THE PREVALENCE AND CONTROL OF HYPERTENSION AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS IN NIGERIA

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SUMMARY

Background:
Diabetes Mellitus (DM) is an endocrine disease with profound vascular morbidity and mortality, and hypertension is known to play a prominent role in this regard. The aim of this study is to determine the prevalence of hypertension and to assess drug control of hypertension among DM patients seen in Enugu, Nigeria.

Methods:
The medical records of 420 adult patients with diagnosis of type 2 DM and hypertension, managed consecutively in the outpatient unit of University of Nigeria Teaching Hospital Enugu were studied.

Results:
Sixty percent of the diabetic patients had hypertension. Only 12% of these patients had their blood pressure controlled to ≤ 130mmHg and ≤ 80mmHg. About 12.3% of the patients who had hypertension were not on anti hypertensive drug treatment. Most of the patients were placed on 1 or 2 drugs. Angiotensin converting enzyme inhibitors were the most frequently prescribed drug.

Conclusion:
This study and similar ones from other parts of Nigeria indicate that the prevalence of hypertension among Nigerians with type 2 DM is high. Clinicians and patients should be reminded that even though blood glucose control is important, aggressive blood pressure control in diabetics is top priority in preventing adverse cardiovascular events which causes the highest mortality in the average population of type 2 diabetics. Appropriate antihypertensive regimen optimizes nonpharmacological therapies, reduces adverse effects on glucose control, minimizes the risk of medication-related side-effects, and provides much needed cardiac and renal protection.

Key words: Hypertension, Prevalence, Diabetes Mellitus, Drug control, Nigerians
INTRODUCTION

Diabetes mellitus (DM) is an endocrine disease, defined by high blood glucose levels, but with a prominent vascular component. The major cause of death in treated diabetic patients is due to cardiovascular problems (70%), followed by renal failure (10%), and infections (6%). The underlying vascular component is so significant that the complications of diabetes mellitus are usually divided according to macrovascular (coronary artery disease, cerebrovascular disease, peripheral vascular disease) and microvascular events (retinopathy, nephropathy, neuropathy).

One of the extremely common cardiovascular risk factors in patients with type 2 diabetes is hypertension. Hypertension may precede diabetes mellitus, be diagnosed at same time as diabetes or may be as a result of diabetic nephropathy. Whenever it occurs, it is the greatest contributor to increased morbidity and mortality in macro-vascular and microvascular events in type 2 DM.

Macro-vascular complications are more common; up to 80% of patients with type 2 diabetes will develop or die of macrovascular disease and the costs associated with macro-vascular disease are greater than those associated with micro-vascular disease. However, while some observational evidence suggests that the level of glycemia is a risk factor for macrovascular disease, experimental studies to date have not clearly shown a causal relationship between improved glycemic control and reductions in serious cardiovascular outcomes.

Hypertension is one of the highly prevalent risk factors for macro-vascular events affecting up to 60% of patients with type 2 DM. Hypertension is known to increase morbidity and mortality among patients with diabetes mellitus. The control of hypertension is dramatically effective in reducing risk for cardiovascular events and mortality and does so within a 4- to 6-year period.

Glucose control is clearly effective only in reducing microvascular end points, but to date only intermediate outcomes have been shown to be reduced. The UKPD study demonstrated that intensive hypertension control is more effective than intensive glycemic control in reducing macro-vascular and micro-vascular events as well as all cause mortality. The benefits of intensive hypertension control (diastolic blood pressure, 87 mm Hg vs. 82 mm Hg) dramatically outweighed those of intensive glucose control (mean hemoglobin A1c level, 7.9% vs. 7.0%), with substantially greater (by two- to fivefold) absolute risk reductions for all published outcomes.

It is not just the UKPD but also the Hypertension Optimal Treatment (HOT) Trial, has demonstrated that cardiovascular mortality and total mortality were reduced by 43% when blood pressure is reduced to <130/80mmHg in diabetic patients with hypertension.

The interruption of the rennin-angiotensin-system (RAS) is considered to be the cornerstone of pharmacologic therapy to reduce macrovascular and microvascular complications in hypertensive type 2 DM patients, mediated by antihypertensive, anti-
inflammatory, antiproliferative, and oxidative stress lowering properties.\textsuperscript{27}

There is evidence, that ACE inhibitors, angiotensin-receptor blockers and diuretics, may be superior to \(\beta\)-blockers and calcium-channel blockers and the latter are probably best used as second- or third-line treatments for hypertension in diabetes \textsuperscript{28-31}

Other antihypertensive drugs may have a role in achieving desired blood pressure targets in patients with type 2 diabetes. However, there is little information on the effectiveness of these drugs in reducing micro-vascular and macro-vascular outcomes.

Previous studies have noted that the antihypertensive drug compliance as well as optimal blood pressure control in diabetic patients is poor and sub optimal in sub Saharan countries, including Nigeria.\textsuperscript{32}

There are few reports of hypertension and its control among DM patients from south western(Ibadan and Benin city), central (Ilorin) \textsuperscript{34}and north eastern belts of Nigeria, \textsuperscript{35}but non from the south east. The aim of this study is to determine the prevalence of hypertension and to assess anti hypertensive drug control among DM patients seen in Enugu, south east, Nigeria.

**METHODOLOGY**

The medical records of 420 adult patients of both sexes (253 females, 167 males) aged between 23 and 81 years with diagnosis of type 2 DM who were seen consecutively in the outpatient unit of University of Nigeria Teaching Hospital Enugu from January 2009 were studied. The first 420 patients that satisfied the inclusion criteria-adult patients of both sexes, with diabetes mellitus type 2, whose blood pressure was > 140/90mmHg or on antihypertensive drugs, were selected.

The anthropometric data- age, sex, weight, height, fasting blood sugar, blood pressure of the patients were documented.

Diagnosis of diabetes mellitus was made using a fasting blood sugar of 7.0 mmol/liter (126mg/dl) according to the World Health Organization guidelines.\textsuperscript{35}

The last clinic blood pressure was recorded, observing the usual standard by taking measurements 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 guidelines\textsuperscript{36} for optimal BP control in patients with diabetes. The Accousson’s mercury sphygmomanometer was used. Hypoglycaemic and antihypertensive drugs given in the last visit were recorded and classified.

**RESULTS**

Out of 420 DM patients studied, those with a combination of diabetes and hypertension were significantly more than those with diabetes only (\(p<0.001\)). There were also more females than males. The diabetic hypertensives were also significantly older than the non diabetic patients ( \(p<0.001\) ) (table 1).

Sixty percent of the diabetic patients had hypertension with systolic and diastolic blood pressures > 140/90mmHg with mean systolic and diastolic blood pressures of
152.6mmHg ±22.2 and 96.6mmHg±9.9 respectively. The blood pressure control pattern is shown in figure 1.

Only 18.3% (46) and 21% (53) of these patients had their mean systolic and diastolic blood pressure controlled to ≤ 130mmHg and ≤ 80mmHg respectively. Altogether 12% (51) DM patients had their blood pressure controlled to below 130/80mmHg. About12.3% (31) of the patients who had blood pressure of more than 135/85mmHg±9.2 were not on anti hypertensive drug treatment.

Forty percent of all the diabetic patients had normal blood pressure with mean systolic and diastolic blood pressures of 123.4mmHg ±3.4 and 72.4mmHg ±10.6 respectively.

The frequency of antihypertensive drugs is shown in table 2. Most patients were on 1 and 2 drugs (63%) and only very few (about 20%) were on 3 and 4 drugs.

<table>
<thead>
<tr>
<th>TABLE 1 : Characteristics of Patients Studied</th>
</tr>
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<tbody>
<tr>
<td></td>
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<tr>
<td>No studied</td>
</tr>
<tr>
<td>Mean Age(yrs)</td>
</tr>
<tr>
<td>M/F</td>
</tr>
<tr>
<td>Mean Dur(yrs)</td>
</tr>
<tr>
<td>Mean BMI(kg/m²)</td>
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<tr>
<td>Mean SBP(mmHg)</td>
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<tr>
<td>Mean DBP(mmHg)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>All Patients</th>
<th>Diabetes Only</th>
<th>Diabetic hypertensive</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>420</td>
<td>176 (42%)</td>
<td>244(58%)</td>
<td>0.001</td>
</tr>
<tr>
<td>59.9±10.2</td>
<td>52.6±9.5</td>
<td>57.9±12.7</td>
<td>0.001</td>
</tr>
<tr>
<td>167/253</td>
<td>70/98</td>
<td>97/155</td>
<td>0.24</td>
</tr>
<tr>
<td>8.2±6.2</td>
<td>8.6±8.7</td>
<td>9.1±5.8</td>
<td>0.68</td>
</tr>
<tr>
<td>27.4±4.5</td>
<td>26.7±5.5</td>
<td>27.9±4.7</td>
<td>0.022</td>
</tr>
<tr>
<td>137.4±11.3</td>
<td>121.5±4.8</td>
<td>152.6±22.2</td>
<td>0.00</td>
</tr>
<tr>
<td>84.4±10.6</td>
<td>73.4±10.4</td>
<td>96.6±9.9</td>
<td>0.00</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 2 : Frequency of antihypertensive drug combination in diabetic patients studied</th>
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<tbody>
<tr>
<td>Number of different drug classes</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>
The classes and pattern of antihypertensive pharmacotherapy are depicted in figure 2. Angiotensin converting enzyme inhibitors was the most frequently prescribed drug for the hypertensive diabetics (64%). Angiotensin receptor blocker was prescribed in only 12% of hypertensive diabetics. Diuretics, calcium channel blockers and central acting agents were prescribed in 35%, 17% and 8% of hypertensive diabetics respectively. No beta blockers were given. Angiotensin converting enzyme inhibitors and angiotensin receptor blockers were also prescribed in 15% of diabetics who had normal blood pressure for renal protective effects.

The study showed that the average prescribed dose of Angiotensin converting enzyme inhibitors (ACEI) and Angiotensin receptor blockers (ARB) were on the low side of recommended dose. The percentage of hypertensive diabetics that achieved the median recommended doses of ACEI/ARB were very low, ranging from 12 to 20%. (table 3)

<table>
<thead>
<tr>
<th>ACEI/ARB drugs</th>
<th>Recommended dose range in mg(median dose in mg)</th>
<th>Average Prescribed dose in mg</th>
<th>% of study patients achieving the median dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lisinopril</td>
<td>10-40(25)</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>Enalapril</td>
<td>5-40(22.5)</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Ramipril</td>
<td>5-20(12.5)</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Valsartan</td>
<td>80-320(200)</td>
<td>160</td>
<td>18</td>
</tr>
<tr>
<td>Losartan</td>
<td>50-100(75)</td>
<td>50</td>
<td>16</td>
</tr>
</tbody>
</table>
DISCUSSION
Hypertension is a major cardiovascular disease risk factor and when present in diabetic patients increases the cardiovascular disease burden substantially. It has been documented that hypertension in diabetic patients markedly increases the risks of coronary heart disease, stroke, nephropathy and retinopathy.\textsuperscript{37,38,39} Indeed, when hypertension coexists with diabetes, the risk of CVD is increased by 75\%\textsuperscript{37,40} Reports of prevalence of hypertension in diabetic patients help to assess the added risks it poses in management. It also exposes the weaknesses and shows the vigour in implementing already recommended guidelines.

The prevalence of hypertension among diabetics in this study, done in Enugu, south eastern Nigeria (60\%) is comparable to that obtained in Ibadan, south western Nigeria (57\%)\textsuperscript{32} and Benin city (59\%)\textsuperscript{33} ,Ilorin (63\%)\textsuperscript{34} and Sweden (56\%),\textsuperscript{41} but understandably lower than that of United kingdom(73\%)\textsuperscript{3} and USA (77\%)\textsuperscript{2} were diet, physical inactivity and obesity have combined to place hypertension and diabetes as competing risk factors of cardiovascular disease in these two countries. The Swedish and American studies were nationwide surveys. Our study and that from Ibadan were hospital based and we await a nation-wide survey to provide the true prevalence of diabetes in Nigeria.

Diabetic patients in Cameroon exhibit a very high prevalence of hypertension (66\%) and are about three times more affected than the general population\textsuperscript{42} A study conducted in Kenya during the year 2005 to determine the proportion of specific cardiovascular risk factors in ambulatory patients with type 2 DM reported that 50\% of the patients had HTN \textsuperscript{43}. The recent EPIDIAM Study conducted in 525 type 2 individuals in three Moroccan regions reported that 70.4\% of the individuals had HTN \textsuperscript{44}.In India about 50\% of diabetic patients have hypertenson\textsuperscript{45}. In a cohort study in China the age- and sex-adjusted prevalence of hypertension among diabetic subjects was twice that of non diabetic subjects (30.6 vs. 16.4\%, \textit{P} < 0.0005).\textsuperscript{46}

Globally, the frequency of diabetic hypertension in diabetic population is almost twice as compared to non-diabetic general population.\textsuperscript{2} Hypertension and diabetes mellitus are really deadly cardiovascular duets. Generally, hypertension in type 2 diabetic persons clusters with other CVD risk factors such as microalbuminuria, central obesity, insulin resistance, dyslipidaemia, hypercoagulation, increased inflammation and left ventricular hypertrophy.\textsuperscript{47} This clustering risk factor in diabetic patients ultimately results in the development of CVD, which is the major cause of premature mortality in patients with type 2 diabetes. In all there is now considerable evidence for an increased prevalence of hypertension in diabetic persons.\textsuperscript{48}

Blood pressure goals in diabetics are lower and thus more difficult to control. Globally, 25\% of hypertensive diabetics achieve control.\textsuperscript{39} The control achieved in this study-(12\%) is comparable to that in Ibadan-Nigeria (12\%)\textsuperscript{32}, Ilorin-Nigeria(11\%)\textsuperscript{34} but lower than that of United Kingdom (<27\%).\textsuperscript{3}Sweden (33.3\%)\textsuperscript{41} and USA (35.5\%).\textsuperscript{3} were there are better care for
patients with cardiovascular risk factors such as hypertension and diabetes mellitus.

The mean systolic and diastolic blood pressure for the hypertensive diabetic patients in our study was high (153/97mmHg). The poor rate of control of hypertension among hypertensive diabetics in this study may be due to inadequate optimization of the antihypertensive agents. The same reason was also adduced for the control in Ibadan and Ilorin studies.

Majority of the antihypertensive prescriptions in this study were 1 or 2 drugs in combination but studies have recommended 3 drugs as required for optimal control of hypertension in diabetics particularly in those whose systolic blood pressure is 25-30mmHg above target goal. In fact the United Kingdom Prospective Diabetic study found out that one-third of patients needed three or more antihypertensive drugs in combination, and two-thirds of treated patients needed two or more for control of blood pressure.

It should be emphasized that blood pressure targets in diabetics should be aggressive. For example, a four point blood pressure difference in the HOT trial (84 to 81mmHg) resulted in a decrease by 50% in cardiovascular events in patients with DM. The study noted that the risk reduction seen with hypertension control in patients with diabetes is substantially greater than that seen in persons in the general population who have similar blood pressure levels.

The ACE inhibitors and particularly the ARB are underutilized in this study (64% and 12% respectively) gave rise to the poor control of hypertension. The Ibadan and Ilorin studies had also recorded ACE inhibitors in only 52% and 44.3% respectively of their prescriptions. The Ibadan study pointed at the high cost of ACE inhibitors/ARB as possible reason for its low patronage. It has been recommended that treating people with diabetes and at least one other major cardiovascular risk factor with an ACE-inhibitor produces a 25-35% lowering of the risk of heart attack, stroke, overt nephropathy or cardiovascular death.

It has been noted that in patients with bilateral renal artery stenosis, ACE inhibitors can cause renal insufficiency. To help detect the presence of undiagnosed bilateral renal artery stenosis, physicians should monitor the serum creatinine level at baseline and one week after initiation of ACE inhibitor therapy.

Diuretics were not used optimally in this study. This finding is in keeping with the Ibadan study. Diuretics are however recommended in the multiple regimen required to control hypertension inspite of their diabetogenic potential. Diuretics, particularly, hydrochlorothiazides when used in low doses, have no significant disturbance on glucose metabolism and are useful in blacks in the control of hypertension.

Thiazide diuretics have been shown to benefit patients with diabetes and systolic hypertension and lower dosages of thiazides (e.g., hydrochlorothiazide 12.5 mg per day) are generally well tolerated and not associated with adverse metabolic effects. Thiazide diuretics are not as effective in patients with renal insufficiency; in such patients, loop diuretics are preferred. In
general, diuretics are effective, affordable and available for the treatment of hypertension in diabetes mellitus.

Calcium channel blockers were prescribed in 17% of the diabetic hypertensive patients studied. Non-dihydropyridine calcium channel blockers were not prescribed in this study and in other studies in Nigeria.

Both the non DHP (diltiazem and verapamil) and the DHP CCBs (amlodipine, felodipine, and others) reduce CVD events in people with diabetes and hypertension.\(^{49,50}\)

NonDHP CCBs significantly reduce albuminuria and may slow the progression of proteinuric renal disease.\(^{51}\) In contrast, DHP CCBs inconsistently reduce albuminuria and are less effective than ACE inhibitors or ARBs in slowing the progression of diabetic nephropathy.\(^{51}\) However, DHP CCBs effectively lower blood pressure and can be safely combined with an ACE inhibitor or ARB to slow the progression of diabetic nephropathy.\(^{51}\) B-blockers were not prescribed in this study unlike in the Ibadan study were it was used in 7% of the patients.\(^{33}\)

Beta blockers worsen hyperglycemia and block adrenergic symptoms. This may produce dangerous hypoglycemia without giving the patient enough time to react by taking food to increase the blood glucose level. It is however useful in post myocardial infarction patients and as an antiarrhythmic agent.

The effectiveness of beta blockers was demonstrated in the UK Prospective Diabetes Study Group, where atenolol was comparable with captopril in reduction of CVD outcomes\(^ {52,53}\). Although these agents have been associated with adverse effects on glucose and lipid profiles and implicated in new onset diabetes in obese patients,\(^ {4}\) they are not absolute contraindication for use in diabetic patients. In fact, carvedilol, which has both alpha and beta receptor blocking properties, has been shown to induce vasodilatation and improve insulin sensitivity\(^ {52}\).

Blood pressure lowering with carvedilol or metoprolol reduces microalbuminuria by 43 and 30%, respectively, when added to ACE inhibitors or ARBs.\(^ {47}\) However, carvedilol is nearly 50% more effective than metoprolol for preventing progression from normoalbuminuria to microalbuminuria.\(^ {54}\)

Central acting drugs were used in only 8% of diabetic hypertensive studied. This drug was not used in any of the centers in Nigeria. This group of drugs are prescribed because they are cheap and affordable.

Our study noted that thirteen percent of the diabetic patients who were hypertensive were not placed on antihypertensives. The reason for this is not clear except that the patients had mild hypertension (135/85mmHg±9.2) and may have been erroneously classified as non hypertensive. These patients are under the threat of renal impairment and other end organ damage.

Our study also showed inertia in the attainment of target doses for the ACEI and ARB was only 12-20% of median doses of ACEI and ARB. It is not clear if the distraction of treating diabetes mellitus and the adverse effects of these drugs contributed to the below target dose prescription of these drugs.
CONCLUSION
It is clear from this study that blood pressure control in hypertensive diabetic patients is unsatisfactory even in a tertiary hospital in Nigeria. The study found out that despite high prevalence of high blood pressure, hypertension was managed less intensively in patients with diabetes. Findings of other tertiary health institutions in Nigeria and other parts of Africa run parallel to that of our study. This is despite the consensus that blood pressure control in diabetic patients has dramatic effects in reducing cardiovascular morbidity and mortality. Clinicians and patients should be reminded that even though blood glucose control is important, aggressive blood pressure control in diabetics is top priority in preventing adverse cardiovascular events which causes the highest mortality in the average population of type 2 diabetics.  

Apart from issues on pharmacotherapy, poor control of hypertension in diabetic patients may be traced to non pharmacological factors which include inadequate recognition of the role of therapeutic lifestyle changes, poverty and proper health education. These non drug measures are obviously not the focus of this study but they can not escape being mentioned here. Availability of generic drugs and health insurance scheme may help to place antihypertensive drugs at the reach of the patients.

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