

## Prevalence and control of hypertension among diabetes patients in hospital universiti sains malaysia, malaysia

### Prevalensi dan kontrol hipertensi pada pasien diabetes di hospital universiti sains malaysia, malaysia

Salwa Selim Ibrahim<sup>1</sup>, Ayman Selim I. Bougalambou<sup>2</sup>, Fita Rahmawati<sup>1,3\*</sup>, Mohamed Azmi Hassali<sup>1</sup>, and Syed Azhar Syed Sulaiman<sup>1</sup>

<sup>1</sup>. School of Pharmaceutical Sciences, Universiti Sains Malaysia, Malaysia

<sup>2</sup>. National Heart Institute, Kuala Lumpur, Malaysia

<sup>3</sup>. Faculty of Pharmacy, Gadjah Mada University, Indonesia

---

#### Abstract

Hypertension in patients with type 2 diabetes mellitus is a prevalent condition that leads to substantial morbidity and mortality. The aim of the study was to determine the prevalence of hypertension in type 2 diabetes attending endocrinology clinics at Hospital Universiti Sains Malaysia (HUSM), to describe antihypertensive treatment patterns, and to evaluate the target of blood pressure achieved by antihypertensive agents. The study was a prospective follow-up descriptive study. Study conducted at diabetic clinic outpatient at HUSM, Kelantan, Malaysia from January to December 2007. A total of 1077 diabetic patients involve in this study. The findings of our study showed that the majority patients type 2 diabetes mellitus 998 (92.7 %) had hypertension. For the patients who were on antihypertensive medications, 254 (23.6 %) of them were on monotherapy and 311 (28.9 %), 179 (16.6 %), and 198 (18.4 %) respectively received two, three and more than three antihypertensive agents. The majority of patients 872 (87.4 %) were on angiotensin converting enzyme inhibitors/angiotensin receptor blockers either alone or in combination with other antihypertensive drugs. A number of 601 (55.8 %) patients achieved blood pressure targets  $\leq 130/80$  mm Hg. Almost all patients with hypertension and diabetes will require a combination of antihypertensive medications. A number of patients was not achieved blood pressure goals  $\leq 130/80$  mm Hg. There is still need to educate both patients and health care providers of importance of achieving target of blood pressure in order to reduce morbidity and mortality in diabetes mellitus patients.

**Key words :** Hypertension, type 2 diabetes mellitus, hypertension treatment

#### Abstrak

Penyakit hipertensi pada pasien diabetes mellitus tipe 2 merupakan penyebab utama mortalitas dan morbiditas. Penelitian bertujuan mengetahui prevalensi hipertensi pada pasien diabetes mellitus tipe 2 di klinik endokrinologi, Hospital Universiti Sains Malaysia (HUSM), gambaran pola antihipertensi, dan mengevaluasi target tekanan darah yang dapat dicapai dengan antihipertensi. Penelitian ini bersifat deskriptif dengan pengambilan data secara prospektif. Penelitian dilakukan pada klinik diabetes rawat jalan di HUSM, Kelantan, Malaysia dari Januari hingga Desember 2007. Sejumlah 1077 pasien diabetes masuk dalam penelitian ini. Hasil penelitian menunjukkan mayoritas pasien diabetes mellitus tipe 2 menderita hipertensi 998 (92,7 %).

Dari pasien yang menggunakan antihipertensi sejumlah 254 (23,6 %) pasien menggunakan monoterapi dan sejumlah 311 (28,9 %), 179 (16,6 %), dan 198 (18,4 %) menerima dua, tiga dan lebih dari tiga antihipertensi. Sebagian besar pasien 872 (87,4 %) menerima *angiotensin converting enzyme inhibitors/angiotensin receptor blockers* baik sebagai obat tunggal maupun dalam kombinasi dengan obat antihipertensi lain. Sejumlah 601 (55,8 %) pasien mencapai target tekanan darah  $\leq 130/80$  mm Hg. Hampir semua pasien hipertensi dan diabetes menggunakan kombinasi antihipertensi. Sejumlah pasien masih belum dapat mencapai target tekanan darah  $\leq 130/80$  mm Hg. Masih diperlukan edukasi baik kepada pasien maupun tenaga kesehatan akan pentingnya pencapaian target tekanan darah pada pasien diabetes sehingga dapat menurunkan morbiditas dan mortalitas.

**Kata kunci :** hipertensi, diabetes mellitus tipe 2, pengobatan hipertensi

## Introduction

Type 2 diabetes mellitus (DM) is one of the world's largest human health problems and a common disease with substantial associated morbidity and mortality (Amos *et al.*, 1997). Most adverse diabetes outcomes are a result of vascular complications, both at a macrovascular level and a microvascular level. Experimental studies have not clearly shown relationship between improved glycaemic control and reductions in cardiovascular outcomes (Rosenbloom *et al.*, 1999). It would seem more logical to focus diabetes care on prevention of macrovascular complications through blood pressure control (Zimmet, 1995).

Patients with diabetes have a much higher rate of hypertension than would be expected in the general population. In Malaysia, about 10.7 % patients with diabetes mellitus are associated with hypertension (Ministry of Health of Malaysia, 2002). The co-existence of diabetes and hypertension in the patient is devastating to the cardiovascular system (Grossman and Messerli, 1996; Grossman *et al.*, 2000). Pharmacological treatment should be initiated in patients with diabetes when the blood pressure (BP) is persistently more than 130 mm Hg systolic and/or more than 80 mm Hg diastolic (World Health Organization, 1999; Schrier *et al.*, 2002; American Diabetes Association, 2002). Barring contraindications, angiotensin converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) are

considered first-line therapy in patients with diabetes and hypertension (Amos *et al.*, 1997; Zimmet, 1995).

Research goal was to determine the prevalence of hypertension in type 2 diabetes mellitus, to describe antihypertensive treatment patterns, and to evaluate the target of BP achieved by antihypertensive agents.

## Methodology

The study was a prospective follow-up descriptive study. Study conducted during January to December 2007 in diabetic clinic outpatients at HUSM, Kelantan, Malaysia. A total of 1077 type 2 DM patients attending into diabetic clinic involve in this study. These patients had been diagnosed and were on treatment for DM for at least 12 months. Patients who were juvenile diabetes, gestational diabetes, advanced chronic kidney disease and diabetes due to other causes were excluded.

Data collection was conducted through patient's medical record. Data included demographical characteristics, duration of having diabetes mellitus, blood pressure measurement, and type of antihypertensive drugs used.

The standard mercury sphygmo-manometer (Accoson Works, London, England) was used with an appropriately-sized cuff on the right arm of the patient who was adequately rested for at least five minutes and seated with the arm supported at his/her heart level. In this study, hypertension was taken as systolic blood pressure (SBP) of 130 mm Hg or greater and/or diastolic blood pressure (DBP) of 80 mm Hg or greater, or they taking of antihypertensive medication (Ministry of Health of Malaysia, 2002). The patients had an average of at least two readings taken two minutes apart.

Table I. Demographic Characteristics of patients in study

Variable	Frequency (%) n=1077
Gender	
Male	476 (44.2)
Female	601(55.8)
Age (years)	
≤35	15(1.4)
36-50	194(18)
51-65	626(58.1)
>65	242(22.5)
Race	
Malay	916(85.1)
Chinese	150(13.9)
Indian	11(1.0)
BMI(kg/m <sup>2</sup> )	
A target < 23 kg/m <sup>2</sup> for asia pacific	199(18.5 %)
Non target > 23 kg/m <sup>2</sup>	878(81.5 %)
Smoking History	
current smoker	66(6.1)
pervious smoker	81 (7.5)
never smoked	930(86.4)
Physical activity	
active > 150 min/wk	471(43.7)
non active < 150 min/wk	606(56.3)
Sistolic blood pressure (mmHg)	
<120	332 (30.8)
120-139	289 (26.8)
140-159	296 (27.5)
> 159	160 (14.9)
Diastolic blood pressure (mmHg)	
<80	753 (69.9)
80-89	33 (3.1)
90-99	213 (19.8)
> 100	78 (7.2)

Initial elevated blood pressure readings would be confirmed on at least two subsequent visits over one week or more.

Statistical Package for the Social Sciences (SPSS) software version 11.0 (Chicago, IL, USA) was used for data analysis.

## Results and Discussion

There were 1077 patients with type 2 DM were enrolled in this study. Descriptive statistics were used to describe the sample as shown in Table I.

About 476 (44.2 %) of patients in this study were male. According to racial distribution, 916 (85.1 %) were Malay, another 161 (14.9 %) were Chinese and Indian. This proportion of ethnic group is generally reprehensible of the Kelantan state population.

The age of patients in this study range was from 18 to 88 years and had been categorized into four groups. Most patients in this study 626 (58.1 %) were the age between 51-65 years.

Table II Antihypertension pattern in type 2 diabetes patients

Variable	Frequency (%) n=998
No medication	56 (5.6 %)
ACEIs	184(18.4 %)
CCBs	70 (7.0 %)
ACEIs and CCBs	168(16.8 %)
ARBs and CCBs	143(14.3 %)
ACEIs, $\beta$ -Blockers and CCBs	95(9.5 %)
ARBs, $\beta$ -Blockers and CCBs	84(8.4 %)
ARBs, $\beta$ -Blockers , CCBs and Diuretics	95(9.5 %)
ARBs, $\alpha$ - blockers , $\beta$ -Blockers and CCBs	103(10.3 %)
Total	998(100 %)

ACEIs = angiotensin-converting enzyme inhibitors,

CCBs = calcium channel blockers,

ARBs = angiotensin II receptor blockers

Diabetes mellitus is mainly diagnosed in adults over 40 years of age, although increasingly, it is being found to have developed in younger people, including children (Rosenbloom *et al.*,1999).

Growing prevalence of diabetes mellitus is now being strongly associated with a longer life expectancy, a more sedentary lifestyle and a greater tendency towards obesity (Zimmet,1995). More than half of patients 606 (56.3 %) in our study had sedentary lifestyle (physical activity less 150 minute/week) and a greater tendency towards obesity 878 (81.5 %) with body mass index (BMI) more than 23 kg/m<sup>2</sup>.

This study was classified blood pressure according to Seventh Report of Joint National Committee on Prevention, Detection, Evaluation of Hypertension (JNC 7). The prevalence of hypertension in patients with diabetes in diabetic clinic HUSM was 998 (92.7 %), which was comparable to studies elsewhere between 20 % until 60 %. (Arauz-Pacheco *et al.*, 2003).

The mean ( $\pm$ SD) of initial systolic blood pressure (SBP) was 136.0( $\pm$ 19.8) mm Hg ranging from 70 to 240 mm Hg and the mean ( $\pm$  SD) diastolic blood pressure (DBP) was 80.6 ( $\pm$ 9.8) mm Hg ranging from 50 to 120 mm Hg. In this study, out of 1077

Patients recruited, 456 (42.3 %) had SBP  $\geq$  140 mm Hg and total of 324 (30.1 %) had DBP  $\geq$  80 mm Hg.

For the patients who were on antihypertensive medications, 254 (23.6 %) of them were on monotherapy and 311 (28.9 %), 179 (16.6 %), and 198 (18.3 %) respectively received two, three and more than three antihypertensive agents. Most diabetic patients with hypertension require combination therapy to achieve optimal blood pressure goals. (Amos *et al.*, 1997; Zimmet,1995). In United Kingdom Prospective Diabetes Study (UKPDS), over 60 % of participants in the more intensively treated group received 2 or more medications, and 29 % received 3 or more medications to achieve a mean blood pressure of 144/82 mm Hg (UKPDS,1998).

According to antihypertension patterns in type 2 diabetes patients, majority of patients 942 (94.4 %) were on various antihypertensive drugs, out of them 872 (87.4 %) were on angiotensin converting enzyme inhibitors (ACEIs)/ angiotensin receptor blockers (ARBs) either alone or in combination with other antihypertensive drugs. ACEIs and ARBs are the agents of choice for diabetes mellitus with hypertension according to the practice guidelines (American Diabetes Association, 2002; Vijan and Hayward, 2003).

Table III. Association between blood pressure target and antihypertension medication pattern in type 2 diabetes patients

Variables	Target $\leq$ 130/80 mmHg	Non target $>$ 130/80mmHg
No Medication Used	114 (19.0%)	21 (4.4%)
ACEIs	122 (20.3%)	62 (13.0%)
CCBs	36 (6.0%)	34 (7.1%)
ACEIs and CCBs	87 (14.5%)	81 (17.0%)
ARBs and CCBs	83 (13.8%)	60 (12.6%)
ACEIs, CCBs and $\beta$ -Blockers	43 (7.2%)	52 (10.9%)
ARBs, CCBs and $\beta$ -Blockers	35 (5.8%)	49 (10.3%)
ACEIs, CCBs, $\beta$ -Blockers and Diuretics	47 (7.8%)	48 (10.1%)
ARBs, CCBs, $\alpha$ -blockers and $\beta$ -Blockers	34 (5.7%)	69 (14.5%)
Total	601 (100%)	476 (100%)

ACEIs = angiotensin-converting enzyme inhibitors,

CCBs = calcium channel blockers,

ARBs = angiotensin II receptor blockers

A number of 184 (18.4 %) were taking ACEIs as monotherapy, 168 (16.8 %) were on combination of ACEIs and CCBs (calcium channel blockers), while 143 (14.3 %) were on combination of ARBs and CCBs. Another 95 (9.5 %) were on combination of ACEIs, CCBs and  $\beta$ -blockers (Table II)

Reducing SBP to less than 130 mm Hg and DBP to less than 80 mm Hg in patients with diabetes has been shown to reduce diabetes-related mortality, microvascular complications, stroke, and all diabetes end points (American Diabetes Association, 2002). As for hypertension control, by performing cross-tabulation between antihypertension medication patterns and blood pressure target in type 2 diabetes patients (Table III) the majority of patients 601 (55.8 %) had achieved BP targets  $\leq$  130/80 mmHg, out of those 122 (20.3 %) were on ACEIs as monotherapy, 87 (14.5 %) were on combination of ACEIs and CCBs, while 476 (44.2 %) had not achieved BP targets (over 130/80 mmHg), out of these 69 (14.5 %) were on combination of ARBs, CCBs,  $\alpha$ -blockers and  $\beta$ -blockers.

Multiple clinical trials have been conducted to compare various antihypertensive agents to placebo or to other active comparators. In The Antihypertensive and

Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), approximately 60 % of participants were controlled to SBP of less than 140 mm Hg (ALLHAT, 2002). In the subgroup of participants with diabetes, the mean SBP ranged from 135 to 137 mmHg across the treatment groups despite the use of 2 medications on average (Whelton *et al.*, 2005). In The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), 53 % of participants reached both their systolic and diastolic blood-pressure targets, but only 32 % of patients with diabetes reached their intensive targets of SBP less than 130 and DBP less than 80 mm Hg (Dahlof *et al.*, 2005).

This study showed that 13.0 % of patients who achieved target were taken triple medication (ACEIs, CCBs, and  $\beta$  Blockers; ARBs, CCBs, and  $\beta$ -blockers). No study has examined the effectiveness of triple drug therapy with a  $\beta$ -blockers, ACEIs or ARBs and CCBs either in patients with or without diabetes. Nevertheless, it is clear from the ALLHAT, ASCOT and UKPDS experiences that the majority of patients with diabetes and high BP will need three or more medications to achieve SBP less than 130 mm Hg (UKPDS, 1998; ALLHAT, 2002, Dahlof *et al.*, 2005).

As clearly stated by recent guidelines most patients with diabetes will require two or more antihypertensive therapies from different classes with complementary mechanisms of action to control their blood pressure. Thiazide diuretics,  $\beta$ -blockers, or CCBs can be added to ACEIs or ARBs treatment to achieve target blood pressure. Combining an ACEIs or an ARBs with a thiazide diuretic may be particularly effective, as such combinations provide additive reductions in BP compared with individual monotherapies, and counteract many of the adverse events that may be associated with the use of high doses of thiazide diuretics (Klauser *et al.*, 1991; Kjeldsen *et al.*, 2005), and abolish any inter racial differences in the response to ACEIs or ARBs monotherapy (Douglas *et al.*, 2003). Certain  $\beta$ -blockers may be preferred as add-on antihypertensive medications for patients with diabetes because of their glycaemic and metabolic effects. Carvedilol, a nonselective  $\beta$ -blockers, has more favorable effects on haemoglobin A1c (HbA1c) levels, insulin sensitivity, total cholesterol levels, and triglyceride levels than metoprolol in patients with type 2 diabetes mellitus and hypertension already receiving an ACEIs or ARBs despite similar effects on blood pressure (Bakris *et al.*, 2004).

Some studies showed that only a very small percentage of patients were optimally managed (Burt *et al.*, 1991; Hyman and Pavlik, 2001). Different results were observed in our study in which the target BP was not achieved in the 476 (44.2 %) of patients with type 2 diabetes mellitus and hypertension.

The poor control of hypertension may result from the inadequate use of antihypertensive agents, may be come from age, and duration of hypertension. Although in most of the antihypertensive intervention studies two, three or even more drugs of antihypertensive classes were used, the necessary target values were not reached in the majority of studies.

There were several limitations to this study. The control of BP may be affected by the patients' adherence, life style and other risk factors, and this study analyzed was based on a clinical population, thus data from other centers are required to determine whether the finding in this study can be generalized to diabetes care setting.

## Conclusion

Hypertension is extremely common in patients with type 2 diabetes. The highest percentage of patients had hypertension treated with combined antihypertensive drug therapy. A number of patients was not achieved blood pressure goals of  $\leq 130/80$  mm Hg. There is an urgent need to educate both patients and health care providers of importance of achieving target of blood pressure treatment in order to reduce morbidity and mortality in diabetes mellitus patients.

## Acknowledgments

We would like to take this opportunity to express our gratitude to Institute of Postgraduate Studies (IPS) Universiti Sains Malaysia which support this study through fellowship programmed.

## Reference

- ALLHAT Collaborative Research Group, 2002, Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker versus diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA*, 288, 2981–2997.
- American Diabetes Association, 2002, Standards of medical care for patients with diabetes mellitus, *Diabetes Care*, 25, 213
- Amos, A. F., McCarty, D. J., and Zimmet, P., 1997, The rising global burden of diabetes and its complications: estimates and projections to the year 2010, *Diab. Med.*, 14 (Suppl. 5), S81–85.

- Arauz-Pacheco, C., Parrott, M.A., and Raskin, P., 2003, American Diabetes Association. Treatment of hypertension in adults with diabetes, *Diabetes Care*, 26, Suppl 1, S80-82
- Bakris, G. L., Fonseca, V., and Katholi, R. E., 2004, Metabolic effects of carvedilol vs metoprolol in patients with type 2 diabetes mellitus and hypertension: a randomized controlled trial, *JAMA*, 292, 2227–2236.
- Burt, V. L., Cutler, J. A., Higgins, M., Horan. M. J., Labarthe, D., and Whelton, P., 1995, Trends in the prevalence, awareness, treatment and control of hypertension in the adult US population: data from the Health Examination Survey, 1960-1991, *Hypertension*, 155, 1855-1860.
- Dahlof, B., Sever, P. S., and Poulter, N. R., 2005, Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial- Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial, *Lancet*, 366, 895–906.
- Douglas, J. G., Bakris, G. L., and Epstein, M., 2003, Management of high blood pressure in African Americans: consensus statement of the Hypertension in African Americans Working Group of the International Society on Hypertension in Blacks, *Arch. Intern. Med.*, 163, 525–541.
- Grossman, E., and Messerli, F.H., 1996, Diabetic and hypertensive heart disease, *Ann Intern Med*, 125, 304–310.
- Grossman, E., Messerli, F. H., and Goldbourt, U., 2000, High blood pressure and diabetes mellitus: are all antihypertensive drugs created equal?, *Arch. Intern. Med.*, 160, 2447–2452
- Hyman, D. J., and Pavlik, V. N. , 2001, Characteristics of patients with uncontrolled hypertension in the United States, *N. Eng. J. Med.*, 345, 479-486.
- Klauser, R., Prager, R., and Gaube, S., 1991, Metabolic effects of isradipine versus hydrochlorothiazide in diabetes mellitus, *Hypertension*, 17, 15–21.
- Kjeldsen, S. E., Os, I., and Hoieggen, A., 2005, Fixed-dose combinations in the management of hypertension: defining the place of angiotensin receptor antagonists and hydrochlorothiazide, *Am. J. Cardiovasc. Drugs*, 5, 17–22.
- Ministry of Health of Malaysia, 2002, Clinical practice guidelines on the management of hypertension 2002
- Rosenbloom, A. L., Joe, J. R., Young, R. S., and Winter, W. E., 1999, Emerging epidemic of type 2 diabetes in youth, *Diabetes Care*, 22, 345–354.
- Schrier, R. W., Estacio, R. O., and Esler, A., 2002, Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes, *Kidney Int.*, 61, 1086-1097.
- UKPDS Study Group, 1998, Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group, *Br. Med. J.*, 317, 703–713.
- Vijan, S., and Hayward, R. A., 2003, Treatment of hypertension in type 2 diabetes mellitus: blood pressure goals, choice of agents, and setting priorities in diabetes care, *Ann. Intern. Med.*, 138, 593-602
- Whelton, P. K., Barzilay, J., and Cushman, W. C., 2005, Clinical outcomes in antihypertensive treatment of type 2 diabetes, impaired fasting glucose concentration, and normoglycemia: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), *Arch. Intern. Med.*, 165, 1401–1409.

World Health Organization, 1999, International Society of Hypertension guidelines for the management of hypertension, *J. Hypertens.*, 17, 151-183.

Zimmet, P. Z., 1995, The pathogenesis and prevention of diabetes in adults: Genes, autoimmunity, and demography, *Diabetes Care*, 18, 1050-1064.

---

<sup>\*)</sup> Correspondent: Fita Rahmawati

Address: Faculty of Pharmacy, Gadjah Mada University

Email: malihahanun@yahoo.com