

## Prescribing pattern of antihypertensive drugs in diabetic patients of Southern Province, Kingdom of Saudi Arabia

El patrón de prescripción de los fármacos antihipertensivos en los pacientes diabéticos de la Provincia del Sur, Reino de Arabia Saudita

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### ABSTRACT

**Background.** Hypertension is extremely prevalent in patients with diabetes. Limited data exist on utilization patterns of antihypertensive in this population are consistent with evidence-based practice guidelines.

**Objective.** To evaluate utilization patterns of antihypertensive agents among diabetic patients with hypertension.

**Design.** Retrospective descriptive cross sectional.

**Patients/Participants.** 149 patients with diabetes and hypertension from outpatient department at Family Medicine Hospital, Ahaderfieda. Khamis Mushait, K.S.A.

**Results.** Over 43% of patients were receiving calcium channel blockers (CCB), 36.2 % of received angiotensin converting enzyme inhibitors (ACEI), followed by angiotensin receptor blockers (ARBs) (34.9%), diuretics (34.2%) and  $\beta$ -blockers (16.2%). Patients on monotherapy were mostly receiving CCB (34.3%) and ACEI (29.9%). The majority (55.03%) of treated patients were on multidrug regimens. In patients with coronary artery disease (CAD), a diuretic with ACEI (25%) and calcium channel blocker with angiotensin receptor blocker (25%) was most commonly prescribed.

**Conclusions.** Patterns of antihypertensive therapy were generally consistent with international guidelines. Areas of improvement include increasing ACEI/ARB and diuretic use, decreasing the number of untreated patients, and increasing the proportion of patients with controlled BP in this population.

**Keywords:** Hypertension, Diabetes, Antihypertensive agents.

### RESUMEN

**Antecedentes.** La hipertensión es muy frecuente en los pacientes con diabetes. Existen datos limitados sobre los patrones de utilización de antihipertensivos en esta población consistentes con las guías de práctica basadas en la evidencia.

**Objetivo.** Evaluar los patrones de utilización de antihipertensivos en los pacientes diabéticos con hipertensión .

**Diseño.** Estudio retrospectivo descriptivo transversal.

**Pacientes/ Participantes.** 149 pacientes con diabetes e hipertensión, del departamento de pacientes ambulatorios en el Hospital de Medicina Familiar, Ahaderfieda. Khamis Mushait, K.S.A.

**Resultados.** Más del 43% de los pacientes estaban recibiendo bloqueadores del canal de calcio (CCB), el 36,2% recibían inhibidores de la enzima convertidora de angiotensina (IECA), seguido de los bloqueadores de los receptores de angiotensina (BRA) (34,9%), diuréticos (34,2%) y bloqueadores  $\beta$  (16,2 %). Los pacientes en monoterapia fueron la mayoría recibiendo CCB (34,3%) e IECA (29,9%). La mayoría (55,03%) de los pacientes tratados se encontraban en regímenes de múltiples fármacos. En los pacientes

con enfermedad de la arteria coronaria (CAD), se les prescribió con mayor frecuencia diurético con IECA (25%) y bloqueador de canales de calcio con bloqueador del receptor de angiotensina (25%).

**Conclusiones.** Los patrones de utilización de antihipertensivos fueron generalmente consistentes con las directrices internacionales. Las áreas de mejora incluyen el aumento de IECA / ARB y el uso de diuréticos, disminuyendo el número de pacientes no tratados, y el aumento de la proporción de pacientes con PA controlada en esta población.

**Palabras clave:** hipertensión, diabetes, agentes antihipertensivos.

## INTRODUCTION

Diabetes mellitus and hypertension are interrelated diseases that strongly predispose an individual to atherosclerotic cardiovascular disease<sup>1</sup>. The prevalence of coexisting hypertension and diabetes appears to be increasing in Saudi Arabia. The World Health Organization estimates that the number of people with diabetes mellitus is projected to increase almost threefold in Saudi Arabia, from 890,000 in 2000 to a staggering 2,523,000 in 2030<sup>2</sup>. Hypertension (HTN), affects about 21% of all Saudi adults between the ages of 18 and 64 years, is an important modifiable risk factor for cerebrovascular disease (CVD)<sup>3</sup>. Studies such as Framingham heart study, United Kingdom Prospective Study-39 (UKPDS), Hypertension Optimal Treatment (HOT), Systolic Hypertension in the Elderly Programme (SHEP), Systolic hypertension in Europe (SYST-Eur), Hypertension in the Very Elderly Trial (HYVET-Pilot) indicated that reduction in either isolated systolic or systolic-diastolic hypertension significantly reduces the risk of micro and macro vascular complications and cardiovascular (CV) death or diabetes-related death<sup>4</sup>. The Seventh Joint National Committee (JNC 7) and American Diabetes Association (ADA) recommends that blood pressure (BP) in diabetics be controlled to levels of 130/80 mmHg or lower<sup>5</sup>. Whatever the goal level, rigorous control of BP is paramount for reducing the progression of diabetic nephropathy to end stage renal disease<sup>6</sup>. However, studies consistently demonstrate that most diabetic patients do not achieve recommended levels of BP control, and the majority have a BP of >140/90mmHg<sup>7</sup>. Saudi Hypertension Management Guidelines recommend either an ACE-I or an ARB, if ACE-I is not tolerated. If BP targets are not achieved, a thiazide diuretic should be added to those with an e Glomerular Filtration Rate  $\geq$  30 or a loop diuretic for those with an estimated Glomerular Filtration Rate < 30<sup>8</sup>. Some studies have demonstrated the beneficial effects of beta blockers and calcium channel blockers in diabetic hypertensive patients<sup>9</sup>. On contrary to above studies, some studies indicate that majority of diabetic patients will require two or more drugs to achieve BP control<sup>8, 10, 11</sup>. The resulting changes in drug use in time and place may have medical, social and economic implications

both for the individual patient for populations. These differences need to be identified, explained and corrected if needed. Drug utilization studies are necessary to this effect with a particular focus on socio- demographic characteristics, co-morbid conditions and pattern of anti- hypertensive drugs usage<sup>12</sup>. Thus in this context, the present study was conducted to examine the utilization pattern of anti-hypertensive in hypertensive diabetic patients and also to explore the adherence of prescribing pattern with existing guidelines.

## MATERIALS AND METHODS

This study is a retrospective descriptive cross sectional drug utilization study conducted in the outpatient department at Family Medicine Hospital, Ahaderfieda. Khamis Mushait, K.S.A. A total of 149 prescriptions of hypertensive outpatients with diabetes above 18 yrs of age were randomly selected employing systematic sampling. The demographic and medication history of the diabetic hypertensive patients were collected to address the following questions:

1. Which antihypertensive drug classes and combinations, respectively, are applied by general physicians in hypertensive diabetic patients?
2. Did drug treatments differ with respect to certain patient characteristics such as age, gender?

### Data analysis

Data analysis was carried out using Microsoft excel. Data were expressed as mean (standard deviation) for continuous variables and as frequency for categorical variables.

## RESULTS

One hundred forty nine prescriptions belonging to 81 (54.4 %) females and 68 (45.6%) males were studied. The mean age of the male patients included in the study was found to be 55.2 $\pm$ 8.5 years and the mean age of the female students included in this study was found to be 58.1  $\pm$  12.9.

The overall use of antihypertensive in diabetes is shown in Table 1. The utilization of the calcium channel blockers supersedes all other groups of antihypertensive in diabetes with hypertension. Use of the calcium channel blockers is around 43% in hypertensive diabetic patients. Amlodipine is the predominantly used CCB. The ACE inhibitors are the antihypertensive class used the most following the CCB's (36.2%). The use of angiotensin II receptor blockers were also nearly the same as ACE inhibitors among the diabetes patients with diabetes (34.9%). Next to the ARBs, diuretics were used widely among these patients (34.2%) and the loop diuretic furosemide is the least prescribed diuretic in diabetes with hypertension.  $\beta$ -Blockers are the least

prescribed antihypertensive in diabetes with hypertension. Table 2 shows the relative use of antihypertensive in both genders. Marked gender based differences have been found to be there between the two groups of diabetes. The utilization of ARBs,  $\beta$ -Blockers and CCBs are more among the female patients whereas the utilization of ACE inhibitors and diuretics are high among the male patients.

In Table 3 the various antihypertensive drugs and the number of patients in whom they were used under the class of monotherapy revealed that, out of 67 patients who underwent monotherapy for the treatment of hypertension, 23 (34.3%) of the patients were prescribed with CCBs, followed by 20 (29.9 %) with ACE inhibitors, 14 (20.8%) of the

patients with ARBs, 6 (9%) of the patients with diuretics and 4 (6%) of the patients with  $\beta$ -blockers.

Table 4 reveals that, out of 68 patients in whom two antihypertensive were prescribed, 17(25%) patients were prescribed with a combination of Diuretics & ACE inhibitors and another 17(25%) patients were prescribed with a combination of CCB & ARBs followed by 13 (19.1%) of patients with Diuretics and ARBs, 7(10.3%) patients with ACE inhibitors, 3 (4.4%) patients with ACE inhibitors and  $\beta$ -Blockers, 2 (2.9%) patients were prescribed with  $\beta$ -Blockers+ARB, another 2 (2.9%) patients were prescribed with CCB+Diuretics and 1 (1.5%) was prescribed with  $\beta$ -Blockers+diuretics.

**Table 1: Antihypertensive Drug Use in Diabetics**

S.No	Antihypertensive Class	Drug	N° of Prescriptions	Percentage
1	CCB	Amlodipine	59	39.6
		Nifedipine	5	3.4
Total			64	43
2	ACEI	Captopril	3	2
		Perindopril	51	34.2
Total			54	36.2
3	$\beta$ -Blockers	Atenolol	8	5.4
		Bisoprolol	11	7.4
		Carvedilol	5	3.4
Total			24	16.2
4	ARBs	Valsartan	27	18.1
		Candesartan	22	14.8
		Losartan	2	1.3
		Telmisartan	1	0.7
Total			52	34.9
5	Diuretics	Furosemide	9	6
		Hydrochlorothiazide	22	14.8
		Indapamide	20	13.4
Total			51	34.2

[Calcium channel blockers (CCB), Angiotensin Converting Enzyme Inhibitors (ACEI), Angiotensin Receptor Blockers (ARBs)]

**Table 2: Relative use of antihypertensive in males and females**

S.No	Antihypertensive class	Males N (%)	Females N (%)
1	CCB	25 (36.8)	39 (48.1)
2	ACEI	37 (54.4)	17 (21)
3	$\beta$ -Blockers	8 (11.8)	16 (19.8)
4	ARBs	22 (32.4)	30 (37)
5	Diuretics	26 (38.2)	25 (31)

[Calcium channel blockers (CCB), Angiotensin Converting Enzyme Inhibitors (ACEI), Angiotensin Receptor Blockers (ARBs)]

**Table 3: Pattern of prescribed single antihypertensive agent (n=67)**

S.No	Antihypertensive Class	Number of prescriptions	Percentage
1	Diuretics	6	9
2	$\beta$ -Blockers	4	6
3	Calcium Channel Blockers	23	34.3
4	ACE Inhibitors	20	29.9
5	ARBs	14	20.8

[Calcium channel blockers (CCB), Angiotensin Converting Enzyme Inhibitors (ACEI), Angiotensin Receptor Blockers (ARBs)]

**Table 4: Pattern of use of antihypertensive drug combinations**

Drug combination	No of prescriptions	% of total prescriptions
<i>2 Drug combination</i>	<i>n=68</i>	<i>45.63%</i>
ARB+Diuretics	13	19.1
CCB+ARB	17	25
$\beta$ -Blockers+ARB	2	2.9
CCB+Diuretics	2	2.9
$\beta$ -Blockers+diuretics	1	1.5
CCBs + $\beta$ -Blockers	6	8.8
ACEI+ Diuretics	17	25
ACEI + CCBs	7	10.3
ACEI + CCBs	3	4.4
<i>3 Drug combination</i>	<i>n=13</i>	<i>8.72%</i>
ACEI + $\beta$ -Blockers + CCBs	2	14.3
ACEI + $\beta$ -Blockers + Diuretics	1	7.1
ACEI + CCBs+ Diuretics	3	21.4
$\beta$ -Blockers+ARB+diuretics	3	21.4
CCB+ARB+Diuretics	3	21.4
CCB+ $\beta$ -Blockers +Diuretics	1	7.1
<i>4 Drug combination</i>	<i>n=1</i>	<i>0.67%</i>
$\beta$ -Blockers +ACEI + CCBs+ Diuretics	1	7.1

[Calcium channel blockers (CCB), Angiotensin Converting Enzyme Inhibitors (ACEI), Angiotensin Receptor Blockers (ARBs)]

## DISCUSSION

We studied patterns of antihypertensive use in patients with diabetes and hypertension, to evaluate whether they were consistent with evidence-based practice guidelines. In present study, ACEI, ARBs and calcium channel blocker were more commonly prescribed drugs, followed by, diuretics and beta-blockers irrespective of mono or poly therapy. Majority of patients were on polytherapy in the present study. As the hypertensive patients were diabetic increased utilization of ACE inhibitors was observed which was in accordance with JNC-7 guidelines which recommend its use for renoprotection in the hypertensive diabetic patients<sup>13</sup>. Among all the ACEI, perindopiril (34.2%) was widely prescribed than any other ACEI. This finding is supported by the EUROPA study which indicated that among patients with stable coronary heart disease without apparent heart failure, perindopril can significantly improve outcome<sup>14</sup>. We found that men were significantly more likely to be prescribed an ACE inhibitor as initial antihypertensive therapy than women (54.4 vs. 21%) this may be due to the fact that men are at high risk of developing atherosclerosis compared to women and also because of the teratogenic risk of ACEI and also reports from clinical trials have consistently documented that women are at higher risk of ACE inhibitor-induced cough than men<sup>15</sup>. Though 34.3% of patients received calcium channel blockers as monotherapy, some studies have shown an excess of selected cardiac events in patients treated with dihydropyridine calcium channel blockers (DCCBs) compared with ACEI<sup>16</sup>.

In a meta-analysis of 42 trials published by Wald *et al.*, it was found that combining antihypertensive drugs from two different classes lowered blood pressure five times more than doubling the dose of a single agent<sup>17</sup>. In addition to synergistic blood pressure lowering, combination therapy allows for lower dosage requirements of each individual agent. This, in turn leads to decreased side effects, thereby improving compliance<sup>18</sup>. In our present study use of multiple drug combinations for controlling blood pressure was also high at 55% compared to those using single drug 44.9% in these patients. Our finding is similar to those observed by Anand *et al.*<sup>19</sup> and Gu *et al.*<sup>20</sup> who indicated that the increased use of multiple antihypertensive drugs apparently has contributed to substantial improvement in BP control in the treated hypertensive population. A combination of diuretics and ACE inhibitor (ACEI) were the important drug combination to be most commonly prescribed in our study and also diuretics were used more often as component of multidrug therapy. This is supported by a previous report which indicated that ACEI-diuretic combinations achieve blood pressure control in approximately 80 percent of patients<sup>21</sup>.

In the present investigation, two-drug combinations were mostly prescribed (45.63%), followed by three-drug combinations (8.27%) and four drug combinations (0.67%) (Table 4). In two-drug combinations, a diuretic with ACEI (25%) and calcium channel blocker with angiotensin receptor blocker (25%) was most commonly prescribed as it is a choice for the treatment of the majority of patients with hypertension, particularly those at high risk of a secondary event<sup>22</sup>, the combined therapy with an ARB and a CCB has a potentially useful antiproteinuric effect in patients with type 2 diabetic nephropathy, even when their renal function is reduced<sup>23</sup> followed by an ARB with a diuretic (19.1 %). ONEAST study results confirm that ARB / diuretic combinations reduce BP further than monotherapies in hypertensive diabetic subjects with an acceptable safety profile<sup>23</sup>.

## CONCLUSIONS

Although this study lacks both breadth and depth, however it provides a reasonable indication of the prescription patterns of antihypertensive agents in diabetic hypertensive population. Our findings suggest that CCBs and ACE inhibitors were used in large proportion of diabetic hypertensive patients and the pattern of antihypertensive therapy was generally consistent with JNC 7 guidelines, those being the current guidelines at the time of our study. However, there remains potential room for improvement in drug utilization and a critical need for better blood pressure control. Further research is needed to qualify rationale for choice of drug based on demographic data, economic status, concomitant conditions and complications to give additional insight into prescribing patterns of antihypertensive in diabetic patients of Aseer region of Saudi Arabia.

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