FACTORS AFFECTING PROGRESSION OF NEPHROPATHY IN TYPE 2 DIABETES MELLITUS

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ABSTRACT:

Background: Hyperglycemia and hypertension are known to be risk factors for the development of proteinuria in patients with diabetes, which leads to progression of end stage renal disease.

Objective: To study the effect of various factors on progression of diabetic nephropathy in type 2 diabetic patients.

Material and Methods: We investigated factors affecting progression of nephropathy by measuring serum creatinine (s-Cr), glomerular filtration rate (GFR) level in 70 (45 men and 25 women) type 2 diabetes mellitus patients on antihypertensive treatment.

Results: The survey was done for 6 months during which 40 (Group 1) - uncontrolled type 2 diabetes mellitus having S. Creatinine <1.2 mg/dl compared with 30 (Group 2) - uncontrolled type 2 diabetes mellitus having S. Creatinine ≥1.2 mg/dl. Mean S. Creatinine 2.1mg/dl, mean SBP 141.37mmHg, mean duration of diabetes mellitus 9.26 years, mean HbA1c 9.0%, mean Serum cholesterol 215.63 mg/dl and mean GFR 36.75 ml/min was seen in group 2 patients. In group 2 mean SBP, Duration of DM, HbA1c and serum creatinine were significantly higher and GFR significantly lower than group1 (P < 0.05).

Conclusion: hyperglycemia (HbA1c), duration of DM and hypertension are the risk factors that lead to progression of diabetic nephropathy with decline in GFR.

KEY WORDS: - Type2 diabetes mellitus (DM), Diabetic nephropathy (DN), serum creatinine, GFR, hypertension.

INTRODUCTION:
The Prevalence of diabetes has reached epidemic proportions. WHO predicts that developing countries will bear the brunt of this epidemic in the 21st Century. While the global prevalence of diabetes is 6.4% with an estimated 50.8 million people living with DM, India has world’s largest diabetes population, followed by China with 43.2 million. 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. 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. Chronic kidney disease (CKD) 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. Recently, interest has focused on the role of the metabolic syndrome (insulin resistance), defined by the presence of abdominal obesity, dyslipidemia, hypertension, and fasting hyperglycemia, in the development of CKD. The Diabetes Control and Complications Trial (DCCT) showed a significant relationship between reduction in glycosylated hemoglobin (HbA1c) levels and the risk of microvascular complications including CKD. In patients with diabetes, poor glycemic control is a risk factor for the development of nephropathy. Similarly, the incidence of a decline in renal function over 5 years was greater among older patients with hypertension. Hypertension has long been recognized as a consequence of renal impairment and an important factor in the progression of CKD, elevated systemic blood pressure transmitted to the glomerulus would contribute to glomerular hypertension and thus accelerate glomerular damage. Raised systolic blood pressure was an independent risk factor for development of albuminuria or renal impairment among patients with type II diabetes. Recent evidence also suggests a role for dyslipidemia in the development and progression of renal disease. Experimental studies have demonstrated that lipids may induce glomerular and tubulointerstitial injury and damage glomerular capillary endothelial and mesangial cells as well as podocytes. 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 various factors like obesity, hyperglycemia, hypertension, duration of diabetes mellitus, dyslipidemia on progression of diabetic nephropathy.

MATERIALS AND METHODS:

An observational cross sectional study was conducted in 2011 with 70 uncontrolled diabetes mellitus type 2 patients under antidiabetic and antihypertensive treatment, in which 45 were males and 25 were females, 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. Fasting blood sample was collected and following investigation done. HbA1c was measured by liquid chromatography. Fasting Serum Cholesterol was estimated by Colorimetry, enzymatic method using cholesterol esterase, cholesterol oxidase and peroxidase. It was performed by end point accucare. Non-fasting blood samples were obtained for measurements 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

Glomerular Filteration Rate (GFR) was calculated by Cockcroft-Gault equation, Estimated creatinine Clearance (ml/min) = (140-age) × weight(kg) / 72 × s. creatinine (mg/dl). Values for female were estimated after multiplying 0.85 to above formula. Patients were grouped according level of serum creatinine as:
Group 1: uncontrolled type 2 diabetes mellitus patients having S. Creatinine < 1.2 mg/dl (N=40)
Group 2: uncontrolled type 2 diabetes mellitus patients having S. Creatinine ≥ 1.2 mg/dl (N=30)

RESULTS:

In present study, mean S. Creatinine levels in group 1 patients was 0.72 mg/dl which was significantly lower than group 2 patients who had S creatinine level of 2.1mg/dl.

Table 1. Mean ± SD and P Value of Various Factors in two Groups.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Group</th>
<th>Value (Mean ± SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1 (N=40)</td>
<td>53.39 ± 5.27</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td></td>
<td>2 (N=30)</td>
<td>58.63 ± 10.77</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1 (N=40)</td>
<td>24.52 ± 2.15</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td></td>
<td>2 (N=30)</td>
<td>24.94 ± 2.96</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>1 (N=40)</td>
<td>126.45 ± 10.33</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>2 (N=30)</td>
<td>141.37 ± 10.56</td>
<td></td>
</tr>
<tr>
<td>Duration of DM (years)</td>
<td>1 (N=40)</td>
<td>5.65 ± 3.32</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>2 (N=30)</td>
<td>9.26 ± 3.16</td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>1 (N=40)</td>
<td>7.97 ± 1.00</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>2 (N=30)</td>
<td>9.00 ± 0.98</td>
<td></td>
</tr>
<tr>
<td>S. cholesterol (mg/dl)</td>
<td>1 (N=40)</td>
<td>214.52 ± 22.09</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td></td>
<td>2 (N=30)</td>
<td>215.63 ± 31.59</td>
<td></td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>1 (N=40)</td>
<td>122.73 ± 37.18</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>2 (N=30)</td>
<td>36.75 ± 9.26</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 shows mean age of two groups was not statistically different. In group 1 patient mean age was 53.39 years and group 2 patients was 58.63 years. Also Mean BMI of group 1 patients was 24.52 kg/m² and group 2 patients was 24.94 kg/m² which was similar.

There was significantly higher Mean SBP in group 2 (141.37 mmHg) compared to group 1 patients (126.45 mmHg). Mean duration of Diabetes of group 1 patients was 5.65 years which was significantly less than group 2 patients where it was 9.26 years. Mean HbA1c of group 1 patients was 7.97 % that was significantly lower than group 2 patients HbA1c of 9.0 %. Mean S. Cholesterol of group 1 patients was 214.52 mg/dl and group 2 patients was 215.63 mg/dl (not statistically different). Mean GFR of group 1 patients was 122.73 ml/min and group 2 patients was 36.75 ml/min which indicated significantly poor renal function in group 2. In our study mean SBP, duration diabetes mellitus type 2, HbA1c are significant different on comparing the two groups and mean S. Cholesterol of both group was found above normal level though not statistically different in the two groups.
DISCUSSION:

In present study we found that GFR was significantly lower in group 2 compared to group 1 patients suggesting the group 2 diabetic patients were having more severe renal affection than group 1 diabetics. The factors like systolic blood pressure, Duration of Diabetes Mellitus and HbA1c were significantly higher in group 2 patients suggesting that above mentioned factors are associated with progression of diabetic nephropathy.

In our study, mean SBP was 141.37 mmHg, mean duration of DM was 9.26 years and mean HbA1c level was 9.0% while mean GFR was 36.75 ml/min in group 2 patients. A similar finding were observed by Grover, et al who studied patients with S. creatinine≥ 1.4 mg/dl and found that mean SBP was 142.8214 mmHg, mean duration DM was 14.09 years, Fasting Blood Glucose was 142.035 mg/dl and mean S. Creatinine 1.6686 mg/dl17.

Kasper Rossing, et al in a follow up study of type 2 DM patients with nephropathy, evaluated renal functions. In this study it was found that rate of decline in mean GFR was 5.2 ml/min/year, mean SBP was 154 mmHg, mean albuminuria was 581mg/24hrs, mean HbA1c was 8.9 %. He suggests that elevated mean albuminuria, SBP, HbA1c, were significantly associated with increased decline in GFR during follow-up18.

Amita Dasmahapatra et al, showed that in overt nephropathy patients , mean duration of diabetes(NIDDM) was15.4 years, mean SBP was 159.2 mmHg, mean HbA1c was 9.2% ,mean AER (albumin excretion rate ) was 981.8 microgram/min, and total: HDL Cholesterol was high suggesting that a significant correlation exist between albuminuria and hypertension , duration of DM, HbA1c and S. cholesterol19.

Jamal S. Alwakeel et al, in a follow up study of NIDDM Saudi patients showed that mean age of patients was 66.9 years, mean duration of DM was 15.4 years and found that GFR deteriorated from baseline value of 78.3 ml/min/1.73 m^2 to 45.1 ml/min/1.73 m^2 at last visit20. Progression of nephropathy was observed in 40.3 % patients, had doubling S. Creatinine in their first hospital visit where SBP, Duration of DM, Persistent proteinuria and HbA1c were significant markers associated with progression of nephropathy.

M.A. Wijesuriya et al in a retrospective analytic study, conducted by reviewing the clinical records of the patients with type 2 diabetes who attended the National Diabetes Centre of Sri Lanka from January 2005 to December 2010 observed that nephropathy was significantly associated with poor glycemic control, high HbA1c, high Fasting blood glucose, high systolic blood pressure21.

The present study tune with all above studies suggest that persistent hyperglycemia as assessed by HbA1c, longer duration of uncontrolled diabetes mellitus and hypertension are the independent factors that affect renal function outcome in type 2 diabetes mellitus patients.

CONCLUSION:  In our study, it was found that persistent higher hyperglycemia, longer duration of DM and higher SBP (systolic blood pressure) with lower GFR in Group 2 patients as compare to group1. Glycemic control (HbA1c), duration of DM and hypertension are the risk factors leading to progression of diabetic nephropathy with decline in GFR earlier. This study may allow one to gain deeper insight into the various differences that may exist between the treatments suggested by previous studies and hence further guide the management of type 2 diabetic nephropathy.

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CONFLICT OF INTEREST: - None declared.

REFERENCES:-

