

Relationship between Serum Homocysteine and Other Parameters in Overt Diabetic Nephropathy

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ABSTRACT

OBJECTIVE: Level of serum homocysteine is remarkably common among patients with moderate to severe renal failure. We assessed whether serum homocysteine concentrations were correlated with proteinuria in overt diabetic nephropathy.

MATERIALS AND METHODS: A cross-sectional study was carried out on 45 patients (29 males, 16 females) with overt proteinuria. All subjects had type 2 diabetes. Data included age, sex, hypertension, serum creatinine, creatinine clearance, 24-hour urine proteinuria, lipid profiles and serum homocysteine.

RESULTS: The mean of serum homocysteine concentrations was 18 ± 7.7 $\mu\text{mol/L}$ (4.6-42), having 31 (70%) hyperhomocysteinemia. The mean of 24-hour urine proteinuria was 1515 ± 996 mg, for serum creatinine 1.9 ± 0.7 mg, and for creatinine clearance, it was 97 ± 26.6 mL/min. Serum homocysteine had a negative correlation with creatinine clearance ($r=-0.4$, $p=0.007$) and revealed no correlation with 24-hour proteinuria ($p=0.9$).

CONCLUSION: In overt nephropathy in diabetes type 2, patients with higher homocysteine had lower creatinine clearance. However, there was no correlation between homocysteine and overt proteinuria.

KEY WORDS: Homocysteine, Diabetic Nephropathies, Proteinuria.

INTRODUCTION

The increased susceptibility of diabetic patients with nephropathy can be explained by risk factors such as genetic susceptibility (1), increased glomerular filtration rate (2), obesity (3), and glycemic control. Therefore, the identification of new risk factors is important. Previous studies have investigated correlation between homocysteine (Hcy) and diabetic nephropathy. However, selected patients had just microalbuminuria (4, 5), or patients with overt nephropathy have been compared with ones without nephropathy (6). We focused just on type 2 diabetic patients

with overt proteinuria and investigated correlations between Hcy and other variables in these patients.

MATERIALS AND METHODS

The study population consisted of 45 type 2 diabetes mellitus patients with overt diabetic nephropathy. Overt nephropathy was diagnosed when 24-hour urine proteinuria was more than 300 mg/day. None of these patients received folic acid, and vitamin b12. Serum concentrations of creatinine, low-density lipoprotein, high-density lipoprotein, triglycerides, uric acid, and C-reactive protein,

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as well as blood hemoglobin concentrations, were measured using standard methods. Blood samples were drawn after a 12-hour fast. Serum Hcy concentrations were measured by enzyme-linked immunosorbent assay (IBL Company, Hamburg, Germany). Hyperhomocysteinemia was defined as a serum Hcy $\geq 15 \mu\text{mol/L}$. Creatinine clearances (CrCl) were calculated with the Cockcroft-Gault formula.

Statistical Analysis

Pearson coefficient was used for correlation analysis. Student *t*-test was used to compare independent samples and continuous variables with normal distribution. Statistical significance was established at $P < .05$. All data were analyzed with SPSS 13.

RESULTS

The mean age of patients was 58 ± 8 (39-79) years. The mean of serum Hcy concentrations was $18 \pm 7.7 \mu\text{mol/L}$ (4.6-42) having 31 (70%) hyperhomocysteinemia. The mean of 24-hour urine proteinuria was $1515 \pm 996 \text{ mg}$, for serum creatinine $1.9 \pm 0.7 \text{ mg}$, and for CrCl $41 \pm 16 \text{ mL/min}$.

There was no significant difference in Hcy level between males and females (19.3 ± 7 vs $17.8 \pm 8.8 \mu\text{mol/L}$, $p > 0.5$).

Table 1 shows the correlation between serum Hcy level and some variables. Serum Hcy was significantly associated with decline in renal function (Fig. 1). Patients with hyperhomocysteinemia had higher serum creatinine, lower CrCl and there was no difference regarding 24-hour proteinuria in comparison with normohomocysteinemia (Table 2).

DISCUSSION

We have demonstrated that patients with higher Hcy had lower renal clearance. Also, patients with hyperhomocysteinemia had higher serum creatinine. The kidney has a major role in the metabolism of Hcy. Therefore, it could explain why renal failure is an important cause of hyperhomocysteinemia in some studies. The Hcy concentrations rise

Table 1- Correlation between Serum Homocysteine Concentration and Other Variables

Variable	r	p
Age(y)	.04	0.3
Systolic BP (mm Hg)	.09	0.5
Diastolic BP (mm Hg)	.16	0.3
FBS (mg/dL)	.3	0.06
Ch (mg/dL)	-.12	0.4
TG (mg/dL)	.2	0.17
Uric acid (mg/dL)	.11	0.45
Serum Cr (mg/dL)	.3	0.03
CrCl (mL/min)	-.4	0.007
24 hours Urine proteinuria (mg)	-.004	0.9

BP, blood pressure; CrCl, creatinine clearance

Table 2- Renal Function and Proteinuria, Relative to Serum Homocysteine Concentration

Parameter	Homocysteine $\geq 15 \mu\text{mol/L}$ (n=31)	Homocysteine $< 15 \mu\text{mol/L}$ (n=14)	P value
Serum Cr (mg/dL)	2.1 ± 0.75	1.6 ± 0.48	0.048
CrCl (mL/min)	36 ± 13.7	52 ± 17.2	0.003
24 hours urine protein (mg)	1670 ± 1100	1970 ± 725	0.5

Cr, creatinine; CrCl, creatinine clearance

with the increase of creatinine especially in chronic renal failure (6, 7). In our study, there was no association between Hcy concentration and overt proteinuria. The previous studies compared Hcy in diabetes with and without micro or macroalbuminuria. Overt nephropathy type 2 diabetic patients had higher Hcy compared with no proteinuria (7-9). Similar findings have also been shown for type 1 diabetes. Wotherspoon et al. (4) have reported mild hyperhomocysteinemia in microalbuminuria diabetic patients compared with normoalbuminuria diabetic patients. We enrolled only patients with overt nephropathy. More than 80% of the patients had renal dysfunction. It seems the CrCl is a main factor that correlates with Hcy. A cohort study showed baseline Hcy cannot predict proteinuria in overt nephropathy after adjustment for serum creatinine. However, Hcy significantly predict proteinuria in patients with no proteinuria (7). Also, Allon et al. (10) showed proteinuria was not significantly associated with Hcy in either the unadjusted or multivariable analysis when serum creatinine is as a marker of renal function. Similar to these findings, we did not

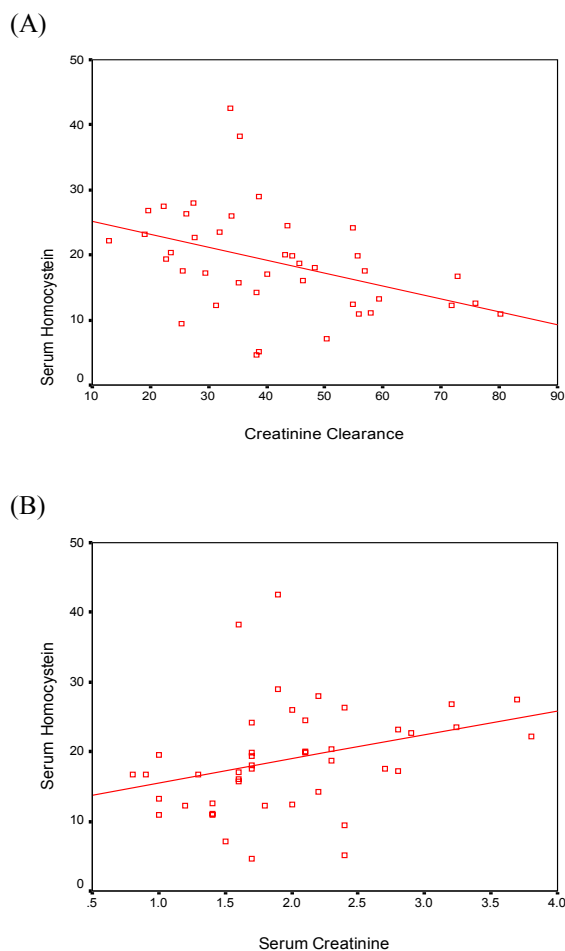


Figure.1- Correlation between Serum Homocystein and Creatinine Clearance (A) or Serum Creatinine (B)

find any correlation between Hcy and

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proteinuria in overt nephropathy.

In our study, there was no significant difference in Hcy between men and women. Some studies have showed that women have lower Hcy levels than men (11, 12). However, this difference even disappears in middle age (13). Because of our patients were on their middle age, this could be the reason for no differences of Hcy regarding different sexes.

In line with the study by Sally et al. (14), we have found no significant correlation between Hcy and systolic or diastolic hypertension.

Agulló-Ortuño et al. (6) observed that Hcy concentrations in type 2 diabetes was positively correlated with TG and Uric acid. However, this correlation was not observed in type 2 diabetic patients. The present study findings support this result.

Finally, in overt nephropathy in diabetes type 2, patients with hyperhomocysteinemia had lower renal clearance. However, there was no correlation between Hcy and overt proteinuria.

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