ORIGINAL ARTICLE

UDC: 577.125:616.61-008.6
DOI: 10.2298/VSP1211961C

Evaluation of lipid parameters and bioindices in patients with different stages of chronic renal failure

Određivanje lipidnih parametara i bioindeksa kod bolesnika u različitim stadijumima hronične bubrežne insuficijencije

Velibor Čabarkapa*, Mirjana Djerić*, Zoran Stošić*, Vladimir Sakač†, Zagorka Lozanov-Crvenković‡, Biljana Vučković*

***Department of Patophysiology, †Department of Internal Medicine, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia, ‡Faculty of Sciences, University of Novi Sad, Novi Sad, Serbia**

Abstract

Background/Aim. Cardiovascular morbidity and mortality are markedly increased in chronic renal failure (CRF). The aim of this study was to evaluate lipid parameters and bioindices in patients with different stages of CRF. **Methods.** In 46 hemodialysed (HD), 50 CRF patients with II, III and IV stage of CRF (non-HD) and 48 control subjects triglycerides (TG), total cholesterol (C), HDL-C, urea, creatinine, creatinuria (standard biochemical methods), apolipoprotein (apo) A-I, apo B, lipoprotein(a), cystatin C (immunoturbidimetric method) were evaluated, and LDL-C, non-HDL-C, LDL-C/HDL-C, non-HDL-/HDL-C, TG/HDL-C, and new bioindices, LTI (lipid tetrad index), logLTI, LPI (lipid pentad index), logLPI, AIP (atherogenic index of plasma), and creatinine clearance were calculated. **Results.** There were significant differences in the levels of TG, HDL-C, LDL-C, non-HDL-C, total C and apo A-I between the HD and non-HD patients, and the HD patients and the controls. LTI and LPI were significantly higher in the HD and non-HD patients compared to the controls ($p < 0.05$), without a good separation by the Box-Whisker plots. The values of TG/HDL-C ratio and AIP were significantly higher in the HD and non-HD-patients compared to the controls ($p < 0.05$), and significantly higher in the HD compared to non-HD patients ($p < 0.05$). AIP > 0.11 was found in 71.7% of the HD, 56% of non-HD and 31.3% of the controls. **Conclusion.** Among lipid parameters and indices, AIP and TG/HDL-C ratio are most suitable for evaluation of lipid disturbances in different stages of CRF. In addition to, non-HDL-/HDL-C, and apoB/A-I ratios, apo A-I, HDL-C and TG are important markers in HD patients. Non-HDL-C is not a suitable marker. LTI and LPI need to be further investigated.

Key words:
kidney failure, chronic; renal, dialysis; lipids; metabolism.

Apstrakt

Uvod/Cilj. U hroničnoj bubrežnoj insuficijenciji (HBI) naročito su povećani kardiovaskularni morbiditet i mortalitet. Cilj studije bio je ispitivanje lipidnih parametara i bioindeksa u različitim stadijumima HBI. **Metode.** Kod 46 bolesnika na hemodijalizi (HD), 50 bolesnika u II, III i IV stadijumu HBI (ne-HD), kao i kod 48 osoba kontrolne grupe određivane su serumske koncentracije ukupnog holesterola (H), HDL-H, triglicerida (TG), ureje, kreatinina, kao i nivo kreatinurije (standardnim biohemijskim metodama), apolipoproteini A-I i B, lipoprotein(a), cistatin C (imunoturbidimetrijskom metodom), i izračunavani su LDL-H, non-HDL-H, odnosi LDL-/HDL-H, nonHDL-/HDL-H, TG/HDL-H, novi bioindeksi lipid tetrada indeks (LTI), logLTI, lipid pentada indeks (LPI), logLPI, AIP (aterogeni indeks plazme), kao i klirens kreatinina. **Rezultati**. Nivoi TG, ukupnog H, HDL-H, LDL-H, non-HDL-H, i apoA-I značajno su se razlikovali kod HD u odnosu na ne-HD bolesnike, kao i u odnosu na kontrolnu grupu. Lipid tetrada indeks i lipid pentada indeks bili su viši kod HD i ne-HD bolesnika u poređenju s kontrolom ($p < 0,05$), ali bez dobrog razdvajanja korišćenjem Box-Whisker grafika. Odnos TG/HDL-H i AIP bili su viši kod HD i ne-HD bolesnika nego kod kontrole ($p < 0,05$), i kod HD nego kod ne-HD ($p < 0,05$). Aterogeni indeks plazme > 0,11 utvrđen je kod 71,7% HD, 56% ne-HD bolesnika, kao i kod 31,3% osoba iz kontrolne grupe. **Zaključak.** Aterogeni indeks plazme i TG/HDL-C najpogodniji su parametri za procenu poremećaja metabolizma lipida u različitim stadijumima HBI. Osim toga, odnosi ne-HDL-/HDL-H, apoB/A-I, kao i vrednosti apoA-I, HDL-H i TG su značajni markeri kod HD bolesnika. LTI i LPI zahtevaju dalja istraživanja.

Ključne reči:
bubreg, hronična insuficijencija; bubreg, dijaliza; lipidi; metabolizam.

Correspondence to: Velibor Čabarkapa, Department of Patophysiology, Faculty of Medicine, University of Novi Sad, Hajduk Veljkova 1, 21 000 Novi Sad, Serbia. Phone/Fax.: +381 21 529 148. E-mail: veliborcabarkapa@gmail.com

Introduction

Epidemiological data indicate that approximately 10% of adult population have some form of chronic renal disease that eventually may progress into a complete loss of kidney function [1]. However, before that, the majority of patients will die from fatal cardiovascular events, particularly from coronary heart disese [2]. Moreover, cardiovascular mortality is 10 to 30 times higher in hemodialysis patients compared to general population [3].

Dyslipidemia is a well-known traditional risk factor for premature atherosclerosis. According to the current guidelines for the diagnosis and treatment of cardiovascular disease (CVD), it is considered a major risk factor [4]. In renal patients, dyslipidemia is being present in 40–60% [5].

Lipid disturbance in chronic renal failure (CRF) are markedly expressed and specific. Due to the dysregulation of numerous enzymes, apolipoproteins and receptors, maturation and metabolism of HDL and metabolism of triglyceride-rich lipoproteins are decreased [5, 6]. A typical lipid profile in CRF is thus characterized by a combination of quantitative and qualitative abnormalities, including hypertriglyceridemia, decreased HDL-C levels, normal, mildly increased, or even mildly decreased total and LDL cholesterol levels, and an abnormal lipid subfraction profile with a predominance of atherogenic low-dense LDL (sd LDL) and HDL particles [7]. The retention of lipoprotein particles of modified structure and size occurs already in the early, pre-dialysis stage, before the elevation of plasma lipids, and persists even after successful transplatation [8]. Plasma lipids and apolipoproteins may hence be unreliable predictors of the cardiovascular risk in CRF-induced dyslipidemia, especially in the early stages of kidney disease.

The mechanism underlying the atherogenic lipoprotein profile associated with renal failure involves delicate metabolic interrelations within the whole lipoprotein system, which is typically present when major traditional risk factors such as hypertension, glucose intolerance and abdominal obesity co-occur [9, 10].

For such patient populations calculations of novel bioindices have recently been proposed, such as lipid tetrad index (LTI), lipid pentad index (LPI) [11, 12] and atherogenic index of plasma (AIP) [13], whose formulas comprise several lipid parameters (total cholesterol, triglycerides, HDL-C, apo A, apo B and Lp(a)). In addition, AIP is an indirect indicator of sdLDL levels [13].

Considering that there are no data about these approaches in CRF patients, the aim of this research was to evaluate the new lipid bioindices (LPI, LTI and AIP) and traditional lipid parameters and ratios (total cholesterol, triglycerides, LDL-C, HDL-C, non-HDL-C, Lp(a), apo A-I and B, apo B/A-I, LDL-C/HDL-C, non-HDL-/HDL-C, triglycerides/HDL-C) in patients with different stages of CRF (hemodialysed and non-hemodialysed).

Methods

The study was carried out in the Clinical Center of Vojvodina, Novi Sad, Serbia in the period January–December 2009. The study had previously been approved by an institutional ethics committee and all the subjects included had consented to participate. A total of 144 subjects were included – 96 with CRF [46 on chronic hemodialysis (HD) and 50 non-hemodialysed (non-HD) patients in different stages of CRF] and 48 controls with normal creatinine clearance (CrCl) and without hypolipemic or antihypertensive therapy.

The inclusion criteria were CRF of various etiologies and stages and chronic hemodialysis treatment lasting more than 18 months. Blood samples were collected on the first day of weekly hemodialysis, before connecting the patient with the dialyser and administering heparin. Patients with nephrotic syndrome, acute infection, liver disease, malignancies, previous or recent myocardial infarction, stroke or peripheral arterial disease were excluded from the study.

Analyses were performed immediately after blood-sampling. Serum levels of creatinine, urea, total C, and HDL-C, TG and creatinuria were measured using the standard biochemical methods, and apo A-I and B, Lp(a) and cystatin C by immunoturbidimetry.

Creatinine clearance was calculated by the formula:

$CrCl = [U_{Cr} \times 24\ h\ urine\ volume\ (ml)]/[S_{Cr} \times 1440\ (min)]$; Note: U_{Cr} urine creatinine (μmol/L) and S_{Cr} – serum creatinine (μmol/L)

The obtained values were normalized to 1.73 m^2 body surface area, sex and age. A deviation above 10% from the expected value in the past 6 months was taken as a criterion for the existence of CRF.

We calculated the values of LDL-C, non-HDL-C, and traditional indICes LDL-/HDL-C, non-HDL-/HDL-C, TG/HDL-C, and new bioindexes Lipid tetrad index (LTI) = TG x total C x Lp(a)/HDL-C; Lipid pentad index (LPI) = TG x total C x Lp(a) x apo B/A-I; Atherogenic index of plasma (AIP) = log (TG/HDL-C). All the parameters were translated into the SI units. The patients were classified accordingly into three risk categories for AIP: low < 0.11, intermediate 0.11–0.21, and high > 0.21 [14]. Since the indices LPI and LTI did not have normal distributions, we used variables logLPI and logLTI.

In addition, body mass index (BMI) was calculated for all subjects [15].

Descriptive statistics, including median, arithmetic mean, standard deviation (SD) and standard error (SE) were used to describe the studied parameters. The differences in distributions of individual parameters between study groups were analyzed using the parametric Student's *t*-test, or the non-parametric Mann-Whitney test in case a distribution showed a significant deviation. Linear regression analysis and Pearson coefficient of linear correlation were used to study the correlation between variables. The differences between the groups were illustrated using Box and Whisker plots and empirical distribution functions. Statistical analysis was performed using the Statistica 8.0 software. A value of $p < 0.05$ was considered statistically significant.

Results

The main characteristics of the study subjects are shown in Table 1. There were significant differences in age and BMI between the HD and non-HD patients.

Laboratory parameters and the calculated indices are presented in Tables 2 and 3.

Total C, TG, HDL-C, LDL-C, non-HDL-C, apo A-I, and non-HDL-/HDL-C levels, and apo B/A-I and TG/HDL-C ratios were significantly different in the HD patients compared with the other two groups. TG/HDL-C ratio was significantly higher in the non-HD patients compared with controls.

Table 1

Basic characteristics of subjects

Basic characteristics	HD patients	Non-HD patients	Control subjects
Number of subjects (f/m)	46 (17/29)	50 (21/29)	48 (19/29)
Age (years), $\bar{x} \pm SD$ (range)	50.4 ± 13.1* (27–76)	56.8 ± 12.1 (24–72)	52.4 ± 10.7 (32–73)
BMI (kg /m^2), $\bar{x} \pm SD$	24.7 ± 5.0*	26.8 ± 4.7	25.8 ± 2.8
Nephroangiosclerosis, n (%)	16 (34.6)	26 (52)	–
Glomerulonephritis chr, n (%)	9 (20)	5 (10)	–
Diabetes mellitus type 2, n (%)	8 (17.3)	3 (6)	–
Nephrolithiasis, n (%)	4 (8.6)	3 (6)	–
IgA nephropathy, n (%)	3 (6.5)	1 (2)	–
Pyelonephritis chr, n (%)	1 (2.2)	5 (10)	–
Other causes, n (%)	5 (10.8)	7 (14)	–

HD – hemodialysis; BMI – Body mass index; *$p < 0.05$ compared to non-hemodialysed patients; Other causes – analgesic nephropathy, polycystic kidney disease, not-recognized nephropaties

Table 2

Laboratory parameters

Parameters	HD patients ($\bar{x} \pm SD$)	Non-HD patients ($\bar{x} \pm SD$)	Control subjects ($\bar{x} \pm SD$)
Urea (mmol/L)	26.6 ± 7.5 ¶,‡	7.9 ± 4.6 * (med. 7.15)	5.3 ± 1.3
Creatinine (μmol/L)	976.9 ± 204.1 ¶,‡	140.6 ± 88.5 ‡ (med. 124.5)	91.9 ± 14.5
CrCl (ml/min/1.73m^2)	–	59.9 ± 26.7 ‡ (med. 57.5)	101.4 ± 15.5
Cystatin C (mg/L)	7.7 ± 1.6 ¶,‡	1.22 ± 0.6 ‡	0.92 ± 0.34
Total cholesterol (mmol/L)	4.6 ± 0.9 ¶,‡	5.33 ± 1.0	5.45 ± 0.79
Triglycerides (mmol/L)	2.1 ± 1.2 †,§	1.79 ± 1.10	1.38 ± 0.73
HDL-C (mmol/L)	1.0 ± 0.2 ¶,‡	1.3 ± 0.5	1.34 ± 0.32
LDL-C (mmol/L)	2.8 ± 0.7 II,‡	3.31 ± 0.8	3.48 ± 0.67
non-HDL-C (mmol/L)	3.6 ± 0.9 §,†	4.03 ± 0.8	4.15 ± 0.72

HD – hemodialysis; CrCl – creatinine clearance; HDL-C – high density lipoprotein cholesterol; LDL-C – low density lipoprotein cholesterol; *$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$ compared to control subjects; §$p < 0.05$, II$p < 0.01$, ¶$p < 0.001$ compared to non-HD patients

Table 3

Laboratory parameters and the calculated ratios

Parameters	HD patients ($\bar{x} \pm SD$)	Non-HD patients ($\bar{x} \pm SD$)	Control subjects ($\bar{x} \pm SD$)
Apo A-I (g/L)	1.1 ± 0.2 ¶,‡	1.3 ± 0.2	1.28 ± 0.14
Apo B (g/L)	0.96 ± 0.2	1.0 ± 0.2	1.03 ± 0.2
Lp (a) (g/L)	0.21 ± 0.3	0.18 ± 0.2	0.2 ± 0.3
LDL-C/HDL-C	2.9 ± 1.1	2.74 ± 0.8	2.71 ± 0.73
nonHDL-C/HDL-C	3.8 ± 1.3 §,*	3.31 ± 0.9	3.31 ± 0.92
Apo B/A-I	0.88 ± 0.3 §	0.76 ± 0.2	0.8 ± 0.22
Triglycerides/HDL-C	2.27 ± 1.7 §,‡	1.6 ± 1.2 *	1.1 ± 0.66
AIP	0.27 ± 0.3 §,‡	0.1 ± 0.3 *	- 0.03 ± 0.27
LTI	1979.2 ± 3118.5 *	2285.2 ± 6248.6 *	1210.8 ± 2412.2
log LTI	6.5 ± 1.6 *	6.4 ± 1.5 *	5.8 ± 1.5
LPI	80.1 x 10^3 ± 15.5 x 10^{5*}	78.1 x 10^3 ± 21 x 10^{5*}	49 x 10^3 ± 107 x 10^5
log LPI	9.98 ± 1.8 *	9.97 ± 1.4 *	9.3 ± 1.7

HD – hemodialysis; HDL-C – high density lipoprotein cholesterol; LDL-C – low density lipoprotein cholesterol; AIP – atherogenic index of plasma, LTI – lipid tetrad index, LPI – lipid pentad index; *$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$ compared to control subjects; §$p < 0.05$, II$p < 0.01$, ¶$p < 0.001$ compared to non-hemodialysed patients.

Distribution of patological values of LDL-/HDL-C, apoB/A-I and non-HDL-/HDL-C ratios in non-HD and HD patients are presented in Table 4.

The values below the upper limit of the confidence interval for the mean of the log LTI (6.23) were recorded in 70.83% of the controls, 46% of the non-HD patients and 36.9% of the HD patients. The values below the upper limit of the confidence interval for the mean of the log LPI (9.80) were recorded in 68.75%, of the controls, 46% of the non-HD patients and 39.13% of the HD patients.

Table 4

Distribution of the patients according to patological values of some lipid indices

Parameters	Categories	non-HD (%)	HD (%)
AIP	> 0.11	46.0	71.7
LDL-/HDL-C	> 3.4	16.0	17.4
Apo B/A-I	> 0.63 (m) > 0.54 (f)	30.0	54.3
Non-HDL-/HDL-C	> 3.25	54.0	62.5

AIP – atherogenic index of plasma; LDL-C – low density lipoprotein cholesterol; HDL-C – high density lipoprotein cholesterol; non-HD – non-hemodialysed patients; HD – hemodialysed patients; m – male; f – female

There was a significant difference in the mean logLPI and logLTI between the controls and the two groups of patients, but not between the HD and non-HD patients (Table 2). This was supported by the non-parametric Mann-Whitney test for LPI and LTI. However, considering great dispersion around both indices their values overlapped. This was illustrated on empirical function distribution plots in Figures 1 and 2.

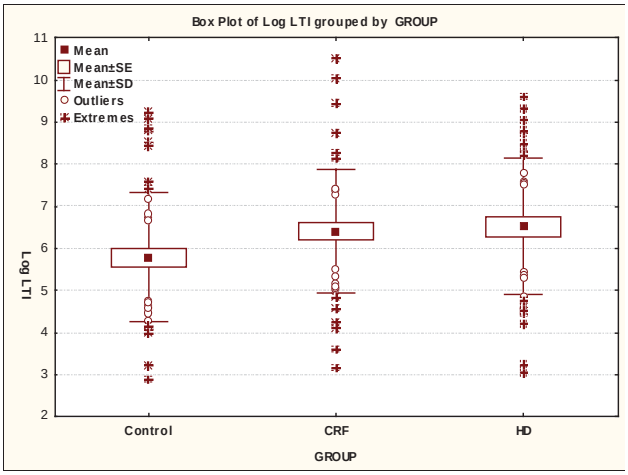

Fig.1 – Box plot of log lipid tetrad index (log LTI)

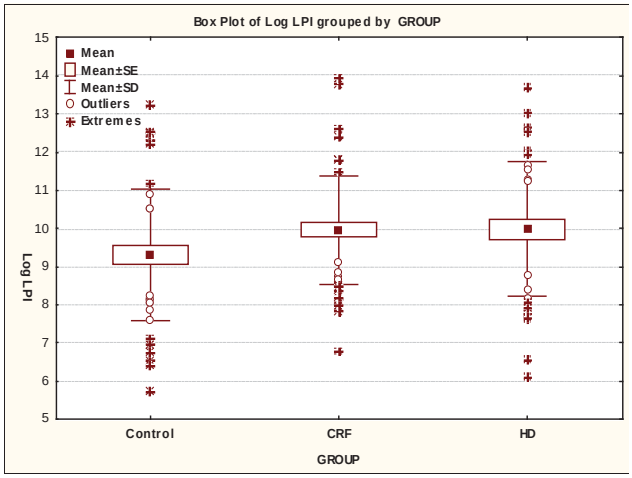

Fig. 2 – Box plot of log lipid pentad index (log LPI)

Similar results were obtained for AIP, however, the significance of the difference in the means in the controls and the HD patients ($p < 0.001$) was higher than in the case of LPI and LTI ($p < 0.05$). Box-plots (Figure 3) showed that most HD patients had AIP over 0.11 (71.7%), which was significantly higher ($p = 0.0001$) compared with the control group, where 31.3% of the subjects had this finding (Table 3).

In the non-HD patients, however, the percentage was insignificantly higher in comparison with the control group (46%, $p = 0.067$).

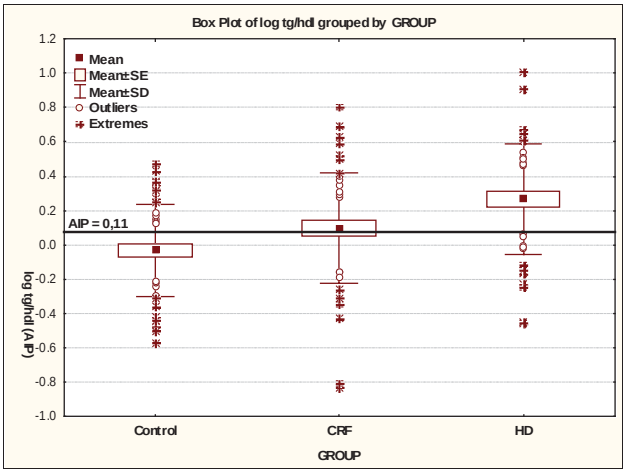

Fig. 3 – Box plot of atherogenic index of plasma (AIP)

Discussion

Cardiovascular morbidity and mortality are present already in mild renal impairment [16, 17] and increased in end-stage renal disease [18].

Among many factors contributing to accelerated atherosclerosis in CRF, dyslipidemia is found in 40–60% patients [5]. Regardless the etiology, patients with CRF develop complex qualitative and quantitative abnormalities, predominantly hypertriglyceridemia and HDL-decrease. In the present

study, the highest triglyceride levels, the lowest HDL-C levels, and the highest values of TG/HDL-C ratio were observed in HD patients. Beside this, the values of TG/HDL-C ratio, that is one of the most potent predictors of cardiovascular disease [8], were significantly higher in the non-HD patients compared with the controls.

More than half of the HD group had high-risk HDL-C levels, which is similar to the results of other authors [19, 20].

Total and LDL cholesterol levels were lowest in the HD patients, compared to the controls and non-HD patients ($p < 0.001$), whereas the levels in the non-HD patients were similar to those of the controls. Most previous studies have also reported similar or lower values [9, 19, 21–23]. Unlike general population, lower plasma cholesterol in CRF has been associated with a higher cardiovascular mortality [24].

Similarly to the results of Schreier at al. [25], the results of our study show that non-HDL-C may not be appropriate marker for risk assessment among CRF patients. The level of non-HDL-C in the HD patients was significantly lower compared with the controls, with no differences among the other groups. The level of non-HDL-C/HDL-C ratio was significantly higher in the HD patients compared with the others groups, mainly due to low HDL-C levels.

More recent research indicates that apolipoproteins are more effective atherogenic markers than plasma lipids: apoA-I is a useful summary index of the antiatherogenic properties of HDL [26–28], apoB of total atherogenic particle number [29–32], and apo B/A-I ratio is better than any cholesterol ratio [26, 33, 34]. In our study, apoA-I was significantly lower only in the HD patients, whereas apoB did not differ significantly, similarly to the results of Alabakovska et al. [19]. The frequency of pathological ratio apoB/A-I was significantly higher than LDL-/HDL-C in both groups of patients in our study.

Although relations between Lp(a) and renal functional status in patients with CRF have been explored in numerous studies, the results obtained are contradictory [19, 35, 36]. In our study, Lp(a) levels in the HD and non-HD patients did not differ significantly from the controls. Furthermore, there was no significant correlation between Lp(a) levels and CrCl ($r = 0.12$, $p = 0.51$), contrary to some other studies dealing with early stages of CRF [37].

Literature data on LTI and LPI in CRF patients are scarce. Despite a significant difference in bioindices between healthy controls and patients with CRF, we did not obtain adequate delineations, which prevented us from determining reference values. An explanation could lie in similar distributions of Lp(a) levels and the existence of extreme pathological values of certain lipid parameters in both controls and patients that is characteristic for our geographic area.

Furthermore, there are no literature data on AIP in patients with CRF. We found the values of > 0.11, which indicated moderate and high atherogenic risk, in 31.3% of the control subjects, 56% of non-HD patients and 71.7% of HD patients. It is significantly different between the groups, particularly controls and HD patients. These findings were expected, since CRF is characterized by the predominance of atherogenic sdLDL particles.

Conclusion

In conclusion, TG, HDL-C, apo A-I, non-HDL-/HDL-C, and apoB/A-I ratios, are important lipid markers only in HD patients. Non-HDL-C is not a suitable marker in CRF patients. Calculations of bioindices LPI and LTI did not show significant benefits in our study population. In contrast, significantly increased pathological values of AIP that we registered in our study in both HD and non-HD patients suggest that this index may have a potential application in routine clinical practice as an indirect indicator of sdLDL levels. Besides AIP, TG/HDL-C ratio could also be a suitable marker for evaluation of lipid disturbances in different stages of CRF.

Acknowledgements

This study was sponsored by the research project of the Serbian Ministry of Science, number 175036.

REFERENCES

1. *Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P*, et al. Prevalence of chronic kidney disease in the United States. JAMA 2007; 298(17): 2038−47.
2. *Hage FG, Venkataraman R, Zoghbi GJ, Perry GJ, DeMattos AM, Iskandrian AE*. The scope of coronary heart disease in patients with chronic kidney disease. J Am Coll Cardiol 2009; 53(23): 2129−40.
3. *Yilmaz FM, Akay H, Duranay M, Yilmaz G, Oztekin PS, Koşar U*, et al. Carotid atherosclerosis and cardiovascular risk factors in hemodialysis and peritoneal dialysis patients. Clin Biochem 2007; 40(18): 1361−6.
4. *National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)*. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002; 106(25): 3143−421.
5. *Đurđević-Mirković T, Ćurić S*. Lipid metabolism disturbance in kidney diseases. In: *Đerić M, Stokić E, Todorović-Đilas Lj,* editors. Hyperlipoproteinemias-current aspects. Novi Sad: Physicians Society of Vojvodina-Serbian Physicians Society; 2005. p. 255−60. (Serbian)
6. *Vaziri ND*. Dyslipidemia of chronic renal failure: the nature, mechanisms, and potential consequences. Am J Physiol Renal Physiol 2006; 290(2): F262−72.
7. *Rajman I, Harper L, McPake D, Kendall MJ, Wheeler DC*. Low-density lipoprotein subfraction profiles in chronic renal failure. Nephrol Dial Transplant 1998; 13(9): 2281−7.
8. *da Luz PL, Favarato D, Faria-Neto JR Jr, Lemos P, Chagas AC*. High ratio of triglycerides to HDL-cholesterol predicts extensive coronary disease. Clinics (Sao Paulo) 2008; 63(4): 427−32.
9. *Bayés B, Pastor MC, Bonal J, Juncà J, Hernandez JM, Riutort N*, et al. Homocysteine, C-reactive protein, lipid peroxidation and mortality in haemodialysis patients. Nephrol Dial Transplant 2003; 18(1): 106−12.

10. *Herzog CA, Ma JZ, Collins AJ.* Poor long-term survival after acute myocardial infarction among patients on long-term dialysis. N Engl J Med 1998; 339(12): 799−805.
11. *Das B, Daga MK, Gupta SK.* Lipid Pentad Index: A novel bioindex for evaluation of lipid risk factors for atherosclerosis in young adolescents and children of premature coronary artery disease patients in India. Clin Biochem 2007; 40(1−2): 18−24.
12. *Bogavac-Stanojević N, Jelić-Ivanović Z, Spasojević-Kalimanovska V, Spasić S, Kalimanovska-Ostrić D.* Lipid and inflammatory markers for the prediction of coronary artery disease: a multi-marker approach. Clin Biochem 2007; 40(13−14): 1000−6.
13. *Dobiásová M, Frohlich J.* The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)). Clin Biochem 2001; 34(7): 583−8.
14. *Holmes DT, Frohlich J, Buhr KA.* The concept of precision extended to the atherogenic index of plasma. Clin Biochem 2008; 41(7−8): 631−5.
15. *Tsigos C, Hainer V, Basdevant A, Finer N, Fried M, Mathus-Vliegen E,* et al. Management of obesity in adults: European clinical practice guidelines. Obes Facts 2008; 1(2): 106−16.
16. *Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY.* Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004; 351(13): 1296−305.
17. *Foley RN, Wang C, Collins AJ.* Cardiovascular risk factor profiles and kidney function stage in the US general population: the NHANES III study. Mayo Clin Proc 2005; 80(10): 1270−7.
18. *Chan DT, Irish AB, Dogra GK, Watts GF.* Dyslipidaemia and cardiorenal disease: mechanisms, therapeutic opportunities and clinical trials. Atherosclerosis 2008; 196(2): 823−34.
19. *Alabakovska SB, Todorova BB, Labudovic DD, Tosheska KN.* LDL and HDL subclass distribution in patients with end-stage renal diseases. Clin Biochem 2002; 35(3): 211−6.
20. *Rajman I, Harper L, McPake D, Kendall MJ, Wheeler DC.* Low-density lipoprotein subfraction profiles in chronic renal failure. Nephrol Dial Transplant 1998; 13(9): 2281−7.
21. *Ozsoy RC, Kastelein JJ, Arisz L, Koopman MG.* Atorvastatin and the dyslipidemia of early renal failure. Atherosclerosis 2003; 166(1): 187−94.
22. *Guerrero A, Montes R, Muñoz-Terol J, Gil-Peralta A, Toro J, Naranjo M,* et al. Peripheral arterial disease in patients with stages IV and V chronic renal failure. Nephrol Dial Transplant 2006; 21(12): 3525−31.
23. *Parsons DS, Reaveley DA, Pavitt DV, Misra M, Brown EA.* Lipoprotein (a) levels in those with high molecular weight apo (a) isoforms may remain low in a significant proportion of patients with end-stage renal disease. Nephrol Dial Transplant 2003; 18(9): 1848−53.
24. *Iseki K, Yamazato M, Tozawa M, Takishita S.* Hypocholesterolemia is a significant predictor of death in a cohort of chronic hemodialysis patients. Kidney Int 2002; 61(5): 1887−93.
25. *Schreier L, González AI, Elbert A, Berg G, Wikinski R.* Utility of non-high-density lipoprotein cholesterol in hemodialyzed patients. Metabolism 2004; 53(8): 1013−5.
26. *Walldius G, Jungner I, Aastveit AH, Holme I, Furberg CD, Sniderman AD.* The apoB/apoA-I ratio is better than the cholesterol ratios to estimate the balance between plasma proatherogenic and antiatherogenic lipoproteins and to predict coronary risk. Clin Chem Lab Med 2004; 42(12): 1355−63.
27. *Francis MC, Frohlich JJ.* Coronary artery disease in patients at low risk--apolipoprotein AI as an independent risk factor. Atherosclerosis 2001; 155(1): 165−70.
28. *Luc G, Bard JM, Ferrières J, Evans A, Amouyel P, Arveiler D,* et al. Value of HDL cholesterol, apolipoprotein A-I, lipoprotein A-I, and lipoprotein A-I/A-II in prediction of coronary heart disease: the PRIME Study. Prospective Epidemiological Study of Myocardial Infarction. Arterioscler Thromb Vasc Biol 2002; 22(7): 1155−61.
29. *Vaverkova H, Karasek D, Novotny D, Jackuliakova D, Lukes J, Halenka M,* et al. Apolipoprotein B versus LDL-cholesterol: Association with other risk factors for atherosclerosis. Clin Biochem 2009; 42(12): 1246−51.
30. *Benn M.* Apolipoprotein B levels, APOB alleles, and risk of ischemic cardiovascular disease in the general population, a review. Atherosclerosis 2009; 206(1): 17−30.
31. *Benn M, Nordestgaard BG, Jensen GB, Tybjaerg-Hansen A.* Improving prediction of ischemic cardiovascular disease in the general population using apolipoprotein B: the Copenhagen City Heart Study. Arterioscler Thromb Vasc Biol 2007; 27(3): 661−70.
32. *Chien KL, Hsu HC, Su TC, Chen MF, Lee YT, Hu FB.* Apolipoprotein B and non-high density lipoprotein cholesterol and the risk of coronary heart disease in Chinese. J Lipid Res 2007; 48(11): 2499−505.
33. *Sniderman AD, Furberg CD, Keech A, Roeters van Lennep JE, Frohlich J, Jungner I,* et al. Apolipoproteins versus lipids as indices of coronary risk and as targets for statin treatment. Lancet 2003; 361(9359): 777−80.
34. *Walldius G, Jungner I.* Apolipoprotein B and apolipoprotein A-I: risk indicators of coronary heart disease and targets for lipid-modifying therapy. J Intern Med 2004; 255(2): 188−205.
35. *Labudovik D, Tosheska K, Alabakovska S, Bogdanska J, Todorova BB.* Apo pro tein(a) isoforms and plasma LP(a) concentration in members of four families. J Med Biochem 2008; 27: 439–46.
36. *Cauza E, Kletzmaier J, Bodlaj G, Dunky A, Herrmann W, Kostner K.* Relationship of non-LDL-bound apo(a), urinary apo(a) fragments and plasma Lp(a) in patients with impaired renal function. Nephrol Dial Transplant 2003; 18(8): 1568−72.
37. *Sechi LA, Zingaro L, De Carli S, Sechi G, Catena C, Falleti E,* et al. Increased serum lipoprotein(a) levels in patients with early renal failure. Ann Intern Med 1998; 129(6): 457−61.

Received on December 21, 2010.
Revised on June 13, 2011.
Accepted on June 23, 2011.