

## Use of antihypertensive medications in patients with diabetes in Ajman, UAE

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### ABSTRACT

**Objectives:** Optimal reduction in blood pressure with antihypertensive agents helps to prevent diabetic microvascular and macrovascular complications. The objective of the study was to evaluate the current utilization pattern of antihypertensive medications among patients with diabetes and co-existent hypertension as per the JNC 7th Report guidelines.

**Materials and Methods:** A cross sectional survey was carried out among patients with diabetes attending the Outpatient Department of Internal Medicine at a tertiary care hospital in Ajman. Medical records of the patients were used to obtain diagnostic, demographic and drug use information. Univariate analysis was performed using Chi square and t-test followed by logistic regression to compute independent predictors.

**Results:** Of 132 patients with diabetes, uncomplicated hypertension (HTN) was coexistent in 107 (81%) patients. Males constituted 49.5% of the total. The mean age of patients with HTN was (55.1±10.1), which was higher than that in those without HTN (49.6±9.9) ( $p < 0.05$ ). 51.4% of patients with HTN were between 45-60 years of age. A higher number of patients with HTN had duration of diabetes <5 years than those >5 years ( $p < 0.05$ ). While adjusting the significant factors, only the duration of diabetes (adjusted OR 1.06; CI (1.003-1.116)) was statistically significant among patients with HTN. 68 (62.6%) prescriptions contained one antihypertensive drug, 29 (30%) two drugs and 8 (7.4%) no anti-hypertensive drug. Angiotensin converting enzyme inhibitors/ angiotensin receptor blockers (ACEI/ARBs) followed by diuretics were commonly prescribed. ARBs with diuretics were the most frequent two drug combination. The antihypertensive utilization pattern was similar in both gender and age groups.

**Conclusion:** The results represent the current prescribing trend for anti-hypertensive agents among patients with diabetes, which is in accordance with JNC-7 recommendations.

**Key words:** anti-hypertensives, diabetes, drug utilization

### INTRODUCTION

Diabetes Mellitus (DM) is one of the endocrine disorders necessitating constant attention to diet, exercise, glucose monitoring, and medication to achieve good glycemic control. The prevalence of diabetes is increasing dramatically, with approximately 171 million people worldwide having diabetes and 350 million adults likely to acquire diabetes by 2030<sup>1</sup>. In the United Arab Emirates (UAE), the prevalence of diabetes is approximately 20%, which is expected to reach 22% by 2025. It is higher among the UAE citizens (25%) than in the expatriates (13–19%), the latter varying with the country of origin<sup>2</sup>.

DM is associated with a higher prevalence of risk factors such as hypertension (HTN) and dyslipidemia, which, in turn leads to major vascular complications (microvascular and macrovascular)<sup>3</sup>. These complications are debilitating to the patient, and also associated with significant economic burden to the patient, family members, and the nation's healthcare budget. Al-Maskari et al. from UAE documented significant association between hypertension and the presence of macrovascular disease among diabetic patients<sup>4</sup>. About 35% of the patients with diabetes had co-existent hypertension. Optimal reduction in blood pressure with antihypertensive agents helps to prevent diabetic microvascular

and macrovascular complications<sup>5</sup>. With each year the number of approved pharmacological treatment options for patients with hypertension is increasing. However, the choice of antihypertensive medication is influenced by many factors, especially the presence of co-morbid conditions. The Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC) stated that angiotensin converting enzyme inhibitors/Angiotensin receptor blockers (ACEI/ARB) is an important component of most regimens to control BP in diabetic patients<sup>6</sup>.

The primary objective of the study was to evaluate and compare the utilization of antihypertensive medications according to JNC 7<sup>th</sup> Report for diabetic patients.

#### **MATERIALS AND METHODS**

This was a cross sectional survey carried out among patients with diabetes attending the Outpatient Department of Internal Medicine at Gulf Medical College Hospital, Ajman. The patients included were those with diabetes and uncomplicated hypertension, 18 years old and above. Patients with incomplete records were excluded. Medical records of patients were used to obtain diagnostic, demographic and drug use information. The data extracted from the medical records were transferred to a pilot-tested structured questionnaire developed by the investigators.

All data collected were analyzed using SPSS, version 19. Univariate analysis was performed using Chi square and t-test followed by logistic regression to compute independent predictors. Multivariate analysis was further tested on variables found significant in Univariate analysis. *p* value less than or equal to 0.05 was considered statistically significant.

#### **RESULTS**

During the study period, a total of 132 prescriptions of patients with diabetes were monitored, of which 25 were excluded as per the exclusion criteria. The remaining 107 (81%) had uncomplicated

hypertension (49.5% were males and 50.5% were females). The demographic and medical characteristics of the 107 hypertensive patients are presented in Table 1.

Of the 107 patients with HTN, 25 had co-existent dyslipidemia. A total of 30 patients had dyslipidemia (22.7%). The mean age of patients with HTN (55.1±10.1) was significantly higher than those without HTN (49.7±10.0 years) (*p*<0.05). The mean ages of males (53.2 ±9.4 years) and females (54.9±10.9 years) with HTN were similar. No gender differences were observed in patients with HTN and those without HTN. Based on the age groups, the majority of the patients were in the age group of 45-60 years. The difference in proportions was statistically significant (*p*<0.05). Among the patients with diabetes and hypertension, it was observed that a significantly greater proportion of patients were with the duration of diabetes >5 years (*p*<0.05). To find the degree of association between mean age of the patient and the duration of diabetes and the occurrence of DM, simple binary logistic regression was applied. It was found that with unit increase in the age (one year) there was a 6% increase in the risk to develop HTN, which was statistically significant (Odds ratio (OR) 1.06; confidence interval (CI) (1.01-1.11)). With respect to the duration of diabetes, there was a 6 times higher chance to develop HTN if the duration of diabetes is above 5 years, although the result was not statistically significant OR 6.5 CI (0.84-51.19).

To eliminate the effect of confounding variables, multiple logistic regression was applied and the results showed that the adjusted OR for duration of DM was not statistically significant but the adjusted OR for the age was 1.06 with a CI (1.003-1.116), which was statistically significant. Thus it can be concluded that the only factor associated with the occurrence of HTN is the duration of diabetes.

Of the total, a single antihypertensive drug had been given in 68 (62.6%) of the prescriptions, a two-drug combination in 29 (30%) prescriptions and a three-drug combination in two prescriptions,

Table 1. Demographic characteristics of patients with and without hypertension among diabetics

Item	Variable	HTN Mean±SD/No. (%)	No HTN Mean±SD/No. (%)	p value
Age	Mean age	55.1±10.1	49.7±10.0	<0.05
Gender	Male	53 (84.1)	10(15.9)	NS
	Female	54(78.3)	15 (21.7)	
Age group	<45 years	16 (64.0)	9 (36.0)	<0.05
	45-60 years	55(82.1)	12(17.9)	
	>60 years	36(90.0)	4(10.0)	
Duration of DM	≤5 years	84(77.8)	24(22.2)	<0.05
	>5 years	23(95.8)	1 (4.2)	

while 8 (7.4%) patients did not receive any drug. Angiotensin receptor blockers were the most commonly prescribed antihypertensive medications and Angiotensin receptor blockers with diuretics were the most frequent two-drug combination. The overall utilization of individual drug classes and as monotherapy and combination therapy is shown in Tables 2 and 3.

Table 2. Antihypertensive medications in monotherapy and combination therapy.

Drug class	Monotherapy	Combination therapy	Overall utilization
ACEI/ARB	42	25	67
BB	19	2	21
CCB	7	7	14
Diuretic	-	23	23

The utilization pattern of the most common

antihypertensive medication based on gender, age groups and duration of DM is listed in Table 4. No statistical significance was noted in the utilization pattern of the common antihypertensive medications (monotherapy and combination therapy) with regard to gender, age groups and duration of DM.

## DISCUSSION

This study evaluated the patterns of antihypertensive drug therapy in diabetic hypertensive patients. It showed that nearly 80% of the patients had co-existing hypertension. The findings of Maskari et al. from the UAE reported that 35% with DM had co-existing hypertension<sup>4</sup>. The co-existence of risk factors such as hypertension and dyslipidemia leads to more harmful effect in the presence of diabetes. Our study revealed that about 62% patients were on single

Table 3. Monotherapy versus Combination therapy of antihypertensive medications

Drug therapy	Drug classes	Number	%
Monotherapy	ACEI/ARB	42	39.2
	BB	19	17.7
	CCB	7	6.5
Two-drug combination	ACEI/ARB +DIU	22	20.5
	ACEI/ARB + CCB	5	4.6
	CCB+BB	1	0.9
	ACEI/ARB +BB	1	0.9
Three drug combination	ACEI/ARB +DIU+CCB	2	1.8

Table 4. Utilization of most common antihypertensive medications based on gender, age groups and duration of DM

Variable	Item	ACEI/ARB (n=42)	BB (n=19)	ARB+DIU (n=22)
Gender	Male	18	12	11
	Female	25	7	11
Age group	<45 years	5	4	2
	45-60 years	20	10	11
	>60 years	18	5	9
Duration of DM	<5 years	32	13	18
	>5 years	11	6	4

antihypertensive therapy and nearly 30% on combination therapy. The use of multiple drugs in combinations is being increasingly recognized as critical to control hypertension in patients with diabetes. Johnson et al. reported that 70% of the patients with HTN among diabetics were on multidrug regimens<sup>7</sup>.

The commonest drug class prescribed was ACEI/ARBs, as shown in previous reports<sup>7,8</sup>, and this pattern of utilization matches the JNC VII recommendation for patients with HTN and diabetics<sup>6</sup>. These findings indicate that medication use among diabetic hypertensive patients was mostly consistent with JNC 7th Report recommendation. ACEI/ARBs were the most commonly prescribed drug classes both in monotherapy and combination therapy. The use of ACEI/ARBs among diabetic hypertensive patients is in accordance with the JNC recommendations for the management of hypertension among diabetic hypertensive patients. ACEI and ARBs are the preferred antihypertensive medication for the management of hypertension among diabetic hypertensive patients. The reported monotherapy and combination therapy use of ACEI/ARBs was 39.2%, which is consistent with reports from Palestine and Bahrain<sup>8,9</sup>. Evidence from the HOPE trial (The heart outcomes prevention evaluation study) suggested the cardiovascular protection benefits of ACEI in hypertension<sup>10</sup>.

Beta-blockers ranked second when considering monotherapy of antihypertensive drug class, which is inconsistent with Sweileh WM et al. wherein diuretics were the second most

common antihypertensive drug class<sup>8</sup>. However, diuretics ranked second when considering the overall utilization of antihypertensive drugs. Combination of ACEI/ARB with diuretic was the most commonly prescribed. Diuretics offer both cardiovascular and renal protection, do not increase the risk for diabetes, and their safety and beneficial effects in this population are well established. They were recommended by JNC VI as one of the preferred therapies in this population. This utilization was consistent with evidence-based practice guidelines<sup>11</sup>.

The combination of ACEI/ARB with diuretic is pharmacologically favorable since it produces an additive antihypertensive effect and minimizes most adverse effects of either the ACEI/ARB or the diuretics, especially hypokalemia<sup>12</sup>. Antihypertensive and Lipid-Lowering Treatment to prevent Heart Attack Trial (ALLHAT study) highlighted the importance of the diuretic agent in hypertension<sup>13</sup>.

The study had the advantage of assessing prescriptions dispensed and was able to assess the prescription volume for a given class and characterize specific prescribing for patients, for example, percentage of patients on multidrug regimen taking a diuretic or those on monotherapy for ACEI.

## CONCLUSION

Our findings showed ACEI/ARB use in a large proportion of diabetic hypertensive patients, representing the current prescribing trend for anti-hypertensive agents among patients with diabetes, which is in accordance with evidence-

based practice guidelines (JNC-7 recommendations).

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