ARTICLE

Serum albumin levels in different stages of type 2 diabetic nephropathy patients

V Viswanathan, C Snehalatha, R Kumutha, M Jayaraman, A Ramachandran
Diabetes Research Centre, Chennai

Abstract

Aim: To study the serum albumin concentration in South Indian type 2 diabetic patients with nephropathy to decide regarding the extent of protein restriction required in these patients.

Research design and methods: Type 2 diabetic patients (n=139) admitted for review in M.V. Hospital for Diabetes, Chennai consisting of 49 patients with normoalbuminuria (< 20 mg of albumin / min), 52 patients with macroalbuminuria (> 200 mg of albumin / min and proteinuria < 3.5 gm /day) and 38 patients with nephrotic syndrome (proteinuria > 3.5 gm /day) were studied. Blood pressure, anthropometry, fasting and post-prandial plasma glucose, HbA1c, total serum albumin, lipid profile, urea and creatinine were measured.

Results: Serum albumin level was significantly lower in the nephrotic syndrome group of patients (p < 0.05) when compared with the macroalbuminuric and normoalbuminuric group of patients. Patients with end-stage renal disease, severe renal failure and moderate renal failure showed lower serum albumin concentrations compared with patients having early renal insufficiency and early renal damage. Serum albumin level decreased significantly in patients with reduced creatinine clearance. Serum albumin showed a significant positive association with creatinine clearance (p < 0.03), negative association with macroalbuminuria (p < 0.0001) and nephrotic proteinuria (p < 0.0001) among the independent variables included in the multiple linear regression analysis.

Conclusion: Serum albumin was significantly lower in patients with heavy proteinuria. Unless there is severe ureamia, drastic reduction in protein intake in south Indian diabetic patients with nephropathy may not be advisable.

Keywords: Type 2 diabetes, Diabetic Nephropathy, Serum albumin, Hypoalbuminaemia, Nephrotic syndrome.

Introduction

Restriction of dietary protein is usually recommended to retard the progression of chronic kidney disease. The Modification of Diet in Renal Diseases (MDRD) study failed to show a statistically significant beneficial effect of protein restriction on kidney function over a 2 – 3 year period. Serum albumin, which makes up approximately 60% of the circulating proteins is the best index of nutritional status as it relates to the outcome. Low albumin level predicts poor survival in end-stage renal disease. We had noted that the protein intake was significantly lower in vegetarian than in non-vegetarian South Indian type 2 diabetic patients, but in both the groups it was within the recommended limits for patients with diabetic nephropathy (0.6 – 0.8 gm / kg body weight / day). Severe protein restriction may lead to hypoproteinaemia and a consequent imbalance in water and electrolytes. The aim of the study was to evaluate whether the South Indian type 2 diabetic patients with nephropathy have evidence of hypoalbuminaemia, which is an established protein deficiency state in nephrotic syndrome.

Research design and Methods

A cross-sectional study was done in 139 type 2 diabetic patients who were admitted in M.V. Hospital for Diabetes for review during a period from October 2002 to March 2003.

The selection criteria were:

1. Type 2 diabetes by the WHO criteria

Address for Correspondence:
Dr V Viswanathan
Diabetes Research Centre
WHO Collaborating Centre for Research, Education and Training in diabetes
4, Main Road, Royapuram
Chennai – 600 013. INDIA.
Email : dr_vijay@vsnl.com
2. Duration of diabetes of 5 years with availability of all clinical and laboratory data at the time of study.

During the study period, 49 patients with normoalbuminuria (albumin excretion rate < 20 mg/min), 52 patients with macroalbuminuria (albumin excretion rate > 200 mg/min and proteinuria < 3.5 gm/day) and 38 patients with nephrotic syndrome (proteinuria > 3.5 gm/day) were available for the analysis. All of them had records of age, duration of diabetes, body mass index (BMI, kg/m²) and measurements of systolic and diastolic blood pressure. Biochemical parameters including plasma glucose, urea, creatinine, total cholesterol, triglycerides and glycosylated haemoglobin (HbA1c) were measured at the time of study. HbA1c was quantitatively determined by immunoturbidimetry. 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 (TG). Total serum albumin was determined by immunoturbidimetry. All the above biochemical tests were done using the reagents from Roche Diagnostics, Mannheim, Germany. Estimation of albuminuria/proteinuria and creatinine clearance in 24 hr urine sample was done by standard procedures. Based on the classification for chronic renal disease recommended by the National Kidney Foundation, the serum albumin levels in the various ranges of creatinine clearance (<15 (ESRD), 15-29 (severe renal failure), 30-59 (moderate renal failure), 60-89 (early renal insufficiency) and >90ml/min (with early renal damage]) was determined.

Statistical analysis

Data with normal distribution were expressed as mean ± SD. Intergroup comparisons were made by one-way ANOVA (HSD PROCEDURE). Multiple linear regression analysis was done to test the dependence of albumin on macroalbuminuria, nephrotic proteinuria, creatinine clearance, duration of diabetes, urea, creatinine, cholesterol, triglycerides, HbA1c and hypertension. Trend chi-square test was done to compare the proportions between the groups.

Result

The comparison of clinical, biochemical and haemodynamic variables in the normoalbuminuric, macroalbuminuric and nephrotic group are shown in Table 1.

Table 1: Characteristics of the study groups

<table>
<thead>
<tr>
<th></th>
<th>Normoalbuminuria</th>
<th>Macroalbuminuria</th>
<th>Nephrotic syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>49</td>
<td>52</td>
<td>38</td>
</tr>
<tr>
<td>M / F</td>
<td>34 / 15</td>
<td>34 / 18</td>
<td>30 / 8</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57 ± 12</td>
<td>56 ± 10</td>
<td>56 ± 9</td>
</tr>
<tr>
<td>Duration (years)</td>
<td>13.4 ± 8.6</td>
<td>15.1 ± 7.1</td>
<td>16.3 ± 6.4</td>
</tr>
<tr>
<td>Body mass index</td>
<td>26 ± 4.4</td>
<td>27 ± 6</td>
<td>24.3 ± 3.6</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>9.3 ± 2.1</td>
<td>9.8 ± 2.3</td>
<td>8.4 ± 2.3</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>133 ± 22</td>
<td>139 ± 21</td>
<td>159 ± 21</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>83 ± 9</td>
<td>86 ± 12</td>
<td>90 ± 11</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>21.7 ± 5.6</td>
<td>27.2 ± 11.3</td>
<td>78 ± 42.1</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.8 ± 0.1</td>
<td>0.9 ± 0.2</td>
<td>3.1 ± 1.9</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>184 ± 43</td>
<td>195 ± 51</td>
<td>211 ± 49</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>153 ± 86</td>
<td>164 ± 78</td>
<td>170 ± 60</td>
</tr>
<tr>
<td>Serum albumin (gm/dl)</td>
<td>4.1 ± 0.4</td>
<td>3.5 ± 0.4</td>
<td>2.8 ± 0.4</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min)</td>
<td>103.4 ± 25.8</td>
<td>84.1 ± 26.1</td>
<td>32.9 ± 15.6</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>33</td>
<td>62</td>
<td>89</td>
</tr>
</tbody>
</table>

Values are mean ± SD,* Macroalbuminuria, Nephrotic syndrome vs normoalbuminuria \{ p value is significantly different at 0.05 level \} # Nephrotic syndrome vs macroalbuminuria \{ p value is significantly different at 0.05 level \}

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There was no significant difference in the mean age and duration of diabetes among the three groups of patients. Nephrotic syndrome group of patients had lesser BMI, significantly lower HbA1c, higher concentration of urea, creatinine and systolic blood pressure in comparison with other groups. A statistically significant difference was found in the prevalence of hypertension among the three groups of patients (Trend $c^2 = 28.8$, $p < 0.0001$).

Serum albumin level was significantly lower in the nephrotic syndrome group of patients when compared with macroalbuminuric ($2.8 \pm 0.4$ vs $3.5 \pm 0.4$ gm/dl, $p < 0.05$) and normoalbuminuric group of patients ($2.8 \pm 0.4$ vs $4.1 \pm 0.4$ gm/dl, $p < 0.05$). Macroalbuminuric group also showed a significantly lower serum albumin values ($3.5 \pm 0.4$ gm/dl) versus normoalbuminuric group ($4.1 \pm 0.4$ gm/dl) ($p<0.05$).

The creatinine clearance level was three-fold higher in the other two groups when compared with the nephrotic syndrome group. The results showed that the serum albumin decreased as the creatinine clearance decreased. One way ANOVA showed that patients with early renal insufficiency and early renal damage had a significantly higher concentrations of serum albumin ($p<0.05$) compared with patients having ESRD, severe renal failure and moderate renal failure (Fig 1).

Since the number of patients was small in each group the total number of patients were included in multiple linear regression analysis. Among the tested variables, the parameters that showed association with serum albumin were creatinine clearance, macroalbuminuria and nephrotic proteinuria. The total variance explained by the above factors was 59%. Cholesterol, triglycerides, duration of diabetes, hypertension, HbA1c, urea and creatinine did not show significant association with the serum albumin values. Creatinine clearance showed a positive association while macroalbuminuria and nephrotic proteinuria showed a negative association with serum albumin (Table 2).

**Discussion**

Hypoalbuminaemia is considered a marker of malnutrition and a strongest predictor of death in patients with renal failure. Albumin is the most extensively studied protein as it is by far the most abundant protein in nephrotic urine. Patients whose serum albumin level is below 3.5 gm/dl have consistently higher morbidity rates. As the serum albumin drops from 3.5 to 3 gm/dl, there is a 15% increase in morbidity and mortality. For patients whose serum albumin concentration is less than 2.0 gm/dl, morbidity and/or mortality approach 100%.

In this study, it was noted that the serum albumin concentration was significantly lower in patients with nephrotic syndrome and macroalbuminuric patients when compared with normoalbuminuric patients.

In a previous study it was reported that there was no need for marked reduction in the protein intake in type 2 diabetic patients with nephropathy particularly in south Indian vegetarians. Innes et al reviewed 185 cases of patients with renal biopsy specimens that were classified solely as hypertension nephrosclerosis. In 18% of patients, serum albumin values were less than 3 gm/dl. Similar finding was also reported by Harvey et al.

In our patients, serum albumin concentration decreased significantly as the creatinine clearance level decreased, showing that albuminuria was related to the deteriorating kidney function. As expected, patients with end-stage renal disease (ESRD), severe renal failure and moderate renal failure showed low serum albumin concentration compared to patients with early renal insufficiency and early renal damage. A prospective study of 1513 type 2 diabetic patients with diabetic nephropathy, had reported that the serum albumin was an independent risk factor in patients with ESRD.

### Table 2: Results of multiple linear regression analysis showing parameters associated with serum albumin

<table>
<thead>
<tr>
<th>Dependent Variable = Serum albumin</th>
<th>R</th>
<th>S.E.R</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independent Variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>-0.51</td>
<td>0.91</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nephrotic proteinuria</td>
<td>-1.01</td>
<td>0.14</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>0.003</td>
<td>0.001</td>
<td>0.03</td>
</tr>
</tbody>
</table>

R = Coefficient    S.E.R = Standard error of R.

Variables not included in the equation significant: Cholesterol, triglycerides, duration of diabetes, hypertension, HbA1c, urea and creatinine.
The National kidney foundation had reported that eight studies addressed the association of low baseline serum albumin with a fast rate of glomerular filtration rate (GFR) decline. The association of low serum albumin with faster rate of GFR decline was more consistent in studies of diabetic patients. The MDRD study has reported that those patients with moderate renal disease assigned to the low protein group had a faster mean decline in GFR. We also note that the serum albumin levels are significantly lower in South Indian type 2 diabetic nephropathy patients. In the light of the observations of the above prospective studies protein restriction in south Indian diabetic patients with nephropathy should be done cautiously, particularly in vegetarians and preferably after considering the GFR and serum albumin level in each patient. Proteins of high biological value should be advised to prevent hypoalbuminaemia.

References