

INFLUENCE OF PROTEINURIA ON DISORDERS OF LIPOPROTEIN METABOLISM

Radmila Obrenović¹, Dejan Petrović², Biljana Glišić¹, Nada Majkić-Singh¹,
Jasna Trbojević³, Biljana Stojimirović⁴

¹Institute of Medical Biochemistry, Clinical Centre of Serbia, Belgrade

²Clinic of Urology and Nephrology, Clinical Centre »Kragujevac«, Kragujevac

³Department of Hemodialysis, Clinical Centre »Dr Dragiša Mišović«, Belgrade

⁴Institute of Urology and Nephrology, Clinical Centre of Serbia, Belgrade, Serbia and Montenegro

Summary: In order to assess the role of proteinuria in the development of lipoprotein metabolism derangements, we investigated 60 patients (32 males and 28 females, mean age 37.15 ± 9.85 years, average clearance of endogenous creatinine 86.27 ± 19.81 mL/min, average body mass index 24.18 ± 2.23 kg/m²), distributed in four groups according to degree of glomerular proteinuria. The control group, with urinary protein excretion <0.25 g/24h, included 15 persons, 6 males (M) and 9 females (F), average age 34.66 ± 4.82 years, with mean endogenous creatinine clearance (CCr) 99.70 ± 12.94 mL/min and mean body mass index (BMI) 23.28 ± 3.50 kg/m². Fifteen patients in the second group (M:F 9:6, average age 37.87 ± 9.65 years, mean CCr 82.85 ± 18.48 mL/min, mean BMI 23.83 ± 1.57 kg/m²) had proteinuria of 0.25–1.0 g/24h. The third group included 15 patients (M:F 8:7, average age 35.67 ± 13.29 years, mean CCr 82.85 ± 18.48 mL/min, mean BMI 23.83 ± 1.57 kg/m²), with proteinuria range 1.0 and 3.0 g/24h. The fourth group, with proteinuria greater than 3.0 g/24h, included 15 patients, M:F 9:6, mean age 40.40 ± 9.75 years, with mean CCr 80.16 ± 20.80 mL/min, and mean BMI 24.83 ± 1.44 kg/m². All patients in the second, third and fourth group had primary glomerulonephritis. Serum concentrations of the following parameters were measured: LDL cholesterol, HDL cholesterol, VLDL cholesterol and lipoprotein(a). Group differences were tested by the Student t-test, Mann-Whitney U test and χ^2 test. Patients with proteinuria greater than 3.0 g/24h had significantly higher VLDL cholesterol ($p < 0.01$) than subjects in other three groups. Furthermore, patients with proteinuria >3.0 g/24h had significantly higher serum HDL cholesterol ($p < 0.05$) than control subjects. Serum lipoprotein (a) level was significantly greater in patients with proteinuria >3.0 g/24h as compared with patients with proteinuria ranging from 1.0 to 3.0 g/24h and control subjects ($p < 0.01$). We therefore conclude that proteinuria causes disorders of LDL, VLDL, HDL and lipoprotein (a) metabolism.

Key words: primary glomerulonephritis, proteinuria, lipoproteins, LDL cholesterol

Introduction

Disorders of lipid metabolism in proteinuric patients appear due to increased hepatic lipid and apoprotein synthesis and deficient hepatic clearance of chylomicrons, very-low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL) and low-density lipoproteins (LDL) (1–4). Lipoprotein(a) (Lp(a))

represents a macromolecular complex present in blood, with covalently bound plasminogen-like glycoprotein (apoprotein(a)) and low density lipoprotein (apoprotein(b)) (2, 3). Its plasma concentration is elevated in proteinuric patients. Patients with low molecular weight isoform of apoprotein(a) (LMW apo(a)) and increased Lp(a) level, develop atherosclerosis and progressive decrease of glomerular filtration rate (3).

Hypoalbuminemia develops as a result of increased urinary loss of proteins and increased protein degradation in proximal tubular cells. It may lead to decrease of plasma colloid osmotic pressure, transition of fluid into interstitial space and increased hepatic

Address for correspondence:

Radmila Obrenović
Institute of Medical Biochemistry, Clinical Centre of Serbia
Višegradska 26, 11 000 Belgrade, Serbia and Montenegro
Tel.: 011/3614122–110
e-mail: radoa@EUnet.yu

lipoprotein and apoprotein synthesis. Furthermore, hypoalbuminemia decreases lipoprotein lipase activity due to increased synthesis of free fat acids (FFA) and, consequently, increased concentration of lipid precursors in the liver. It also leads to decrease of lecithin-cholesterol acyltransferase (LCAT) activity, caused by increased concentration of free lysolecithin (1–4).

Total cholesterol, phospholipids, triglycerides, LDL and VLDL serum concentrations are elevated in patients with nephrotic syndrome. Triglycerides and VLDL concentrations increase when serum albumin concentration is <20 g/L. Serum HDL level may be normal, elevated or reduced, depending on proteinuria level. When serum albumin concentration decreases below 20 g/L, serum HDL₂ also decreases. The higher the proteinuria and the lower the albuminemia, the lower the HDL₂ serum concentration. Serum HDL₃ concentration decreases when serum albumins are <10 g/L (1, 2). According to classification by Frederickson, patients with nephrotic syndrome exhibit *hyperlipoproteinemia type IIa, IIb* and *V*.

The aim of this study was to assess the influence of various degrees of proteinuria on disorders of lipoprotein metabolism.

Patients and Methods

The study included 60 patients, treated at the Institute of Urology and Nephrology, Clinical Centre of Serbia in Belgrade. All subjects had creatinine clearance greater than 50 mL/min, proteinuria lower than 10 g/24h and body mass index (BMI) lower than 27 kg/m². None was receiving immunosuppressive and antilipoproteinemic therapy. The patients were monitored during a period of one year. All subjects gave informed consent to participate in the study, according to the Helsinki Declaration on Medical Research.

The variables investigated were: clearance of endogenous creatinine (CCr), proteinuria, serum albumin concentration, plasma colloid osmotic pressure (COP), LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol and lipoprotein(a) serum concentrations.

Patients were divided into four groups based on the degree of glomerular proteinuria. The first (control) group had proteinuria < 0.25 g/24h, the second group had proteinuria of 0.25–1.0 g/24h, the third group had proteinuria of 1.0–3.0 g/24h, while patients in the fourth group had proteinuria >3.0 g/24h (Table 1). Patients in the second, third and fourth group all had glomerulonephritis, which was diagnosed on the basis of standard clinical and biochemical parameters. The diagnosis was confirmed by renal biopsy and patohistological findings.

Blood and urine analyses were performed at the Institute for Medical Biochemistry, Clinical Centre of

Serbia, in Belgrade. Lipoprotein concentration in the blood was determined after 12 to 14 hours of fasting. Patients ceased taking medicines which might influence serum lipid and lipoprotein levels three weeks prior to commencement of the study.

Serum creatinine was determined by colorimetric method, on *Monarch plus IL* apparatus (Milano, Italy), normal values being 57–95 μmol/L for women, and 69–111 μmol/L for men. Creatinine concentration in 24-hour urine was measured by the same method, using ten times higher dilution. Serum urea concentration was measured by complete enzyme method (urease-glutamyl-dehydrogenase), on the same apparatus, normal values being 3.5–7.5 mmol/L. Serum albumin was determined by bromine-cresol-green method, a commercial test by *Randox* company, on *Monarch plus IL* apparatus (Milan, Italy). Total serum cholesterol was measured by enzyme method (cholesterol esterase – cholesterol oxidase), normal values being 3.37–6.48 mmol/L. HDL lipoprotein was determined by colorimetric method, normal value being 0.78–1.55 mmol/L. LDL concentration was calculated using the following equation: $CLDL = C_{HOL-tot} - (TGL/2.2) - C_{HDL}$; where C_{LDL} stands for LDL plasma concentration, C_{HOL} represents total cholesterol plasma concentration, C_{HDL} is HDL plasma concentration, and TGL – triglycerides. Serum triglycerides concentration was determined by enzyme-colorimetric method, normal values being 0.45–1.88 mmol/L. Serum lipoprotein(a) level was determined by *Behring Nephelometer System* and *N-Latex Lp(a)* reagent, normal values being < 0.3 g/L. Proteinuria in 24h urine was determined by *Coomassie brilliant blue G 250* (CBB) color, which binds to proteins forming colored complexes. The complexes' absorbance was determined on *Stassar III* spectrophotometer. Normal protein concentration in 24h urine is <150 mg/24h.

Clearance was calculated using the following equation: $C_x = \frac{U_x \cdot V_u}{P_x}$ mL/min, where C_x is clearance of examined substance, U_x – concentration of the substance in 24h urine (mmol/L), V_u – volume of 24h urine (L), P_x – concentration of examined substance in plasma (mmol/L).

Plasma colloid osmotic pressure (COP) was calculated using the following equation (6): $COP(\text{mmHg}) = \alpha(P-\text{Alb})^2 + \beta[\text{Alb} \times (P - \text{Alb})]$, where P is plasma total protein concentration (g/L) and Alb is plasma albumin concentration (g/L), while end values depend on the degree of proteinuria. For proteinuria > 3.5 g/24h $\alpha = 0.13$ and $\beta = 2.07$; while for proteinuria <3.5 g/24h $\alpha = -1.15$ and $\beta = 3.03$. Normal plasma COP is 24–26 mmHg.

Results are presented as mean standard deviation (SD). Group differences were tested by the Student t-test, Mann-Whitney U test and χ^2 test.

Results

Patients' renal function was assessed by 24h creatinine clearance and serum creatinine and urea concentrations and values of parameters are presented in *Table I*.

Patients in the second and third group (proteinuria levels of 0.25–1.0 g/24h and 1.0–3.0 g/24h respectively) had significantly higher serum urea and creatinine ($p < 0.05$) and significantly lower creatinine clearance ($p < 0.05$) than control subjects, with proteinuria < 0.25 g/24h (*Table I*). Healthy subjects also had significantly lower serum urea and creatinine ($p < 0.01$) and significantly greater creatinine clearance ($p < 0.01$) than patients with proteinuria > 3.0 g/24h (*Table I*). No statistically significant difference was found between other groups of patients regard-

ing serum urea and creatinine, and creatinine clearance ($p > 0.05$) (*Table I*).

Patients with proteinuria greater than 3.0 g/24h had significantly lower total protein and albumin serum concentration ($p < 0.01$), as well as significantly lower plasma COP ($p < 0.01$), as compared with control subjects and patients in the second and third group (*Table I*). No statistically significant difference was found regarding serum total protein, serum albumin and plasma COP between other groups ($p > 0.05$) (*Table I*).

Patients with proteinuria > 3.0 g/24h had significantly higher serum LDL cholesterol ($p < 0.01$) compared to patients with proteinuria range 0.25–1.0 g/24h and patients with proteinuria range 1.0–3.0 g/24h (*Table II*). There were no statistically significant

Table I General patients' characteristics and biochemical parameters

Variables	Groups – proteinuria (g/24h)			
	I (<0.25)	II (0.25–1.00)	III (1.00–3.00)	IV (>3.00)
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$
Number (n°)	15	15	15	15
Sex (M/F)	6/9	9/6	8/7	9/6
Age (years)	34.66 ± 4.82	37.87 ± 9.65	35.67 ± 13.29	40.40 ± 9.75
BMI (kg/m ²)	23.28 ± 3.50	24.77 ± 1.53	23.83 ± 1.57	24.83 ± 1.44
Healthy subjects	15	/	/	/
Urea (mmol/L)	4.57 ± 1.15	6.22 ± 1.34*	6.45 ± 2.39**	7.12 ± 3.31***
Creatinine (mol/L)	78.00 ± 19.05	98.60 ± 17.33*	99.73 ± 21.09**	105.93 ± 35.20***
CCr (mL/min)	99.70 ± 12.94	82.37 ± 21.19*	82.85 ± 18.48**	80.16 ± 20.80***
Total proteins (g/L)	70.00 ± 3.57•	70.47 ± 3.94••	69.00 ± 3.95•••	51.60 ± 5.37
Albumins (g/L)	42.93 ± 3.61•	41.86 ± 4.27••	39.80 ± 2.51•••	25.13 ± 4.02
COP (mmHg)	26.44 ± 2.71•	26.22 ± 2.94••	24.69 ± 2.59•••	14.73 ± 3.04
Probability (p)	*pI,II<0.05; **pI,III<0.05; ***pI,IV<0.01 •pI,IV<0.01; ••pII,IV<0.01; •••pIII,IV<0.01			
CCr – creatinine clearance; COP – coloid-osmotic pressure; BMI – body mass index				

Table II Lipoprotein concentration and atherosclerosis index depending on the range of proteinuria

Variables	Groups – proteinuria (g/24h)			
	I (<0.25)	II (0.25–1.00)	III (1.00–3.00)	IV (>3.00)
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$
LDL-cholesterol (mmol/L)	2.82 ± 0.49	3.14 ± 0.49**	3.28 ± 1.35***	5.00 ± 1.48****
HDL-cholesterol (mmol/L)	1.41 ± 0.16♦	1.32 ± 0.42	1.31 ± 0.30	1.15 ± 0.39
VLDL-cholesterol (mmol/L)	0.88 ± 0.43	0.68 ± 0.57**	0.61 ± 1.10***	2.57 ± 1.94****
HOL/HDL	•3.42 ± 0.63*	4.40 ± 1.60**	4.34 ± 1.44***	6.93
LDL/HDL	2.04 ± 0.48*	2.40 ± 0.74**	2.87 ± 1.27***	4.65 ± 1.91****
(LDL – HDL)/LDL	0.48 ± 0.14	0.54 ± 0.16**	0.57 ± 0.22***	0.75 ± 0.10****
Lipoprotein (a) (g/L)	0.14 ± 0.10*	0.23 ± 0.27	0.32 ± 0.26	0.35 ± 0.27*
Probability	♦pI,IV<0.05; •pI,II<0.05; *pI,III<0.05; **pII,IV<0.01; ***pIII,IV<0.01; ****pI,IV<0.01; *pI,III<0.01; **pI,IV<0.01			

differences in serum LDL cholesterol between other groups of patients. Patients with proteinuria greater than 3.0 g/24h had significantly lower serum HDL cholesterol ($p < 0.05$) than control subjects. No statistically significant differences were found between other groups of patients regarding serum HDL cholesterol (Table II).

Patients with proteinuria > 3.0 g/24h had significantly higher serum VLDL cholesterol ($p < 0.01$) than control subjects and patients in the second and third group. Serum VLDL cholesterol concentrations did not differ significantly between other patients' groups. Patients with proteinuria greater than 3.0 g/24h had significantly higher HOL/HDL atherosclerosis index ($p < 0.01$) than control subjects, patients with proteinuria range 0.25–1.0 g/24h and patients with proteinuria range 1.0–3.0 g/24h. Furthermore, HOL/HDL atherosclerosis index was significantly higher for patients in the second and third group (proteinuria range 0.25–1.0 g/24h and 1.0–3.0 g/24h respectively) than for control subjects ($p < 0.05$) (Table II).

Patients with proteinuria > 3.0 g/24h had significantly higher LDL/HDL atherosclerosis index ($p < 0.01$) than patients in the second and third group (Table II). Patients with proteinuria range 1.0–3.0 g/24h had significantly higher LDL/HDL atherosclerosis index ($p < 0.05$) than control subjects.

Patients with proteinuria greater than 3.0 g/24h had significantly higher (LDL – HDL)/LDL atherosclerosis index than patients in the control group, patients with proteinuria range 0.25–1.0 g/24h and patients with proteinuria range 1.0–3.0 g/24h (Table II).

Patients with proteinuria range 1.0–3.0 g/24h and patients with proteinuria greater than 3.0 g/24h had significantly higher serum lipoprotein(a) ($p < 0.01$) than patients in the control group. No statistically important differences were found between other groups of patients regarding serum lipoprotein(a) concentration (Table II).

Discussion

A number of studies confirmed that proteinuria leads to disorders of lipid metabolism. In renal patients, these disorders represent an independent risk factor for cardiovascular diseases and progression of renal failure. Due to damage of glomerular basement membrane, lipoproteins accumulate in mesangium, where they bind to specific receptors on mesangial cells' surface, inducing mesangial proliferation, increased formation and release of proinflammatory and vasoactive mediators, as well as increased formation and accumulation of extracellular proteins. All these changes eventually lead to glomerulosclerosis. Furthermore, lipoproteins bind to specific receptors on epithelial cells in proximal tubules, stimulating me-

sangial cells to increase production of proinflammatory and vasoactive mediators. These mediators are released through basolateral surface of proximal tubular epithelial cells in interstitium, where they stimulate fibroblast activity and induce scarring process.

The aim of this study was to investigate the influence of various degrees of proteinuria on disorders of lipoprotein metabolism. Subjects were divided into four groups according to the degree of proteinuria. Patients were matched for age, sex and BMI. Proteinuric patients had significantly lower creatinine clearance than healthy controls (Table I). Disorders of lipid metabolism are present when creatinine clearance falls below 50 mL/min. Since patients included in this study all had $CCr > 50$ mL/min, creatinine clearance had no significant influence on lipid metabolism (7).

Increased albumin degradation in proximal tubular epithelial cells and increased urinary loss of proteins lead to hypoproteinemia and hypoalbuminemia. As anticipated, patients with proteinuria greater than 3.0 g/24h had significantly lower serum total protein and albumin levels ($p < 0.01$) than control subjects, patients with proteinuria range 0.25–1.0 g/24h and patients with proteinuria range 1.0–3.0 g/24h (Table I). Higher urinary loss of proteins is followed by lower serum total protein and albumin concentration (Table I). Hypoalbuminemia is followed by decrease of plasma colloid osmotic pressure. Therefore, patients with proteinuria > 3.0 g/24h have significantly lower plasma COP ($p < 0.01$) than control subjects, patients with proteinuria range 0.25–1.0 g/24h and patients with proteinuria range 1.0–3.0 g/24h (Table I).

Increased urinary loss of protein, hypoalbuminemia and decreased plasma COP stimulate hepatic lipoprotein and apoprotein synthesis, and decrease hepatic clearance of chylomicrons, VLDL, IDL and LDL, which in turn contributes to disturbance of lipid metabolism in proteinuric patients (1–4). When serum albumin concentration is below 20 g/L, there is an increase in triglycerides, LDL and VLDL levels. Depending on the degree of proteinuria, high density lipoproteins (HDL) can be either normal, increased or decreased. Serum albumin concentration below 20 g/L is accompanied by decrease of serum HDL₂ concentration, and when albuminemia falls under 10 g/L it is followed by the decrease of serum HDL₃ concentration (2–4). Lipoprotein electrophoresis shows hiperlipoproteinemia type IIa or IIb is present in 60% of patients with nephrotic syndrome. Some 30% of patients with nephrotic syndrome have hiperlipoproteinemia type V, while 10% of patients with nephrotic syndrome have hiperlipoproteinemia type III or IV (2, 3).

Patients with proteinuria greater than 3.0 g/24h had significantly higher serum LDL cholesterol and VLDL cholesterol ($p < 0.01$) than patients in all other groups (Table II). Patients with proteinuria > 3.0 g/24h had significantly reduced serum HDL chole-

terol ($p < 0.05$) than control subjects, which confirms previous statements (*Table II*).

Disturbance of lipid metabolism strongly contributes to development of atherosclerosis, cardiovascular complications and progression of renal failure. Our results demonstrate that patients with proteinuria greater than 3.0 g/24h have significantly higher HOL/HDL, LDL/HDL and (LDL – HDL)/LDL indexes of atherosclerosis compared to patients in all other groups. Furthermore, patients with proteinuria range 1.0–3.0 g/24h have significantly higher HOL/HDL and LDL/HDL indexes of atherosclerosis than control subjects ($p < 0.05$), which puts them at higher risk of atherosclerosis (*Table II*).

Plasma concentration of Lp(a) is elevated in proteinuric patients (8, 9) which mainly originates from increased protein synthesis in the liver. Plasma Lp(a) concentration in patients with nephrotic syndrome is proportional to the degree of proteinuria and disproportionate to plasma albumin (10). In this study, patients with proteinuria greater than 3.0 g/24h and patients with proteinuria range 1.0–3.0 g/24h had significantly higher serum lipoprotein(a) than control subjects (*Table II*), which is in agreement with data published on the subject. Higher proteinuria levels are associated with higher serum concentration of lipoprotein(a). Together, they cause faster development of atherosclerosis and higher incidence of cardiovascular diseases. Patients with Lp(a) concentration > 0.3 g/L have 2.7 times higher risk of coronary disease than patients with Lp(a) plasma concentration < 0.3 g/L. Patients with increased Lp(a) plasma concentration and increased isoform of LMW apo(a) develop atherosclerosis and progressive renal damage (3). Therefore, guidelines for follow-up of patients with renal diseases should include: measuring lipoprotein(a) concentration in all renal patients, determining apo(a) phenotype in all patients with increased Lp(a) concentration, and strict follow-up of

other risk factors for atherosclerosis (such as anemia, hypertension, hyperglycemia, hyperchromocystinemia) in all patients with increased Lp(a) serum concentration (3).

Disorders in lipid metabolism contribute significantly to the progression of renal failure and progressive decrease of glomerular filtration rate. These derangements are always associated with glomerular damage to influence the development and progression of renal failure. Immunofluorescent staining of renal tissue proved presence of apo B (LDL), apo(a) (Lpa) and apo E (VLDL) in various glomerular diseases. Lipid deposits were found in mesangial and visceral epithelial cells. Presence and density of lipid deposits are connected with the degree of mesangial hypercellularity, glomerular sclerosis, interstitial changes, proteinuria and hypercholesterolemia. Based on morphological data, it was found that lipoproteins play a major role in the progression of glomerular diseases (12–15).

Clinical studies have shown that renal function decreases by 20%, during follow-up period of five years, in patients with LDL/HDL ratio higher than 4.4 compared to patients with LDL/HDL ratio lower than 3.2 (13). HMG-CoA reductase inhibitors (statins) decrease total cholesterol and LDL cholesterol concentrations, increase HDL cholesterol concentration, decrease proteinuria and improve glomerular filtration rate (15).

Having in mind that disorders of lipid metabolism represent an independent risk factor for progression of renal failure and development of cardiovascular complications, early detection of such derangements is mandatory, as are adequate treatment and achieving target levels of lipoproteins ($LDL \leq 2.6$ mmol/l).

Acknowledgements: The present work was supported by the Ministry for Science and Environmental Protection of Serbia, on the basis of Contract No 1260.

UTICAJ PROTEINURIJE NA POREMEĆAJE METABOLIZMA LIPOPROTEINA

Radmila Obrenović¹, Dejan Petrović², Biljana Glišić¹, Nada Majkić-Singh¹,
Jasna Trbojević³, Biljana Stojimirović⁴

¹Institut za medicinsku biohemiju, Klinički centar Srbije, Beograd

²Klinika za urologiju i nefrologiju, Klinički centar »Kragujevac«, Kragujevac

³Odeljenje hemodijalize, Klinički centar »Dr Dragiša Mišović«, Beograd

⁴Institut za urologiju i nefrologiju, Klinički centar Srbije, Beograd, Srbija i Crna Gora

Kratak sadržaj: Cilj ovog istraživanja bio je da se ispita uticaj proteinurije na poremećaje metabolizma lipoproteina. Ispitano je 60 bolesnika (32 muškog i 28 ženskog pola, srednje starosti $37,15 \pm 9,85$ godina, srednjeg klirensa kreatinina $86,27 \pm 19,81$ mL/min, srednjeg indeksa telesne mase $24,18 \pm 2,23$ kg/m²) koji su svrstani u četiri grupe u zavisnosti od stepena glomerularne proteinurije. Kontrolnu grupu, s proteinurijom manjom od 0,25 g/24h činilo je 15 osoba, 6 muškog i 9 ženskog pola, srednje starosne dobi $34,66 \pm 4,82$ godina,

srednje vrednosti klirensa kreatinina (CCr) $99,70 \pm 12,94$ mL/min i srednjeg indeksa telesne mase (BMI) $23,28 \pm 3,50$ kg/m². Bolesnici s proteinurijom 0,25–1,0 g/24h (9 muškaraca i 6 žena, starosti $37,87 \pm 9,65$ godina, srednjeg CCr $82,85 \pm 18,48$ mL/min i srednje vrednosti BMI $23,83 \pm 1,57$ kg/m²) činili su drugu grupu. U treću grupu je uključeno 15 bolesnika s proteinurijom 1,0–3,0 g/24h (8 muškaraca i 7 žena, srednje starosti $35,67 \pm 13,29$ godina, srednjeg CCr $82,85 \pm 18,48$ mL/min i srednje vrednosti BMI $23,83 \pm 1,57$ kg/m²), dok je četvrtu činilo 15 bolesnika s proteinurijom većom od 3,0 g/24h (9 muškaraca i 6 žena, starosti $40,40 \pm 9,75$ godina, srednjeg CCr $80,16 \pm 20,80$ mL/min i srednjeg BMI $24,83 \pm 1,44$ kg/m²). Svi bolesnici u drugoj, trećoj i četvrtoj grupi su imali primarni glomerulonefritis. Određivani su sledeći biohemijski parametri u serumu: LDL holesterol, HDL holesterol, VLDL holesterol i lipoprotein(a). Dobijene vrednosti statistički su analizirane studentovim t-testom, Mann-Whitney U-testom i χ^2 testom. Bolesnici s proteinurijom preko 3,0 g/24h imali su statistički značajno više vrednosti VLDL holesterola ($p < 0,01$) nego bolesnici u ostalim grupama. Bolesnici sa proteinurijom preko 3,0 g/24h imali su statistički značajno više vrednosti HDL holesterola ($p < 0,05$) nego bolesnici u kontrolnoj grupi. Serumska vrednost lipoproteina(a) bila je statistički značajno viša u grupi bolesnika sa proteinurijom preko 3,0 g/24h nego kod bolesnika sa proteinurijom između 1,0 i 3,0 g/24h i bolesnika u kontrolnoj grupi ($p < 0,01$). Proteinurija uzrokuje poremećaj metabolizma LDL, VLDL, HDL i lipoproteina(a).

Ključne reči: primarni glomerulonefritis, proteinurija, lipoproteini, LDL, holesterol

References

- Harris RC, Ismail N. Extrarenal Complications of the Nephrotic Syndrome. *Am J Kidney Dis* 1994; 23: 477–97.
- Wheeler DC, Bernard DB. Lipid Abnormalities in the Nephrotic Syndrome: Causes, Consequences and Treatment. *Am J Kidney Dis* 1994; 23: 331–46.
- Kronenberg F, Utermann G, Dieplinger H. Lipoprotein(a) in Renal Disease. *Am J Kidney Dis* 1996; 27: 1–25.
- Sechi LA, Zingaro L, Catena C et al. Lipoprotein(a) and apolipoprotein(a) isoforms and proteinuria in patients with moderate renal failure. *Kidney Int* 1999; 56: 1049–57.
- Wheeler D. Lipid abnormalities in the nephrotic syndrome: the therapeutic role of statins. *J Nephrol* 2001; 14 [Suppl 4]: 70–5.
- Geranton F, Chantrel F, Boullier M et al. Prediction of colloid osmotic pressure in renal patients. *Clin Nephrol* 2000; 53: 269–75.
- Attman P-O, Alaupovic P, Tavella M et al. Abnormal lipid and apolipoprotein composition of major lipoprotein density classes in patients with chronic renal failure. *Nephrol Dial Transplant* 1996; 11: 63–9.
- Doucet C, Mooser V, Gonbert S. et al. Lipoprotein(a) in the Nephrotic Syndrome: Molecular Analysis of Lipoprotein(a) and Apolipoprotein(a) fragments in the Nephrotic Syndrome: Molecular Analysis of Lipoprotein(a) and Apolipoprotein(a) Fragments in Plasma and Urine. *J Am Soc Nephrol* 2000; 11: 507–513.
- De Sain-Van Der Velden MG, Reijngoud DJ, Kaysen GA et al. Evidence for increased synthesis of lipoprotein(a) in the nephrotic syndrome. *J Am Soc Nephrol* 1998; 9: 1474–81.
- Noto D, Barbagallo CM, Cascio AL. et al. Lipoprotein(a) levels in relation to albumin concentration in childhood nephrotic syndrome. *Kidney Int* 1999; 55: 2433–9.
- Feeman WE, Caldwell LR, Iliff D et al. Guidelines for Diagnosis and Treatment of High Cholesterol. *JAMA* 2001; 285: 2486–97.
- Klahr S, Schreiner G, Ichikawa I. The progression of renal disease. *N Engl J Med* 1988; 318: 1657–66.
- Saito T, Oikawa S, Sato H. et al. Lipoprotein Glomerulopathy and Its Pathogenesis. In: Keane WF, Hörl WH, Kasiske BL, eds. *Lipids and the Kidney*. Contrib Nephrol, Karger, Basel, 1997: 30–8.
- Olbricht CJ. The potential role of lipids in the progression of glomerular diseases. In: Koch KM, Stein G, eds. *Pathogenetic and Therapeutic Aspects of Chronic Renal Failure*. Marcel Dekker, New York, 1997; 21–31.
- Nakamura T, Ushiyama C, Hirokawa K. et al. Effect of cervistatin on proteinuria and urinary podocytes in patients with chronic glomerulonephritis. *Nephrol Dial Transplant* 2002; 17: 798–802.
- Fried LF, Orchard TJ, Kasiske BL. Effect of lipid reduction on the progression of renal disease: a meta-analysis. *Kidney Int* 2001; 59: 260–9.
- Lavey AS. Clinical practice: non-diabetic kidney disease. *N Engl J Med* 2002; 347: 1505–11.
- Vogt L, Laverman GD, Dullaart RPF. et al. Lipid management in the proteinuric patients: do not overlook the importance of proteinuria reduction. *Nephrol Dial Transplant* 2004; 19: 5–8.

Received: March 15, 2005

Accepted: June 18, 2005