RESEARCH ARTICLE

EFFECT OF BLOOD PRESSURE ON DIABETIC NEPHROPATHY

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ABSTRACT

Background: Hypertension is known to be risk factor for the development of proteinuria in patients with uncontrolled diabetes mellitus type2, leads to progression of end stage renal disease

Aims & Objective: To study the effect of hypertension on diabetic nephropathy in type 2 diabetic patients.

Material and Methods: We investigated, progression of diabetic nephropathy by measuring arterial blood pressure , serum creatinine and glomerular filtration rate(GFR) level in 60 (35 men and 25 women) type 2 uncontrolled diabetes mellitus patients on antihypertensive treatment.

Results: The survey was done for 6 months during which 30 (group 1) -uncontrolled diabetes mellitus patients with normal blood pressure were compared with 30 (group 2) -Uncontrolled diabetes mellitus patients with hypertension who had mean systolic blood pressure (SBP) was 148.86 ± 5.12 mmHg. In group 2 the mean level of serum creatinine (1.71 ± 0.46 mg/dl) was significantly higher and mean GFR (54.57 ± 35.26 ml/min) was significantly lower than group 1 ($P < 0.05$).

Conclusion: Uncontrolled hypertension leads to progression of diabetic nephropathy with decline in GFR earlier than normotensive uncontrolled diabetic patients.

KEY-WORDS: GFR; Serum Creatinine; Type 2 Diabetes Mellitus; Hypertension

Introduction

Diabetes has emerged as a major healthcare problem in India. In 2011, India had 62.4 million people with type 2 diabetes, compared with 50.8 million the previous year, according to the International Diabetes Federation (IDF) and the Madras Diabetes Research Foundation. As the economy started growing, so did the incidence of diabetes. The nationwide prevalence of diabetes in India now tops 9%, and is as high as 20% in the relatively prosperous southern cities. By 2030, the IDF predicts, India will have 100 million people with diabetes.[1]

Diabetic nephropathy is a clinical syndrome characterized by persistent albuminuria, arterial blood pressure elevation, progressive decline in glomerular filtration rate (GFR), and a high risk of cardiovascular morbidity and mortality.[2] Approximately 40% of people with diabetes will develop nephropathy. Diabetic nephropathy (DN) is a leading cause of end-stage renal disease. However, the decline in GFR is highly variable, ranging from 2 to 20 ml/min/year.[3-6] Chronic kidney disease can be quantitatively defined as a GFR < 60 ml/min/1.73m^2 and the rate of rise in serum creatinine, a well-accepted marker for the progression of DN, (creatinine value 1.4 to 3.0 mg/dl) is the indicator for impaired renal function.[7,8]

Hypertension and proteinuria contribute to the progressive loss of renal function, while other progression promoters, for example, glycemic control and lipids are still debatable as reviewed by Rossing.[6] These renal functional changes develop as a consequence of structural abnormalities, including glomerular basement membrane thickening, mesangial expansion with extracellular matrix accumulation, changes in glomerular epithelial cells (podocytes), including a decrease in number and/or density, podocyte foot process broadening and effacement, glomerulosclerosis, and tubulointerstitial fibrosis.[9] Diabetic nephropathy occurs only in a

minority of subjects with either type 1 or type 2 diabetes and seems to result from the interaction between genetic susceptibility and environmental insults, primarily metabolic and hemodynamic in origin. Over the last decade, the cellular and molecular mechanisms by which these insults translate to structural and functional abnormalities leading to diabetic nephropathy have been increasingly delineated.[9] In particular, it has been determined that both metabolic and hemodynamic stimuli lead to the activation of key intracellular signaling pathways and transcription factors, thus triggering the production/release of cytokines, chemokines, and growth factors, which mediate and/or amplify renal damage.[9] The identification of promoters of progression of renal damage in diabetics is important for the creation of new powerful treatment modalities impeding the development of end-stage renal disease. This study was designed to assess the effect of hemodynamic stimuli like hypertension on progression of diabetic nephropathy.

Materials and Methods

An observational cross sectional study was conducted in 2011 with 60 poorly controlled (uncontrolled) diabetic mellitus type 2 patients (HbA1c >7%) in age group of 40- 70 years in G.G. hospital, Jamnagar district. Individuals who had already been treated for diabetes and hypertension were included in the study. The research protocol was approved by Institutional ethical committee and informed consent obtained from each subject prior to inclusion in the study. Personal history and medical history was collected in pre-designed proforma. After taking consent, Blood Pressure (BP) was measured with an appropriately sized cuff in the sitting position after resting for 10 min. Three measurements on different days were recorded, and the average was used for the analysis. Blood samples were drawn for measurement of serum concentrations of creatinine. Serum creatinine was estimated by modified Jaffe's kinetic reaction with Initial Rate Colorimetric and single reagent density by using picric acid.[10-12] Glomerular Filteration Rate (GFR) was calculated by Cockcroft-Gault equation,

$$\text{Creatinine Clearance}\left(\frac{\text{ml}}{\text{min}}\right) = \frac{(140 - \text{Age}) \times \text{Weight (kg)}}{72 \times \text{S. Creatinine}\left(\frac{\text{mg}}{\text{dl}}\right)} \times \text{GF}$$

Where GF is a Gender Correction Factor, for female 0.85 and 1.00 for male.[13] Patients were grouped according to their SBP as

Group-1: Normotensive uncontrolled type 2 diabetes mellitus (SBP < 140 mmHg).

Group-2: Hypertensive uncontrolled type 2 diabetes mellitus (SBP ≥ 140 mmHg)

Data was collected and statistically analyzed. BP, serum creatinine and GFR was reported as mean ± SD. The effect of Blood pressure in uncontrolled diabetes mellitus patients on progression of diabetic nephropathy by measuring serum Creatinine and GFR was tested statistically by T-test (Unpaired) by SPSS trial version 20 software, the difference was taken as significant if p value was less than 0.05.

Results

The study included total 60 uncontrolled diabetes mellitus Type2 patient under antihypertensive treatment, in which 35 were males and 25 were females.

Table no. 1 shows the comparison of general characteristics of group 1 and group 2. The mean age of group 1 was 56.41 years and in group 2 was 60.85 years, mean BMI of group1 and group 2 was 24.68 kg/m^2 and 24.69 kg/m^2 respectively, mean HbA1c of group1 was 8.11% and group 2 was 9.05% and mean duration of DM type 2 of group 1 and group 2 was 8.62 years and 9.69 years respectively. All above parameters in group 1 and group 2 were not significantly different.

Table-1: General Characteristics of Patients in Two Groups (Values in Mean ± SD)

	Group 1	Group 2
No. of patients	30	30
Age (years)	56.41 ± 12.5	60.85 ± 11.37
BMI (kg/m^2)	24.68 ± 2.57	24.69 ± 2.26
HbA1c%	8.11 ± 1.06	9.05 ± 2.47
Duration of DM 2 (years)	8.62 ± 2.98	9.69 ± 3.25

Table no. 2 shows mean SBP in group 1 was 125.61mmHg while in group2 was 148.86 mmHg which was significantly higher (P<0.05). Mean S. creatinine was significantly lower in group 1 (1.14 mg/dl) compared to group 2 (1.71 mg/dl) and the mean GFR in group 1 was 103.92 ml/min that was significantly higher than 54.57 ml/min in group 2 (P<0.05).

Table-2: Comparison of Systolic Blood Pressure (SBP), S. Creatinine & Glomerular Filtration Rate (GFR) in Group 1 and Group 2 (Values in mean ± SD)

	Systolic blood Pressure (mmHg)	Serum Creatinine (mg/dl)	GFR (ml/min)
Group 1 (N=30)	125.61 ± 7.64	1.14 ± 0.59	103.92 ± 50.53
Group 2 (N=30)	148.86 ± 5.12	1.71 ± 0.46	54.57 ± 35.26
P value	< 0.05	< 0.05	< 0.05

Discussion

In our study mean S. creatinine is significantly higher and mean GFR is significantly lower in Group2 patients (uncontrolled DM Type 2 with hypertension). Similar findings were found by Grover G.et al[14] who showed that affected participants (diabetic group) had mean FBG (fasting blood glucose) 142.035 ± 14.39 mg/dl, SBP (systolic blood pressure) 142.8214 ± 13.8815 mmHg and S. creatinine 1.6686 ± 0.28233 mg/dl. Ravi Retnakaran et al[15] suggest that history of hypertension were associated with an increased risk of doubling of plasma creatinine. Amita Dasmahapatra et al[16] study observed that hypertension was present in 72.4% nephropathy patients and particularly overt diabetic nephropathy was significantly more prevalent in hypertensive group. Study by Kasper Rossing et al [17] found that diabetic type 2 with diabetic nephropathy had HbA1c 8.8%, SBP 158 mmHg, GFR 83 ml/min/1.73 m^2.

Cox propotional hazards regression model was used by George L.Bakris et al[18] to assess the hazard risk profile of baseline SBP. That study found that increase in SBP (hypertension) progressively affect renal outcome of Type2 diabetic nephropathy patients. Also the hypertensive patients with SBP>140 mmHg had HbA1c 8.5 ± 1.6%, S. creatinine 1.9 ± 0.5 mg/dl and GFR 40.4 ± 11.9ml/min/1.73m^2 and also found in this study that a baseline SBP range of 140 to 159 mm Hg increased risk for ESRD or death by 38% (P=0.05) compared with those below 130 mmHg.

The present study tune with all above studies suggests that Blood pressure is one of the independent factors that affect renal function outcome in type 2 diabetes mellitus patients.

Conclusion

In our study, it was found that S. creatinine level was higher and GFR was lower in Group 2 patients as compare to group 1 which was statistically significant. Our study concludes that uncontrolled hypertension leads to progression of diabetic nephropathy with decline in GFR earlier than normotensive diabetic patients.

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