 (71.1%)
Employment states	Employees	54 (28.9%)	114 (35.3%)
	Retired/non-employees	133 (71.1%)	209 (64.7%)
Area of residency	Rural area	60 (31.7%)	96 (29.5%)
	Urban area	129 (68.3%)	229 (70.5%)
Smoking	Current smoker	56 (29.9%)	105 (32.7%)
	Former/non-smoking	131 (70.1%)	216 (67.3%)
Physical activity	No	121 (64.0%)	190 (58.1%)
	Yes	68 (36.0%)	137 (41.9%)
Obesity	Non-obese	134 (71.3%)	214 (66.9%)
	Obese/overweight	54 (28.7%)	106 (33.1%)
ACEI	No	147 (77.8%)	238 (72.8%)
	Yes	42 (22.2%)	89 (27.2%)
BB	No	94 (49.7%)	142 (43.4%)
	Yes	95 (50.3%)	185 (56.6%)
CCB	No	118 (62.4%)	181 (55.4%)
	Yes	71 (37.6%)	146 (44.6%)
ARBs	No	80 (42.3%)	141 (43.1%)
	Yes	109 (57.7%)	186 (56.9%)

Table 4 (Continued). Univariate analysis of the variables associated with blood pressure control

		BP control	
		Frequency (%) or Mean (\pm SD)	
		Controlled	Uncontrolled
Thiazide diuretics	No	114 (60.3%)	210 (64.2%)
	Yes	75 (39.7%)	117 (35.8%)
DPP4 inhibitors*	No	141 (74.6%)	212 (64.8%)
	Yes	48 (25.4%)	115 (35.2%)
Insulin	No	89 (47.1%)	146 (44.6%)
	Yes	100 (52.9%)	181 (55.4%)
Metformin	No	29 (15.3%)	38 (11.6%)
	Yes	160 (84.7%)	289 (88.4%)
GLP1 receptor agonist	No	105 (55.6%)	162 (49.5%)
	Yes	84 (44.4%)	165 (50.5%)
SU	No	122 (64.6%)	202 (61.8%)
	Yes	67 (35.4%)	125 (38.2%)
Dyslipidemia	No	51 (27.0%)	92 (28.1%)
	Yes	138 (73.0%)	235 (71.9%)
cerebrovascular disease	No	165 (87.3%)	283 (86.5%)
	Yes	24 (12.7%)	44 (13.5%)
Ischemic heart disease	No	120 (63.5%)	187 (57.2%)
	Yes	69 (36.5%)	140 (42.8%)
Renal failure	No	164 (86.8%)	290 (88.7%)
	Yes	25 (13.2%)	37 (11.3%)
Microvascular complications	No	90 (47.6%)	165 (50.5%)
	Yes	99 (52.4%)	162 (49.5%)
Retinopathy*	No	92 (48.7%)	191 (58.4%)
	Yes	97 (51.3%)	136 (41.6%)
Neuropathy	No	160 (84.7%)	263 (80.4%)
	Yes	29 (15.3%)	64 (19.6%)
Foot damage	No	170 (89.9%)	279 (85.3%)
	Yes	19 (10.1%)	48 (14.7%)
Anxiety	No	153 (81.0%)	248 (75.8%)
	Yes	36 (19.0%)	79 (24.2%)
Depression	No	166 (87.8%)	294 (89.9%)
	Yes	23 (12.2%)	33 (10.1%)
HbA1c*		13.83 (\pm 81.86)	8.29 (\pm 1.75)
Fasting serum glucose		162.67 (\pm 72.39)	174.07 (\pm 75.57)
HDL*		1.09 (\pm 0.31)	1.16 (\pm 2.30)
LDL		2.44 (\pm 0.99)	2.67 (\pm 3.49)
Total cholesterol		4.37 (\pm 1.25)	5.01 (\pm 10.33)
TG		2.18 (\pm 1.22)	4.23 (\pm 32.39)
GFR		67.00 (\pm 25.15)	71.24 (\pm 27.13)

Note. ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; BB: Beta-blocker; CCB: Calcium channel blocker; DPP4: Dipeptidyl-peptidase 4; GLP1: Glucagon-like peptide 1; SU: Sulfonylurea; SGLT2: Sodium-glucose cotransporter-2; TG: Triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; GFR: Glomerular filtration rate; & *Significant at $p < 0.05$

Table 5. Multivariate analysis of the variables associated with blood pressure control

Variable	OR (95% CI)	p-value
Retinopathy: No vs. yes	1.468 (1.020-2.113)	0.039*
DPP4 inhibitors: No vs. yes	0.633 (0.423-0.946)	0.026*
Hb A1c	0.997 (0.988-1.005)	0.452
HDL	1.022 (0.906-1.154)	0.720

Note. DPP4: Dipeptidyl-peptidase 4 & *Significant at $p < 0.05$

The significant variables were receiving dipeptidyl-peptidase 4 (DPP4) inhibitors ($p=0.035$), having retinopathy ($p=0.024$), glycemic control ($p=0.006$), and HDL value ($p=0.025$).

Binary regression model was conducted to evaluate variables association with BP control (Table 5). The results revealed that patients who were suffering from retinopathy had significantly higher odds to be in the uncontrolled BP group when compared to those who were not (OR=1.468 (95%CI 1.020-2.113), $p < 0.05$). Furthermore, patients who were receiving DPP4 inhibitors had lower odds to be in the

uncontrolled BP group when compared to those who were not (OR=0.633 (95%CI 0.423-0.946), $p < 0.05$).

DISCUSSIONS

Currently, hypertension is acknowledged as a substantial risk factor for early mortality and disability, with prevalence rates varying greatly between countries and projected to increase by 68% by 2025 [13]. Besides, the coexistence of hypertension and diabetes has been observed in previous research [14-17] and was associated with a four-fold increase in mortality [18], as well as microvascular and macrovascular complications [19]. Controlling BP in diabetic patients is extremely important objective in reducing the consequences associated with the two coexisting diseases [20]. Consequently, the aim of this study was to explore the factors associated with uncontrolled BP in hypertensive patients with type 2 diabetes.

The current study results obviously showed uncontrolled BP in the majority of the participants (63.4%), which was in line with the findings reported in studies conducted in Iran [9], Saudi Arabia [21], India [22], Ethiopia [23], Thailand [24], and Spain [25]. Another Ethiopian study reported that nearly 44% of the participating hypertensive patients comorbid with diabetes failed to reach optimal BP control [7]. Furthermore, most of the hypertensive patients were found to have poorly controlled BP in studies conducted in Ethiopia [26-28] and Ghana [29]. More than one third of the hypertensive patients enrolled in several other studies had poorly controlled hypertension [30-32]. Other studies conducted among hypertensive patients with chronic kidney disease found that more than 60% of the patients had uncontrolled BP [33, 34]. These findings highlight the value of investigating the primary contributing variables of poor BP control in hypertensive patients with diabetes in order to create effective strategies for controlling BP and overcoming the challenges in obtaining such a target among these patients.

Retinopathy is one of the microvascular complications of diabetes that results from the disease's long-term effect on the ocular system [35]. Patients who were suffering from retinopathy in the present study had significantly poorer BP control than their counterparts. This relationship has been supported in previous research conducted on diabetic patients [22, 36-39]. High blood sugar levels in diabetic patients increase their chance of developing diabetic retinopathy by harming the small blood vessel network that supplies blood to the retina [40]. Strict glycemic control and a healthy lifestyle are indeed recommended to prevent the development or worsening of diabetic retinopathy, consequently limiting subsequent diabetes complications.

Another major predictor of BP control in the current investigation was the use of DPP4 inhibitors, with patients who did not take a DPP4 inhibitor having considerably lower BP control when compared to DPP-4 inhibitors users. Controversial results were reported in the literature regarding the effect of DPP4 inhibitors on BP with some studies reporting that DPP4 inhibitors decrease BP, others claiming that DPP4 inhibitors have no effect on BP, and others reporting that DPP4 inhibitors can increase BP. A case report study conducted on a 54-year-old hypertensive diabetic patient reported a favorable effect of vildagliptin, a DPP4 inhibitor, on the central SBP of this patient, and suggested that this group of medications could have a glucose-independent beneficial cardiovascular effect in patients with hypertension and diabetes [41]. Another study found that four weeks of vildagliptin treatment enhanced endothelium-dependent vasodilation in type 2 diabetes individuals and indicated that it may have positive cardiovascular effects [42]. In a Japanese trial, the DPP4 inhibitor Sitagliptin was also observed to lower systolic BP in hypertensive patients with type 2 diabetes [43]. A systematic review and meta-analysis study reported that DPP4 inhibitors may exert a modest BP-lowering effect in patients with type 2 diabetes [44]. On the other hand, a randomized, double-blind, crossover study which was conducted among hypertensive patients with type 2 diabetes reported that DPP4 inhibition increased catecholamine concentration without affecting BP readings in patients receiving sustained ACE inhibitor treatment [45]. More interestingly, an American study conducted among rats found that DPP4 inhibition do increase arterial BP [46]. The evidence regarding the impact of DPP4 inhibitors on BP is conflicting, which makes it necessary to

move forward with more studies that would improve our understanding of this complicated interaction and guide the development of effective management programs for individuals with combined hypertension and diabetes.

It is worth mentioning that earlier research studies focused solely on BP control among patients with hypertension, whereas the present study specifically targeted those with hypertension and type 2 diabetes as a comorbid disease. This, together with the paucity of research in the field, contributes to a deeper understanding of BP control in hypertensive patients with type 2 diabetes, and provides a broader picture of the key contributing variables that impede obtaining adequate BP control in this group of patients. Nevertheless, the current study has some limitation. The retrospective research design has an inferior level of evidence compared with prospective studies. Furthermore, the recruited sample might not be representative of the general population and prone to selection bias.

CONCLUSIONS

Uncontrolled BP increase the potential of cardiovascular events among patients with hypertension and type 2 diabetes. The current study revealed a margin for improving BP control among this group of patients. Having retinopathy and not receiving dipeptidyl-peptidase 4 inhibitors were independent determinants of poor BP control among patients with hypertension and type 2 diabetes. Targeting retinopathy and considering dipeptidyl-peptidase 4 inhibitors drug therapy should be considered by the clinicians in the future strategies which aim at controlling BP among hypertensive patients who have type 2 diabetes as a comorbid disease.

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Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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