Impact of Joint National Committee VII Recommendations on Diabetic Microvascular Complications

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Abstract
Aims and Objectives: To determine the impact of the Seventh Report of the Joint National Committee recommendations on microvascular complications in South Indian type 2 diabetic patients.

Material and Methods: In this study, 457 type 2 diabetic patients and 500 age-matched healthy control subjects, with no history of hypertension were enrolled. Based on blood pressure measurements, they were assigned as Group I: Normal (SBP < 120 and DBP < 80 mmHg); Group II: Prehypertension (SBP 120-139 or DBP 80-89 mmHg); Group III: Stage I hypertension (SBP 140-159 or DBP 90-99 mmHg) and Group IV: Stage II hypertension (SBP ≥ 160 or DBP ≥ 100).

Results: Blood pressure readings in controls and diabetics were: normal in 46.8% and 16.2% (χ² = 101.1, p < 0.0001), prehypertension in 33.2% and 52.5% (χ² = 35.7, p < 0.0001), stage I hypertension in 15.2% and 26.3% (χ² = 17.3, p < 0.0001), stage II hypertension in 4.8% and 5% respectively. Prevalence of retinopathy increased with increasing incidence of hypertension (trend χ² = 10.7, p < 0.01). In the multivariate analysis, cholesterol was associated with prehypertension, and cholesterol and family history of hypertension were associated with stage I hypertension. Albuminuria, family history of hypertension and serum triglycerides were associated with stage II hypertension.

Conclusion: More than half of the diabetic subjects were prehypertensives. As expected prevalence of other complications increased with increasing levels of blood pressure. This emphasizes the need to have regular check up for hypertension to reduce the morbidity from other complications.

INTRODUCTION
Hypertension is an extremely common comorbid condition in diabetes, affecting approximately 20-60% of patients with diabetes, depending on obesity, ethnicity and age. Hypertension substantially increases the risk of both macrovascular and microvascular complications, including stroke, coronary artery disease (CAD), and peripheral vascular disease, retinopathy, nephropathy and possibly neuropathy. Epidemiological data have shown a clustering of cardiovascular risk factors in non-diabetic Southern Indians. The United Kingdom Prospective Diabetes Study (UKPDS) reported that the prevalence of hypertension was significantly lower in the Asians than in the White Caucasian and Afro-Caribbean patients. Although the prevalence of stage I and II of hypertension, as defined by the recent Seventh Report of the Joint National Committee (JNC VII) may be lower, the prevalence of the prehypertensive stage may be high in India, especially among the diabetic subjects. In a population study, from Diabetes Research Centre, the age-adjusted prevalence of hypertension was found to be 21.8% in subjects aged ≥ 40 years. The CUPS study also showed that in the South Indian subjects aged ≥ 20 years, the standardized prevalence of hypertension was 17%. Many cases of hypertension remain undiagnosed also. This study was undertaken to determine the impact of JNC VII recommendations on microvascular complications in South Indian type 2 diabetic patients.

MATERIALS AND METHODS
Ethical approval of the study protocol was obtained from the Institution’s ethics committee. Consecutive patients of type 2 diabetes (n=457; M/F: 313/144, Mean age: 53.4 ± 10.6 years) admitted in MV Hospital for Diabetes during a period of 3 months were studied. The selection criteria were type 2 diabetes by the WHO criteria, with availability of all clinical
and laboratory data at the time of study and with no history of hypertension and without previous antihypertensive treatment. Age-matched normoglycaemic control subjects (n=500, M/F: 330:170, Mean age : 53 ± 2.1 years) were selected from a population survey for diabetes, in Chennai. All control subjects also were tested with the standard oral glucose tolerance test (OGTT). The study subjects gave their informed consent for the study.

Based on blood pressure measurements, the recruited subjects were assigned into four different categories. Group 1 : Normal (systolic blood pressure (SBP) < 120 and diastolic blood pressure (DBP) < 80 mmHg); Group 2 : Prehypertension (SBP 120-139 or DBP 80-89 mmHg); Group 3 : Stage I hypertension (SBP 140-159 or DBP 90-99 mmHg) and Group 4 : Stage II hypertension (SBP ≥ 160 or DBP ≥ 100 mmHg). All of them had a detailed clinical examination and blood pressure measurements. Blood pressure was determined at the beginning of the study as the mean of three measurements. Blood urea and creatinine were estimated by immunoturbidimetry. All the above biochemical tests were done using the reagents from Roche Diagnostics, Mannheim, Germany. Blood urea and creatinine were estimated by standard enzymatic procedures. Fasting serum sample was used to estimate total cholesterol and its fractions like high density lipoprotein cholesterol (HDLc), low density lipoprotein cholesterol (LDLc), very low density lipoprotein cholesterol (VLDLc) and triglycerides. Albuminuria (by immunoturbidimetry) and creatinine clearance were estimated in 24-hour urine sample. They were expressed as µg/min and ml/min respectively.

**Biochemical Tests**

Blood samples were collected to determine the biochemical parameters including plasma glucose, urea, creatinine, total cholesterol, triglycerides and glycosylated haemoglobin (HbA1c). HbA1c was quantitatively determined by immunoturbidimetry. All the above biochemical tests were done using the reagents from Roche Diagnostics, Mannheim, Germany. Blood urea and creatinine were estimated by standard enzymatic procedures. Fasting serum sample was used to estimate total cholesterol and its fractions like high density lipoprotein cholesterol (HDLc), low density lipoprotein cholesterol (LDLc), very low density lipoprotein cholesterol (VLDLc) and triglycerides. Albuminuria (by immunoturbidimetry) and creatinine clearance were estimated in 24-hour urine sample. They were expressed as µg/min and ml/min respectively.

**Statistical analysis**

Data with normal distribution were expressed as mean ± SD. Comparison of the group means was performed by unpaired Student’s ‘t’ test. Intergroup comparisons were made by one - way ANOVA (HSD procedure). Chi square test was used wherever relevant. Trend chi - square test was done to compare the proportions between the groups. Multiple logistic regression analysis with stepwise addition of independent variables was done to find out the parameters associated with each stage of hypertension. The odds ratio (OR) was estimated as the exponential of b (i.e. OR = exp(β)), which was the regression coefficient obtained using the maximum likelihood calculation. P values less than 0.05 were considered as statistically significant. All the tests were performed using SPSS package, version 4.0.1.

**RESULTS**

Blood pressure categories in the control and diabetic subjects are shown in Table 1. Diabetic subjects had higher prevalence of prehypertension (52.5% vs 33.2%, χ² = 35.7, p < 0.0001), and stage I hypertension (26.3% vs 15.2%, χ² = 17.3, p < 0.0001) compared with the controls. Stage I and stage II hypertensive diabetic patients were significantly older when compared with respective non-diabetic hypertensives (age 54.4 ± 10.9 vs 53.3 ± 2.1 yrs, p = 0.02 and 57.9 ± 10.6 vs 53.3 ± 1.8 yrs, p < 0.0001). BMI was significantly higher in prehypertensive diabetic patients (25.5 ± 4.2 kg/m²) than in control subjects (24.5 ± 4.0 kg/m²) (p < 0.001).

Table 2 shows the comparison of clinical, biochemical and haemodynamic variables of diabetic patients in four different blood pressure categories. There was no significant difference in the sex, mean age and duration of diabetes among the four groups of patients. Mean BMI was significantly higher in all hypertensive groups compared with Group I (p < 0.05). Group IV patients had a higher level of creatinine and lower range of creatinine clearance (p < 0.05) in comparison with Group II and III. Total cholesterol level was significantly higher in Group II and III vs Group I (p < 0.05). A statistically significant trend was noted in the prevalence of normoalbuminuria, albuminuria (trend χ² = 15.6, p < 0.0001) and diabetic retinopathy (trend χ² = 10.7, p < 0.01) among the four groups of patients.

A sub-analysis was done in the diabetic patients to evaluate the profile of newly detected hypertension in normoalbuminuric (n=309, AER < 30 µg/min) and albuminuric (n=148, AER ≥ 30 µg/min) patients. Among the normoalbuminuric patients, blood pressure readings were normal in 51 (16.5%), prehypertension in 181 (58.6%), stage I hypertension in 71 (23%) and stage II hypertension in 6 (1.9%) whereas in albuminuric patients, 23 (15.5%) with normal, 59 (39.9%) with prehypertension, 49 (33%) with stage I hypertension and 17 (11.5%) with stage II hypertension were noted. The prevalence of stage I and stage II hypertension were significantly higher in albuminuric vs normoalbuminuric (χ² = 4.8, p = 0.03 for stage I), (χ² = 17.1, p = 0.00004 for stage II), while in the normoalbuminuric group the prehypertension alone showed a significantly higher prevalence (χ² = 13.3 p = 0.0002).

Table 3 shows the significant associations of risk factors
with each hypertensive stages, evaluated by multiple logistic regression analyses. Cholesterol had a significant association with prehypertension (OR = 1.007, p = 0.02). Cholesterol (OR = 1.01, p = 0.006) and family history of hypertension (OR = 2.85, p = 0.02) were significantly associated with stage I hypertension. The risk factors associated with stage II hypertension were in the order of albuminuria (OR = 8.08, p = 0.003), family history of hypertension (OR = 5.04, p = 0.03) and triglycerides (OR = 1.007, p = 0.01). The strongest associated was between stage II hypertension and albuminuria.

**DISCUSSION**

In this study we have investigated the profile of newly detected hypertension and the risk variables associated with patients with increasing incidence of hypertension. The study population showed a higher prevalence of prehypertension among the diabetic patients in comparison with non-diabetic subjects. The JNC VII Report advocates that patients with prehypertension are at increased risk for progression to hypertension. Moreover, recent data from the Framingham Heart Study has reported that those in the 130/80 to 139/89 mmHg blood pressure range are at twice the risk to develop hypertension as those with lower values. The prevalence of hypertension in the diabetic population is 1.5 - 3 times higher than that of non-diabetic age-matched groups. Several confounding factors are present in diabetic patients that makes the assessment of the prevalence of hypertension attributable to diabetes difficult.

As expected, an increasing trend was noted in the prevalence of diabetic retinopathy with increasing incidence of hypertension. This finding was relevant since extensive epidemiological evidence indicated that diabetic individuals with hypertension had increased risk of diabetic retinopathy. In Pima Indians, blood pressure levels above 130/85 mmHg were associated with more severe progression of exudative retinopathy than in those having blood pressure less than 120/70 mmHg. In a recent study from South India, Ramachandran et al, showed that hypertension is a strong risk factor for diabetic retinopathy. Hypertension accelerates the progression of diabetic nephropathy in type 1 and type 2 diabetic patients. In a study by Lewis et al., it was shown that antihypertensive treatment with captopril reduced the doubling time of serum creatinine by 48% and reduced by 50% the combined end-points of death, dialysis and renal transplantation.

The sub-analysis from the total diabetic population based on albuminuric status revealed that the prevalence of stage I and stage II hypertension increased with increased urinary albumin excretion compared with normoalbuminuric group. This was in confirmation of our earlier report showing that prevalence of hypertension increased proportionally with increasing albumin excretion in type 2 diabetic patients. We
also found that the coexisting hypertension increased the risk of complications in the proteinuric group.

In our study, cholesterol showed an independent association with prehypertension and stage I hypertension, while family history of hypertension also contributed to the latter group. Albuminuria was found to be strongly and independently associated with stage II hypertension followed by family history of hypertension and serum triglycerides. Similar observations were reported in studies in other populations. Mogensen et al, in a cross-sectional study had reported that increased albumin excretion rate was associated with increase in blood pressure. In the San Antonio Heart Study, diabetes, hypercholesterolemia and hypertriglyceridemia showed association with hypertension.

We also noted a high prevalence of stage I and stage II hypertensive diabetic patients with increased age in comparison with non-diabetics. In a meta-analysis, it was shown that for individuals aged 40-70 years, each increment of 20 mmHg in systolic blood pressure or 10 mmHg in diastolic blood pressure doubles the risk of CVD across the entire blood pressure range from 115/75 to 185/115 mmHg. In a cross-sectional study of 447 Asian Indian diabetic subjects, Ramachandran et al, had reported a high prevalence of hypertension in CAD group compared to non-CAD group.

Sex was not an important determinant of risk of hypertension in our study groups. This finding was consistent with the observation in the NHANES study. However, some other studies had reported a higher incidence of hypertension in women.

The study projects the high prevalence of prehypertension followed by stage I and stage II hypertension in diabetic subjects in India. Prevalence of retinopathy and albuminuria increased with increasing levels of blood pressure. The study underscores the need to diagnose the early stages of hypertension and to institute tight control of blood pressure, in the attempt to prevent the occurrence and/or worsening of vascular complications associated with diabetes.

**References**