

## Control of hypertension in Nigerians with Diabetes Mellitus: A report of the Ibadan Diabetic / Kidney Disease Study Group.

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### Abstract

The prevalence of high blood pressure (BP) is high among Nigerians with diabetes mellitus. This study of Nigerian patients with diabetes examines the adequacy of BP control and antihypertensive therapy as a baseline for establishing conformity with current guidelines. A total of 256 patients with diabetes, aged between 21 and 83 years (mean  $59.1 \pm 12.8$  years) attending the Diabetes/Endocrine Clinic of the University College Hospital Ibadan, Nigeria were involved in the study. Fifty seven per cent had co-existing hypertension and 15.5% of these patients were not receiving any antihypertensive agent. There was a significantly higher systolic BP among females compared to males ( $p < 0.05$ ). Diabetic patients with hypertension were significantly older than those with diabetes alone ( $p < 0.001$ ). The body mass index (BMI) was higher than 25 in 66% of patients with both diabetes and hypertension compared to 48% in those with diabetes alone ( $p < 0.005$ ). A satisfactory mean systolic ( $<130$  mmHg) and diastolic BP ( $<80$  mmHg) BP was obtained in only 38.5% and 42.2% of all patients respectively. The association between BMI and blood pressure was found to be significant only for the diastolic pressure ( $p < 0.05$ ). Only 52% of the patients with hypertension were receiving angiotensin converting enzyme inhibitors as part of their treatment. The high prevalence and poor control of high BP among Nigerians with diabetes pose an increased risk of future development of nephropathy. There is need for a more intense awareness programme for doctors in developing countries regarding current blood pressure management guidelines and the need for adhering to them.

**Key words:** Hypertension, Nigerians, Diabetes Mellitus

### Introduction

Hypertension is commonly associated with diabetes mellitus (DM). Its presence may antedate the onset of DM by many years or it may develop several years after the onset. Its pathogenesis also differs in type 1 and type 2 DM. A rising blood pressure is usually accompanied by the onset and progression of renal disease in type 1 DM, whereas in type 2 disease, elevated blood pressure is often present as at the time of, or shortly after, the diagnosis.

Several risk factors for the development and progression of renal disease in diabetes have been identified. Notable among these factors are hypertension, poor glycaemic control and albuminuria. These three conditions tend to have an anomalous relationship, poor glycaemic control being a predictor of microalbuminuria or incipient nephropathy, while the co-existence of nephropathy with hypertension presents a faster rate of renal function decline.<sup>1</sup> An aggressive treatment and control of hypertension in patients with diabetes is therefore highly desirable in

preventing or slowing down the progression of renal disease.

Recently, new guidelines for the treatment of hypertension in patients with diabetes have recommended the use of angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) either singly or in combination with other drugs depending on the blood pressure.<sup>2-5</sup> Several studies in particular have documented the benefit of the use of ACE inhibitors in preventing or treating microalbuminuria (and thus preventing the progression of renal disease), as well as in overt renal disease.<sup>6-8</sup>

However, it has been observed that antihypertensive drug compliance as well as optimal BP control are often unsatisfactory in developing countries,<sup>9-10</sup> often due to financial constraints. The high cost of these newer and beneficial drugs in developing countries like Nigeria makes compliance poor so that their reno-protective benefits are missed.

This preliminary study evaluates the magnitude of the problem of inadequate blood pressure control as a contributory risk factor for progressive renal disease in Nigerian patients with diabetes.

### Materials and methods

Two hundred and fifty six (256) patients with diabetes

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**Table 1:** Characteristics of patients studied

	All patients	Diabetes alone	Diabetes and hypertension	p value
Number (%)	256	148 (57.8%)	108 (42.2%)	
Male/Female	110/146	59/89	51/57	0.21
Mean Age (yrs)	55.4 ± 11.9	51.9 ± 13.5	57.8 ± 10.0	0.00
Mean Duration (yrs)	9.1 ± 7.5	8.1 ± 6.3	9.68 ± 8.1	0.91
Mean BMI (kg/m <sup>2</sup> )	26.5 ± 5.9	24.9 ± 5.1	27.5 ± 6.2	0.01
Mean Systolic BP (mmHg)	138.8 ± 24.0	125.9 ± 18.6	147.6 ± 23.4	0.00
Mean Diastolic BP (mmHg)	83.93 ± 13.8	79.5 ± 14.4	87.0 ± 12.5	0.00

attending the Endocrine Clinic of the University College Hospital, Ibadan were evaluated as part of an on-going study of chronic kidney disease in Nigerian patients with diabetes. Only patients who had been diagnosed and were receiving treatment for diabetes for at least 3 months were included in the study.

Informed consent was obtained from all patients following which a structured questionnaire covering demographic data, duration of disease, co-morbid conditions like hypertension, asthma and liver disease, the mode of treatment of diabetes and the compliance both with clinic attendance and therapy, was administered to each patient.

Each patient was physically examined, recording the anthropometric parameters of height and weight and calculating the body mass index (BMI) as weight (kg)/height (m<sup>2</sup>). A BMI value of 25 was taken as the cut-off point for the normal range while values above 25 and up to 30 were regarded as overweight and values above 30 classified as obese.

Blood pressure (BP) was measured in each patient using an Accouson Mercury Sphygmomanometer in the sitting position on two occasions at least 15 minutes apart and the average recorded.

Assessment of BP control was based on the American Diabetes Association and KDOQI guidelines for optimal blood pressure treatment goals in patients with diabetes<sup>2, 4</sup> with our patients being classed as follows:

- i. Satisfactory systolic BP: systolic <130mmHg and satisfactory diastolic blood pressure <80mmHg
- ii. Unsatisfactory systolic BP: systolic 130 - 139mmHg and unsatisfactory diastolic blood pressure 80 - 89mmHg
- iii. Poor systolic BP systolic ≥140mmHg and poor diastolic blood pressure ≥ 90mmHg

A record was taken of the antihypertensive drug prescriptions of the patients, allocating these into their respective drug classes.

Patient compliance with medication was obtained from each patient and regarded as poor if patient failed to use at least one of the prescribed antihypertensives for a minimum of five consecutive days within the previous three months. Compliance with clinic attendance was poor if the patient failed to keep clinic appointment at least once in the previous 12 months.

### Statistical analysis

Data were reported as mean ± SD. Mean values from different groups were compared using the students *t*-test of significance for unpaired groups or the ANOVA test of variance for comparison of more than two groups. Association between categorical variables was tested for using the Chi square test of significance. A value of *p* <0.05 was taken as significant.

### Ethical Clearance

Ethical clearance for this study was obtained from the University of Ibadan/UCH Ethical Committee of the Institute of Advanced Medical Research and Training Certificate Number UI/IRC/03/0055 of 2004.

### Results

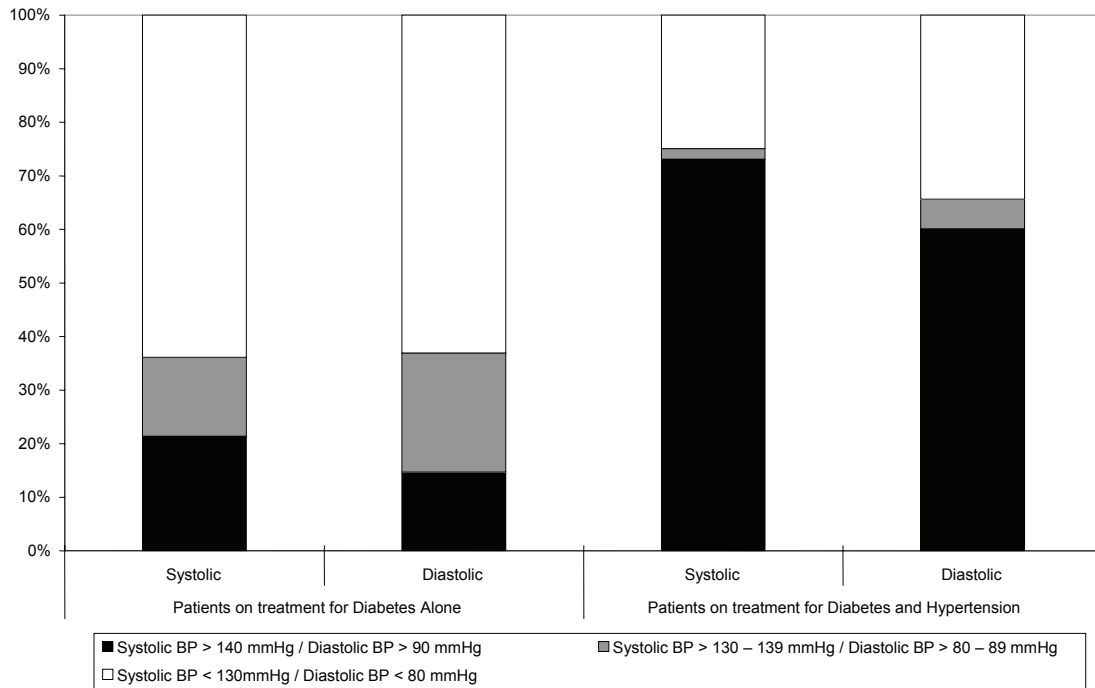
Two hundred and fifty six (256) patients were recruited and studied. Table 1 shows the characteristics of the study population. The age of patients ranged from 21 to 83 years while duration of diabetes mellitus ranged from 4 months to 34 years.

The mean systolic and diastolic BP of the entire study population was unsatisfactory. Female patients had a significantly higher mean systolic pressure than males (142.2 ± 24.0 mmHg and 135.0 ± 22.6 mmHg respectively, *P*<0.05). The difference in mean diastolic pressure of female (84.3 ± 13.2 mmHg) and male (83.1 ± 12.5 mmHg) patients was not statistically significant.

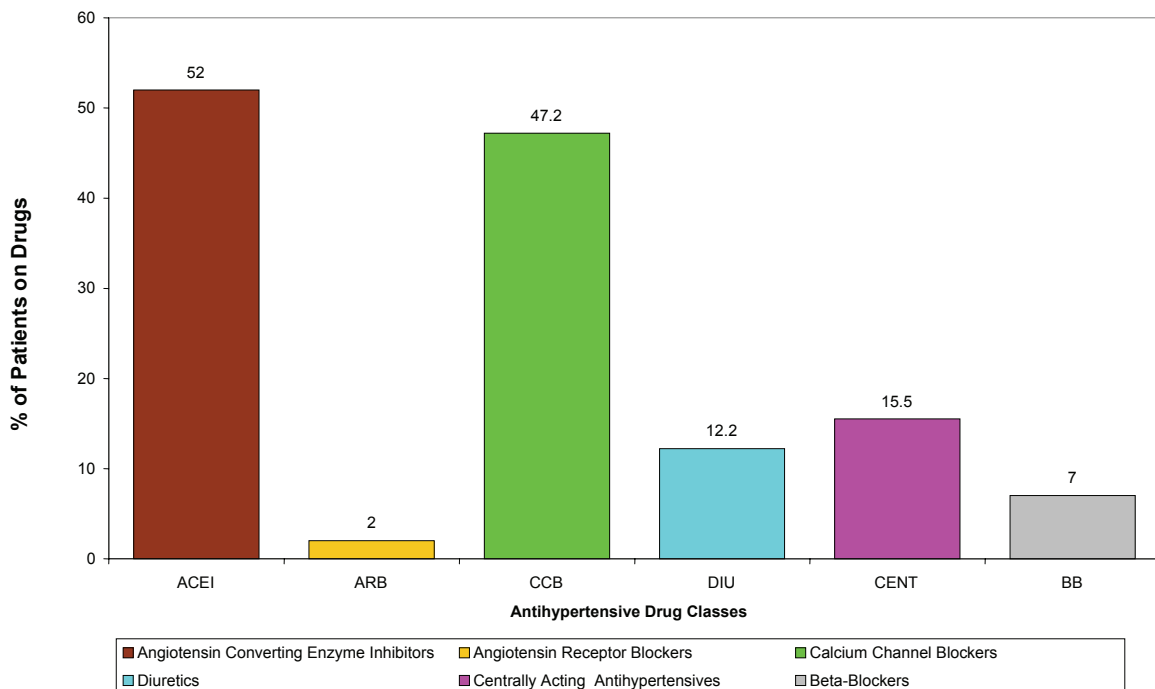
Satisfactory systolic and diastolic blood pressure control was obtained in only 38.5% and 42.2% of the study population, respectively. Figure 1 shows the distribution of patients into blood pressure control groups. For the non-hypertensive diabetics, the mean systolic and diastolic blood pressure of the control groups was 116.1 ± 12.2, 138.0 ± 0.0, 149.1 ± 8.3 mmHg, and 75.0 ± 9.4, 85.0 ± 21.2, 90.1 ± 18.8 mmHg for satisfactory, unsatisfactory and poor BP, respectively. For the hypertensive patients the mean for the groups

**Table 2:** Frequency of drug combination therapy in treatment of hypertension

Number of different drug classes	N (%)
0	23 (15.5)
1	59 (39.9)
2	58 (39.2)
3	8 (5.4)



**Figure 1:** Blood pressure control groups showing satisfactory BP, systolic BP < 130 mmHg/diastolic BP < 80 mmHg (empty); unsatisfactory BP, systolic BP  $\geq$  130 – 139 mmHg/diastolic BP  $\geq$  80 – 89 mmHg (grey); and poor, systolic BP > 140 mmHg/diastolic BP > 90 mmHg (black)



**Figure 2:** Shows the pattern of antihypertensive drugs prescription in percentages. ACEI: Angiotensin Converting Enzyme Inhibitors, ARB: Angiotensin Receptor Blockers, CCB: Calcium Channel Blocker, DIU: Diuretics, CENTRAL: Central Acting Drugs, BB: Beta Blocker.

were  $122.4 \pm 9.3$ ,  $135.0 \pm 1.0$ ,  $159.4 \pm 18.4$  mmHg and  $79.2 \pm 10.0$ ,  $86.7 \pm 15.3$ ,  $90.4 \pm 11.9$  mmHg. Among the hypertensive diabetic patients, the systolic BP was higher than 130 mmHg and diastolic blood pressure was higher than 80 mmHg in 28.8% and 28.9%, respectively.

There was significant association between inadequate systolic blood pressure control ( $BP \geq 130$  mmHg) with age greater than 50 years ( $p=0.00$ ),  $BMI > 30$  ( $p=0.02$ ) but not with duration of diabetes. Inadequate diastolic pressure was only associated with age over 50 years ( $p=0.04$ ).

Figure 2 shows the antihypertensive drug classes prescribed for patients with hypertension while Table 2 shows the frequency of drug combination therapy. The ACE inhibitor class of antihypertensives was the most frequently prescribed. Eighteen (17.3%) of the non-hypertensive diabetics were on ACE inhibition therapy. The majority of patients claimed good compliance with medication as well as clinic attendance (87.9% and 89.1%, respectively).

### Discussion

Hypertension is a common accompaniment of diabetes mellitus (DM). Studies have shown hypertension to be a definite risk factor towards the development as well as progression of nephropathy and cardiovascular disease in diabetics. Recent guidelines have recommended a target blood pressure (BP) level below 130/80mmHg to reduce these risks in patients with diabetes<sup>11, 12</sup>. Desirable as this goal may be, certain obstacles to its attainment are envisaged in developing countries. These include financial incapability to purchase or the unavailability of the recommended drugs (especially the renoprotective ACEIs and ARBs, which are regarded as 'preferred drugs' in this condition), poor compliance with treatment and clinic check-ups, and ignorance of new guidelines on the part of many primary care physicians.<sup>9</sup>

Inadequate BP control in the majority of a group of patients with DM was reported in a recent study carried out in Nigeria in which only 11% of diabetic patients with hypertension had their BP controlled to levels below 140/90mmHg.<sup>10</sup> In our study, a similar observation was made with approximately 12% of our patients achieving BP control below the currently recommended target level of 130/80 mmHg.

In a different study of BP control among hypertensive patients in a tertiary health care setting in Nigeria, a normal blood pressure control incidence of approximately 43% was reported using a blood pressure cut-off value of 140/90 mmHg.<sup>9</sup> Several other studies in more economically advanced environments showed that achieving the target blood pressure goal is often difficult<sup>13, 14</sup>, as only a minority of the patients studied had their BP controlled below the recommended target.

Multiple drug therapy is often required to achieve this satisfactory BP control in patients with diabetes.<sup>7, 8, 15</sup> In fact it has been suggested that a combination of at least three

drugs are required in patients whose systolic BP is about 25-30 mmHg above the target goal.<sup>16, 17</sup> The majority of our patients were treated for hypertension with either one or two drugs (Table 2). Considering the poor BP control rate among our patients, it becomes necessary to stress the need for multiple drug therapy with at least three different classes of antihypertensives for hypertensive diabetic patients optimally controlled. This point needs to be specifically emphasized to the attending doctors.

Various antihypertensive drugs were found to be in use in our diabetic clinic in the management of hypertension. It was, however, observed that the use of ACE inhibitors was the highest among all of the prescribed antihypertensive drugs. We expect, however, a higher rate of their prescription as current guidelines have classified them as drugs with compelling indications in people with DM with or without hypertension, or in chronic kidney disease.<sup>16, 17</sup> Cost constraints, however, represent a possible major reason for the limitation in the prescription of these drugs in this country. The occurrence of side effects, in particular ACE inhibitor-related cough is a less prominent reason for these drugs not being used. Nevertheless, educational programmes specifically addressing adherence to guidelines as advocated by previous authors<sup>7, 18</sup> on the merit of ACE inhibitor and ARB drug prescription for patients with diabetes should be organised for medical personnel involved in the treatment of these patients.

The use of diuretics is often avoided in the treatment of hypertension in patients with diabetes due to their potential diabetogenic effect. This may be responsible for the low rate of their use as reported in this study (Fig. 2). Several guidelines and reports on the drug treatment of hypertension in diabetes recommended the inclusion of a diuretic (especially thiazide) in the multiple drug therapy required for intensive BP control.<sup>2, 7</sup> We are of the opinion, therefore, that disturbance of glucose control should not justify the exclusion of diuretics from the therapy of our patients. In fact, a previous study in Nigeria<sup>10</sup> demonstrated an association between thiazide use and better control of BP in a group of hypertensive patients with DM. The study also highlighted the cost-effectiveness of including a thiazide in the combination therapy, an important and relevant factor in a developing economy.

Another important observation from this study is that many of the patients classified as hypertensive were not on any antihypertensive treatment (15.5%, Table 2). Similarly, a number of the patients classified as being diabetic alone actually have blood pressures well above the recommended optimal level for patients with diabetes (Figure 2). Our concern is that these patients represent an important group of patients at increased risk of renal function deterioration should they develop nephropathy.

In summary, this study shows that there exists both a high prevalence and poor control of elevated BP in Nigerians with diabetes, with many patients remaining untreated even in a tertiary health care setting. The use of ACE inhibitors

and angiotensin receptor blockers remain inadequate, despite the strong recommendation for their increased use in most current guidelines. These observations necessitate the need for more emphasis on intensive BP control through educational programmes for the medical personnel and primary care physicians involved in the care of patients with diabetes in order to reduce or prevent the trend towards end stage renal failure.

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