LIPOPROTEIN LIPASE ACTIVITY AND DYSLIPIDEMIA IN UREMIC PATIENTS TREATED WITH HEMODIALYSIS

1. **Prof. Dr. Nasir Behxheti, MD,PhD**[1] , 2. Doc. Dr. Sci. Med. Lutfi Zylbeari MD, PhD[1,2] ,

3. Mr. Dr. Zamira Bexheti[1], 4. .Mr. Dr.Gazmend Zylbeari[2],5. Mr.Phar. Mirlind Behxheti[1]

1. The State University of Tetovo, Medical Faculty, Tetova, Macedonia
2. Special Private Hospital for Nephrology and Hemodialysis ,, Vita Medical Group" -Tetova, Macedonia

Abstract. There are documented facts that uremic patients present clinical picture of dyslipi-demia associated with the earlier representation of atherosclerosis and serious cardiovascular complications, peripheral arterial lessions with large number and the youngest in comparison with the older population. It is supposed that in uremic patients the subtle changes in the morphology of lipid molecule further increase their atherogenicity (due to greater affinity for sticking to the subendothelial wall of oxidized cholesterol (oxLDL-ch) and changed. Subfraction β 1-HDL-ch is minor subfraction who acts as a initial acceptor of cholesterol Initiation of vaccum created by his own cells and transport under the influence of lecithin acyl cholesterol transferase (LCAT) fractionβ□1-HDL-ch passes in β migrant cholesterol -HDL. LCAT in normal plasma affects maturation (maturation) to HDL-ch reconstructed into spherical HDL poorer with lipids in HDL-ch with lipids. Reduced activity of Lipoprotein lipase (LPL) for approximately 33-46% is due to the excessive cumulation of toxins or cytokine-us (Interleukin-1, Interleukin-6, Interleukin- 1α, Interleukin-1 β and this phenomenon counted among the main causes of pathological adjustments in lipid metabolism of uremic patients with lower concentrations of HDL-ch, elevated concentrations triglycerides (TG), total cholesterol (TCh) and LDL-ch. Purpose of paper:The aim of the paper was to verify the effect and activity Lipoprotein Lipase (LPL), its impact on the presentation of hypertriglyceridemia and dyslipidemia in uremic patients treated with chronic HD intermitent randomized by age sex and basic disease that has lead them to uraemia with values obtained from lipid parameters and LPL from the group of healthy individuals who served as the control group. The paper also aimed to document the correlation between lipid profile and LPL and influence of their disorders in the appearance of uremic dyslipidemia with consequences of early atherosclerosis (Atherosclerosis uraemica praecox). The paper aims also in proposing measures for drug prevention and treatment and correction of hypertriglyceridemia and cholesterolemia with what would influence the prevention and inhibition of early atherosclerotic processes of uremic patients. The material and methodsIn the prospective cohort study, (,, cross-section ") in total are included N 0 = 520 examined of whom 260 were of uremic patients treated with dialysis while 260 were healthy individuals who served as the control group. Of the total number of patients (N O = 260) treated with HD-110 (45%) were girls while-150 (55%) were male, with an average age: 18.0 □58.20 years, treated with dialysis more than 6 years in nephrology-Skopje Clinic and Hospital Clinical examination Tetova.And high prevalence of coronary artery atherosclerosis and cerebral. Disorders of lipid meta-bolism in patients with terminal chronic renal insufficiency (TCRI) are first documented in 1827 by Dr. Bright (1).

Term Index: Lipoprotein Lipasae (LPL), ESRD, hemodialysis (HD), Lipids profiles

1 Introduction

Patients with terminal chronic renal failure (TCRF) most often suffer from hyperlipoproteinemia of type IV of secondary hyperlipoproteinemia (accor-ding to Frederickson's classification) in which predo-minate higher concentrations of triglycerides (TG) (high values of 30-100%) (2). Cholesterol and tryglicerides in fact are not actually hidrosolubile, however their solubility in water preferably is improved if they relate to the carrier (carrier) known as plasma special apoproteine that allow their

transport through the blood in the form of lipoproteinemic molecules (4,5,6).
Lipid abnormalities during uremia of all lipopro-teinemic particles (LPS) .At uremic patients LCAT activity is reduced approximately by 30-46%. Clinical trials with (incubation inhibitor plasma LCAT in uremic patients) have verified and documented the above mentioned position and in conclusion shows that uremic accelerating atherosclerosis is due to changed catabolism of the Pre β1HDL-ch (3) .

Prof. Dr. Nasir Behxheti,MD,PhD[1]- The State University of Tetovo, Medical Faculty, Tetova, Macedonia

Doc. Dr. Sci. Med. LUTFI ZYLBEARI, MD, PhD[1,2]- The State University of Tetovo, Medical Faculty, Tetova, Macedonia , Special Private Hospital for Nephrology and hemodialysis "Vita Medical Group" - Tetova, Macedonia
3. Mr. Dr. Zamira Bexheti[1]-Special Private Hospital for Nephrology and hemodialysis "Vita Medical Group" - Tetova, Macedonia

4. .Mr. Dr.Gazmend Zylbeari[2]- Special Private Hospital for Nephrology and hemodialysis "Vita Medical Group" - Tetova, Macedonia

5. Mr.Phar. Mirlind Behxheti[1] - The State University of Tetovo, Medical Faculty, Tetova, Macedonia ,

Hypertriglyceridemia dominates due to its growth in the composition and structure of VLDL, IDL, HDL-ch, LDL-ch. Cholesterol shows no significant difference between uremic patients and the population without uremia. The composition of cholesterol is higher in the composition of the VLDL is faction, while lowest in the composition of HDL-ch faction. Carriers of molecules of lipids-apoproteins belong to class A, V and S. Concentrations of Apolipoproteines AI (ApoA-I in the structure of LDL-ch are more decreased while the apolipopoteines-A-IV (or a-IV) are more increased . Concentrations Apo B_{48} / B_{100} are increased in the composition of the VLDL class, while $APOC_2$ / C_3 are each lower respectively increased while the structure of the LDL-ch. Low HDL concentrations ch to patients with terminal chronic renal failure (TCRF) influence the reduction of reverse transport of cholesterol in the liver terms with what created even more favorable conditions for the accumulation of cholesterol through ekstrahepathale tissue (7). The ratio of reduced bet-ween $APOC_2$ / $APOC_3$ to reducing signifycantly affects activity of Lipoprotein lipase (LPL). The pres-nce of elevated concentration of Apo B_{48} / B_{100} and the Apo-A faction in the composition of VLDL, VLDL Namely in / LDL suggests to the increased presence *of β- VLDL Alimentary in circulation. The presence of ApoA + ApoC in the composition of LDL-ch leads to functional insufficiency (functional defect) to LPL, while reducing activity of lecithin-cholesterol-acyl-transferase (LCAT) and low HDL concentrations significantly affect the disorder of the utilisation of cholesterol in tissue.*(8,9 , 10, 11). It is assumed that hypertriglyceridemia and reduced concentrations of HDL-ch proathe-rogenic are one of the main causes of decreasing LPL activity and its the lower concentra-tion (12,13,14,15) . Factors such as, poor nutrition, physical inactivity, uremic toxins, and inflammation (MIA syndrome-Malnutritio-Atherosclersosis-Infla-matio) which factors are frequent in uremic patients counted as additional factors in the reduction of *enzy-me* LPL- activity *much important in lipid metabolism*. More further during each dialysis treatment, the use of heparin inhibits the release of LPL which also reduces LPL activity. This results in a degradation of enzyme activity and lack of activity of LPL for 10 hours since the beginning of hemodialysis. Thus, the use of anticoagulant during hemodialysis therapy, besides other consequences, a lack of the function and activity of LPL which contri-butes significantly in occurrence of harmful effects on metabolism regula-tion in lipids. Some studies have confirmed that some uremic toxins as angiopoietina, protein 3 and 4, accumulate in the blood of uremic patients treated with HD significantly reduces LPL activity (this argu-ment is verified in animal experime-nts they have caused chronic kidney injuries artificially). To avoid blood coagulation in HD, and for reducing the effect of heparin inhibition to LPL activity, the successful anticoagulant widely used is the heparin with low molecular weight. Lipoprotein lipase (LPL), together with TG come to vascular endothelium with limiting of the lipolitic enzyme(16). Reduced hepatale synthesis of ApoA-I in uremic patients is considered funda-mental cause for low plasma concentrations so as a result is increased compensatory synthesis of Apo B.Egsist documented facts that pararatireoid hormone (PTH) prevents and inhibits the synthesis of hepata-le lipase and Lipoprotein Lipase (LPL) however does not affect to the membranous expres-sion of receptor for HDL-ch (SR-B1) and synthesis apolipo-proteine-I (Apo-I). Improved genetic expression and increased synthesis of specific mRNA $ApoA_1$ in uremic environ-ments (uremic patients) is the main postulate on the definitive and radical solution to dyslipidemia in this group of patients. (17). The uremic patients hipetrygli-ceridemia in parallel is associated with increased

concentrations of V sub-class composed of LDL-ch . Of uremic patients treated with hemodialysis proatherogenic effects of HDL-ch are degraded and extremely low which tells us structural changes and increased affinity with the produ-ction of his own to oxidized cholesterol (oxLDL-ch). All factions of lipoprotein have equal affinity to aterogen regardless faction in uremic patients. Atherosclerotic risk of uremic patients treated with HD and presumed to have been closely associated with electronegative charged subfraction of LDL ($LDL^{-)}$ (18,19,20).
The regular application of heparin during hemodialysis intravenously *(2500-10000 IU pro dialysis)* can not stimulate activity of Lipoproten Lipase (LPL) but still reduces and inhibits the synthesis (the already reduced) of LPL (especially synthesis of hepatale lipase) which selectively eliminates from circulation ,, by *remaining cells - remmnant cells "* (21). With the mentioned high inhibitor impact on the activity of LPL, the *ratio between APOC-II* ↓ / ↑ *APOC-III* . Because it is known that HDL-ch is reservoir for APOC-II and therefore in cases where the concentration is reduced then is a lot easier to justify inverse correlation which is found between hypertriglyceridemia and low concentrations of HDL ch. It is assumed that the uremic patients treated with HD exist circulating inhibitors of lipases (22). The application of heparin (during dialysis) further reduces the activity of LPL, however attempts of leadership in hemodialysis does not show any significant lipolitic positive effect (23). A large number of studies have established that there exists some significant difference in the improvement of dyslipidemia among patients with preterminal chronic renal insufficiency compared to patients with TCRI treated with hemodialysis, which means that the very TCRI (because of silent inflammation) may affect the reduction of LPL activity (24) .

2 MATERIAL AND METHODS

In the prospective cohort study, (,, cross-section ") in total are included N^{0} = 520 examined of whom 260 were of uremic patients treated with dialysis while 260 were healthy individuals who served as the control group. Of the total number of patients (N^{O} = 260) treated with HD-110 (45%) were girls while-150 (55%) were male, with an average age: 18.0 □58.20 years, treated with dialysis more than 6 years in nephrology-Skopje Clinic and Hospital Clinical examination Tetova. Healthy controller group (voluntary blood donors) also were 110 (45%) women and 150 (55%) men with the same group of patients according to age, gender and religious affiliation and national belonging. Average age, gender and nationality of patients examined and controlling group are presented in a table 1-4. According to the average age difference between female and male gender proved non significant for *p = 0.0005* which shows a homogeneous group. Of all patients treated with HD during the seanses we applied dialysis molecule heparin the highest weekly dose of: 8500-18750 IE. Blood was taken for routine analysis in the 8 am breakfast at room temperature of 19-24 ^{0} C, before the start of dialysis procedure after fast minimum 12 hours in order to avoid the effect of lipid apsorbtion by intestines.In all the patients in the control group there were examined following parameters: total Lipids (TL), Triglycerides (TG), total cholesterol (TCh), HDL-ch, LDL-ch, Lipoprotein lipase (LPL), serum urea (URS) , serum creatinine (CRS), serum uric acid (Aus). In our paper we analyzed the patients with the most common underlying disease that has led to dialysis with: glomerulonefritis patients with chronic arterial hypertension, diabetes mellitus (Nefron-made diabetic) and undifferentiated basic disease (Tables number: 8- 10). Of all parameters that were examined once a month with three consecutive measurements and results obtained represent the average value of the three measurements of parameters examined in identical conditions.

Table number 1: Presentation of the total number of examiners **(N^{O} = 520-** uremic patients and check on control group), by gender

Gender	The total number N^{O} = 520 (uremic+Control goup)	%
Male	300	57.70
Female	220	42.30

Table number 2: Presentation of uremic patients (N ^{O} = 260) according to **nationality** and **sex**

Gender	Macedonian N ^{O} = 100	Albanian N ^{O} = 160
Male	55 (60 %)	90 (65 %)
Fenale	4 5 (45 %)	70 (35 %)

Of the total group of patients there were 100 Macedonian nationality uremic patients (60% male and 40% female), while 160 were of Albanian nationality (65% male and 35 women) (tab. Number 2).

Table number 3: The average age of uremic patients

Number	Average	Minimum	Maximum	± SD
260	58.20	18:00	74	13:40

Table number 4: The average age of uremic patients according to gender

Gender	Number	Average	Minimum	Maximum	± SD
Men	145	57.40	19	74	14:50
Women	115	59.50	18	68	12.80

The average age of uremic patients by gender was = 58.90 ± 13.60 years old (table 4). The average age was identical between the sexes nosignificant contrast to p = 0.0005 which shows a homogeneous group of patients.

Table number 5: reference values of lipid parameters and LPL and authors according to which method was defined

Lipid Fraction	Reference Values	Autor
TL	4-10 g / l	Zollner & Kirsch (43)
TG	0.68 - 1.70 mmol / l	G. Bucolla & H.David (44)
TCh	3.1 - 5.2 mmol / l	CCAllain et al. (45)
LDL-ch	<3.4 mmol / l, high risk> 4.1 mmol / l	Friedewalde & Frederickson (46)
HDL-ch	1.6 mmol / l, the highest risk <0.9mmol / l	G.Warnick et al (47)
LPL	5.6 - 51.3 u / L	Tietze et al ..Steinberg WM NW, SS Goldstein, ND Davies et al., Leybold A W.1 Junge (48,49,50).

Statistical analysis of the examined material

Statistical basic methods that were used are the arithmetic mean value and standard devijacioni X ± SD. Comparative statistics and LPL lipid parameters betwe-en the two groups was analyzed by test called STUDENTOV and for examples of

dependent or independent and non-parametric tests were used the tests: Mann-Whitney and Wilcoxon's test. Statistically significant The differences between the Group of patients and control group obtained the values of lipid parameters and test LPL analyzed the so-called ,, Anonova Two-Factor "with the amounts of domestic statistics for p <5%, Namely p <statistical 0.0005.Dependence between parameters that are examined is calculated with linear regression formula (y = Bx + A) it is also calculated the coefficient of correlation ,, r "with statistical accuracy for ,, p 'of less averages and proportional / x, p /) were tested with accuracy higher than 95%, or rather, for Mr. > SEM 1.78.The results of the lipid profile and LPL are presented in the form of graph-cones, table and in than 1% Namely p <0.0001. And the frequency distribution was tested with test c ^{2} The amount of change (z) between the mean values of parameters analyzed / arithmetic averages and proportional / x, p /) were tested with accuracy higher than 95%, or rather, for Mr.> SEM 1.78.The results of the lipid profile and LPL are presented in the form of graphicones, table and in the form of processed diagrams made with standard statistical program (Statistic for Windows, version 6.0 A, Stat.softincTulsa, OK USA.

the form of processed diagrams made with standard statistical program (Statistic for Windows, version 6.0 A, Stat.softincTulsa, OK USA.

3 RESULTS OBTAINED BY THE ANALYSIS OF PRODUCTS OF DEGRADED NITROGEN, LIPIDS AND LIPOPROTEIN LIPASE

Table number 6: average serum urea (sUr), serum creatinine sCr) and uric acid (sAU) of uraemia patients treated with HD

Parameters at	Female = 115 (45%)		Men = 145 (55%)		Total = 260 (100%)	
	Average	± SD	Average	± SD	Average	± SD
sUr (mmol / l)	34 .80	6 .30	34 .60	6 .50	33 .80	6 45
sCr mmol / l	870.60	184, 80	905.0	254 .70	875.60	219.60
sAu □□mol / l)	394.20	75.40	375.90	64.60	382.5	68.90

In table number 6 is observed higher value of the urea, creatinine and uric acid in patients screened-expected results from this group of patients.
In the next tables will present average values obtained from analyse of uremic patients treated with HD for parameters: LT, TG, CHT, LDL-ch, ch HDL and LPL by gender and between their correlation

Table number 7: Presentation of average values of the parameters of examined patients - **female gender**

Parameters	Number	Average	Minimum	Maximum	± SD
LPL	115	22:33	2.80	62.80	16:00
TL	115	10.7	3.80	13:00	1.82
TG	115	20.3	30.1	4.60	0.86
TCH	115	19.5	30.1	30.7	28.1
HDL-ch	115	18.1	0.80	1.80	0.60

LDL-ch	115	3.80	**1.80**	4:40	0.70

Table number 8: Presentation of average values of parameters of examined patients-**male gender**

Parameters	Number	Average	Minimum	Maximum	± SD
LPL	**145**	19:35	**1.80**	58.00	13:00
TL	145	6.12	**2:50**	15:00	10.2
TG	145	2.80	**20.1**	310	0.70
TCH	145	27.5	**0.80**	7.80	1:57
HDL-ch	145	12.1	**12:50**	10.2	12:50
LDL-ch	145	3.78	**1:40**	20.4	0.80

Table number 9: Presentation of average values of the examined parameters of patients with under basic disease, **chronic glomerulonephritis**

Patients Chronic Glomerulonephritis N ^{O} = 85 *(32.70.%)*						***Group controller***		
Parameter	**Number**	**Average**	**Minimum**	**Maximum**	**± SD**	**Average**	**± SD**	***p***
TL	88	27.8	**2:50**	15:00	2.83	6:50	0.60	0.0001
TG	85	3:40	**1:40**	4:50	0.75	30.1	0.63	0.0001
T Ch	85	23.5	**1.80**	7:40	12.1	4.95	22.1	0.0053
HDL-ch	85	1.0 2	**0.80**	1. 15	0. 40	1.60	0.7 0	0.0001
LDL-ch	85	3:40	**1:40**	4.80	1018	2.75	1:03	0.0001
LPL	**85**	**1 2:50**	**1.80 ↓↓**	**38.00**	**8.60**	**24.20**	**9.2 0**	**0 .0001**

Table nr.9 shows significant differences between average values between examined parameters which appear in patients with chronic glomerulonefrit and group controller. Of the two groups with a significant difference it is higher with p <0.0001 compared with values obtained from the control group, except the TCH where p = 0.0053.

Table number 10: shows the average values of the examined parameters of patients with basic disease: **Essential Hypertension**

Patients with Ess Hypertension. = N ^{O} 70 (27.00%)						***Group controller***		
Parameter	**Number**	**Average**	**Minimum**	**maximum**	**± SD**	**Average**	**± SD**	***p***
TL	70	30.7	5:00	11:50	1.70	6:50	0.60	0.0001
TG	70	**14.3**	1:40	4.60	1.66	30.1	0.63	0.0001
T Ch	70	5:00	30.1	30.7	1:46	4.95	22.1	0.3 400
HDL-ch	70	**1. 06**	0.80	3. 50	0.60	1.60	0.71	0.0001
LDL-ch	70	3.80	1.80	4.80	0.72	2.75	1:03	0.0001

LPL	**70**	**10.60**	**2.5 0 ↓↓**	**29.80 0**	**8.60**	**24.20**	**22.9**	**0.0 001**

By table number 10, it is observed that differences that appear in average values between examined parameters of both groups is a high significant difference for p <0.0001, exept in TCH p> 0.05. Parameter values: LT, TG, LDL-ch, are higher in patients with **HTA** compared with values obtained from the group controll. Lower values are registered only HDL -ch (1.06) and LPL (2.50 u / L) from the group of patients compared with the group controll an extremely high contrast significant for p <0.0001.

Table numer 11: Shows the average values of the examined parameters of patients with basic disease: **Diabetes mellitus**

Patients with Diabetes Mellitus N O = 55 (21:15%)						***Number controller***		
Parameter	**Number**	**Average**	**Minimum**	**maximum**	**± SD**	**Average**	**± SD**	***p***
TL	55	7.62	2:50	12.60	2.82	6:50	0.60	0.0001
TG	55	**3.85**	2:40	4.60	0.70	30.1	0.63	0.0001
T Ch	55	5:34	20.4	30.7	0.91	4.95	22.1	0.0210
HDL-ch	55	**1:03**	12:50	2.60	0.92	1.60	0.71	0.0001
LDL-ch	55	3:46	1:50	4.80	0.92	2.75	1:03	0.0001
LPL	**55**	6:00	**1:15 ↓↓**	15.0	10:20	24.20	22.9	0.0001

Table number 11, shows significant differences between the parameters of p in examined the patients with diseases **Diabetes- mellitus and control group.** The difference was shown between the average values of the examined parameters (of the two groups) is statistically significant value for parameters: LT, TG, LDL-ch, Thol which values are higher in uremic patients compared with control group values for p <0.0001. Furthermore the lowest values were observed only in patients HDL-ch (1.03), LPL (15.1 u / L) compared with control group.

Table numer 12: Shows the average values of the examined parameters of pacieneteve with basic disease, **nephropathy of undifferentiated**

Patients with Undifferentiated Nephropathy N O = 50 (19:23%)						**Number controller**		
Parameter	**Number**	**Average**	**Minimum**	**Maximum**	**± SD**	**Average**	***± SD***	***p***
TL	50	7.72	6:00	11:00	1:53	6:50	0.60	0.0001
TG	50	3.60	30.1	3.90	0.88	30.1	0.63	0.0001
T Ch	50	4.74	2:40	7.60	1.70	4.95	22.1	0.0103
HDL-ch	50	15.1	0.80	2:50	0.61	1.60	0.71	0.0320
LDL-ch	50	3:57	1.80	4.80	1:03	2.75	1:03	0.0001
LPL	**50**	**2 0:50**	**12 .60?!**	**3 4:20**	**1 1:40**	**24.20**	**22.9**	**00258**

Table number 12, shows significant differences between the parameters of p examined in the patients with diseases **of undifferentiated nephropathy and control group.** The difference was shown between the average values of the examined parameters (of the two groups) is statistically significant value for parameters: LT, TG, LDL-ch, Thol which values are higher in uremic patients compared with control group values for p <0.0001. Furthermore the lowest values were observed only in patients HDL-ch. To this group of patients LPL values (12.60 u / L) compared with the control group did not show any statistically significant difference (p> 0:05) . We suppose that this result is due to the fact that all patients with undifferentiated disease were with the short duration (no more than 10 months) of starting treatment with HD.

Table number 13: Shows the average values of the examined parameters of the patients of **group controller healthy individuals N ^{O} = 260**

Parameters at	Number	Average	± SD
LPL	260	2 4:20	9.2 1
TL	260	6:50	0.60
TG	260	30.1	0.63
TCH	260	4. 95	22.1
HDL-ch	260	1.60	0.71
LDL-ch	260	2.75	1:03

Table numer14: Shows the average values of the examined parameters of **uremic patients N ^{O} = 260**

Parameters at	Number	Average	± SD	*p*
LPL	260	1 0:20	6:40	0.0001
TL	260	7:39	2:00	0.0001
TG	260	18.3	0.80	0.0001
TCH	260	18.5	1:50	0.1980
HDL-ch	260	12.1	00:49	0.0001
LDL-ch	260	3.74	0.87	0.0001

Table nr.13-14: Shows the differences between the examined parameters of uremic patients and control group were at a statistically significant for p <0.0001. No significant difference was verified only the total cholesterol to p = 0.1980 which value can be accidental case of uremic patients.

Table number 15: Presentation of ***Mann-Whitney U*** test for the difference of the average values obtained from the examined parameters of **uremic patients** group **(women + men).**

Parameter	U	Z	*p-level*
LPL	1215.00	0.60	00:01
TL	1345.50	10.2	00:02
TG	1260.50	12:42	12:20
TCH	1520.00	-0.56	12:32
HDL-ch	1165.00	12:50	12:20
LDL-ch	1240.50	00:55	00:30

From table 15 is noticed a registered diference of average values between uremic patients (male and female gendered) treated with HD compared with the results obtained from control group of healthy individuals is a statistically significant higher for p <0.0001 .

]

Table number 16: Represents the correlation coefficient between examined parameters in serum urea (sUr), serum creatinine (sCr) and serum uric acid (sUA) and lipid parameters and LPL

Parameter	Coefficient of correlation - r	Coefficient of correlation - r	Coefficient of correlation - r
	sUr	sCr	sAU
TL	-0.07	- 12:10	- 0.04
TCH	00:05	- 00:01	- 00:05
TG	0. 48	- 12:40	12:12
HDL-ch	- 12:35	- 12:10	0.24
LDL-ch	00:46	-0.01	-0.01
LPL	- 00:06	00:04	0.15

4 DISCUSSION

Lipoprotein lipase is an enzyme which has an important role in the hydrolysis of triglycerols and changes of lipoproteinemic lipid molecule in the bloodstream. In literature they are found over 100 different types of genetic mutations LPL (33,34). It is verified that the gene for LPL is the main factor involved in the pathogenesis of hypertriglyceridemia and lipid disorders in patients with uremic patients with CRTI. In uremic patients treated with HD, cardio-vascular diseases, pancreatites, etc.. In the general population there are observed some types of genetic variations of LPL (-93T / G, D9N,, W86R, V108V, N291S, S447X ...). In the science of medicine has an important role first mutation detection of LPL W86R who has been the cause of hypertriglyceridemia of family inherited type. LPL for the first time before 60 years was discovered by Hahn PF when during heparin application he noticed reduction of lipemia after food. LPL activity is detected in extrahepatale tissue, skeletal muscle, lung, heart, nerve cells, thoracic aorta , adipose tissue, glands during lactation etc. (25,26,27.33,34). During the passage of time scientists proved that Apolipop-rotein-C_2 (Apo-C_2) (which is composed of lipoproteines with high density (HDL) and low density lipoproteines VLDL) is the main action factor and the main stimulus of an enzyme which was verified that is lipase enzyme is pure and nominated as Lipoprotein lipase (LPL) which has an important role in lipid metabolism (28,29). It is verified that the structure of LPL is a glycolised dimer who participates in the metabolism of lipids with the help of apolipoproteines-C2 (Apo-C2, heparan-sulfate-proteoglycans as well as specific receptors with the help of method (by the pancreas) has verified that the structure of LPL-that contains two structural domains (a greater percentage of amino acid residues 1-312 and a smaller amount of aminoacidic debris 313-448 (30,31) LPL gene is in magnitude of 30 colibases contains two structural domains, and is located in the shorter *arm of chromosome 8 and contains 10 exons.* Today it is known that this protein has an ability to connect simultaneously lipoprotein receptor cells (proteoglycans) which is one of skills and presents noncatalitic role of proteins and cell enables lipoprotein cumulation (32). There are verified facts that LPL has an important role in presenting the disturbance of lipids (hypertriglyceridemia, hypercholesterole-

mia), decrease of the enzymes activity, early atherosclerotic processes with CVD events to presentation, renal diseases, cerebral and peripheral arteries. The main physiological effects of LPL are endogenous and exogenous metabolism of lipoprotein and cholesterol transportation. LPL is an enzyme that has a key role in the hydrolysis of triglycerides (TG) from hilomicrons and VLDL from the circulation and helps change of lipid between VLDL and HDL cholesterol (HDL-ch) or rather, between cholesterol and HDL-ch. Synthesis of TG-rich lipoprotein begins with the synthesis Apo-B_{48} in hilomicrons while Apo-B_{100} of VLDL in ribosomes reticulum and then enter the lipoprotein composition of the smooth endoplasmic reticulum, which is the main place where triglycerids are synthesized (35 , 36). LPL in the wall of a blood vessel is connected with the aid of negative electricity chain proteoglycan heparin sulfate. For LPL activation are necessary phospholipids and apolipoprotein-C_2 (or Apo $C_{2)}$. HDL amount of cells is in inverse correlation with the concentration in triglycerides (TG) and LPL(37). LPL affects Reverse cholesterol transport because of reduced activity of LPL due to increase of TG concentrations, reduced the amount of HDL-ch. Large number of studies have documented that LPL helps the proliferation of smooth muscle cells of a blood vessel (38). From hyperlipoproteinemias under Fredricksonit due to lack of syntesis of LPL or lack of Apo-C2 is introduced the hyperlipoproteinemia type IV but may appear chylomicrons and triglycerides and so called family chylomicronemia.(39,40,41 42,) An overwhelming number studies show that the activity of lipoprotein lipase (LPL) is quite reduced in patients with treatment duration greater with dialysis. To our patients we noticed a decreased activity of LPL and from lipid fractions triglycerides are dominant faction manifested with *hypertri-glyceridemia. Apearance of* hypertriglyceridemia is deficit reduction of the LPL activity (51) which results in reduction of the lipoprotein lipolisis rich in TG (VLDL). The presence of serum LDL rich in TG, suggests for a partial deficit of lipase hepatale. The aforeme-ntioned disorders of the metabolism of fats to treat uremic patients with HD can be improved with use of beta adrenergic blocators , increased concentrations of carbohydrates in food, the use of dialysis bicarbonate, glucose apsorbim the peritoneal cavity of CAPD, use of biocompatible membranes -with updates (High Flux) clad with tocopherol and portal to reduced circulation in the context of a weakened heart (52,53,54) .Deficit or decrease of LPL activity in patients with dialysis-associated with hypertri-glyceridemia as independent major factor in the early appearance of atherosclerosis with atherosclerotic manifestations on the coronary arteries, cerebral but not limited to patients with uremia but also the general population. Treatment of hypertriglyceridemia (TG ↑) should be proportional to the degree of dyslipidemia. From basic diseases (tab.nr.8-11) LPL minimum concentrations lower activity of LPL were remarks of patients with diabetic nephropathy (LPL = 15.1 u / L) then with time: GMN chr (LPL = 1.80 u / L), then the HTA with nephroartherosclerose (LPL = 2.50u /L of interstitium (LPL = 3:40), while highest concentrations of LPL we won our study of patients with chronic renal disease without differentiating with LPL = 12.60u / L, we assume that this value is result from treatment with the short duration of the patients (there were more than 8 months to treat HD). Reduction of LPL activity (due to the action of heparin) and HTGL (hepatic lipase triglycerides) of patients with dialysis assumed by action to uremic toxins as well as high concentrations of APOC-III and parathyroid hormone (HPT). Always during uremia conditions dominate the reduced concentrations of ApoA-I and HDL-ch while higher concentrations of LDL-ch, APOC-III and TG (55) . Garber with associates. in his study verified and documented the activity of LPL reduction in patients treated with HD is responsible for delayed and compromised lipolysis of this population(56). Of patients with nephrotic syndrome were found lower concentrations of the Lipase LPL and hepatic lipase (HL), compared with patients that suffer from any other renal disease. Lipolitic activity of LPL isolated from in vitro heart patients with nephrotic syndrome is decreased to 90% compared with the control group of healthy patients (57.58).THBI patients due to kidney parenchyma reduction can not be synthesized some of apoproteines , because in these patients

the concentrations of triglycerides are for 50-70 ... 90% increased, while the concentrations of HDL-ch are reduced to 20 -40% (59). Exist two classes of circulating lipoproteins which differ according to their content: apolipoprotein -I and apolipoprotein-B as basic constituent. Lipoprotein which in itself is comprising mostly ApoA-I is a high density (HDL-ch) and calculated as antiaterogjen, while Apo-B is associated and mostly in separate composition containing lipids and is leading the construction of the structure of the VLDL, LDL-ch IDLdhe and is accounted as atherogenic apoprotein. Dyslipidemia in patients treated with HD includes complex changes in the composition of Apo-B with relative growth of APOC-III (60). Sintesis of lipids is under direct control of food and lipometabolic rate . In some studies it is verified that LPL and HTGL have important roles generating " *Remnant "* lipoprotein LDL-ch and positively correlated with lipoproteinemic abnormalities to patients treated with HD. LPL activity and HTGL in patients with esrd is quite reduced compared with the control group. Some studies show that the concentration of VLDL and IDL are increased in THBI patients even though it is not detected dyslipidemia (61.62). Some studies show that between hypertriglyceridemia activity and level of IDL in patients with THBI is shown the opposite significant correlation . A large number of studies have verified that supplementary therapy with rHuEpo (human Eritropoetin) that was given for correction of renal anemia it reduces the level of ,, *Remnant "*lipoproteinic cholesterol particles (RLPs- *("Remnant Lipoprotein-Particles," -RLP)* and "Remnant" lipoproteinic particles of triglycerides (RLPs-TG) of patients with HD, with increasing concentrations of LPL and triglyceride Hepatale lipase (TGHL). Lipoproteinic waste particles are atherogenic and their growth shows that they are one of the factors the risk of complications and platelet atheros-clerose of uremic patients (63,64,65). Some authors have documented over the apparent invol-vement of LPL and RLPs HTGL in metabolism, while supplementary therapy with rHuEpo in patients with uremia significantly reduces the level of RLPs in plasma, with increased concentration of LPL and LTGH. It is proven that early treatment with rHuEpo not only controls and regulates renal anemia but also prevents left ventricular hypertrophy, but is increasing the activity of LPL and LTGH which can also be effective for the prevention of atherosclerosis (Ath) that of uremic population. It is confirmed that for the therapy that lasts with Eritropoetin,in the patients treated with HD, are registered changes in lipid profile and LPL (66). Besides the abovementioned lipid abnormalities , the presentation of early atherosclerosis and atherosclerotic lesions in blood vessels (heart, brain, peripheral vessels ...), also lipid peroxidation is calculated as a key factor in the progress and presentation of premature atherosclerosis. Free radicals of oxygen and hydrogen are able to " activate" irreversible fixing of LDL-ch for arterial endothelium. In this way it is enabled possible cumulation of subendotelial and endothelial sparkling cells phagocytosed, generating and secondary dystrophy of calcium and forming of atheromatic tablets . Oxidized cholesterol (LDLox) enables local manufacturing of chemoattrctant protein monocytes (MCP-1: Monocyte-Chemoat-tractant-Protein) and the granulocyte macrophage stimulating factor (GM-CSF, granulocyte macro-phage-and-Colony-Stimulating Factor) from endothelial cells. These substances damage vascular wall by attracting circulating monocytes that enter through the tunica media endothelin blood envelope, also under the influence of GM-CSF are transformed into macrophages .In some studies it is proven that LPL and TGLH have an important role in generating ,, Remnant " particles of LDL-ch lipo-proteins and positively corres-ponding to abnormal plasma lipoprotein, to patients treated with hemodialysis. Hepatic lipase is converting α-HDL migrants in pre-β1 HDL CETP under influence of (Cholesterol-Ester Transfer Protein) , the process of hydrolysis. In patients with CRTI (Chronic Renal Terminal Insuficiency) treated with hemodialysis have lower conce-ntrations of hepatic lipase (LH) due to the lower values of CETP. At the end we resume that patients with CRTI treated with hemodialysis reserve cholesterol transport is extremely dama-ged. Oxidized LDL (LDLox), IDL and VLDL speeding the secretion of inflammatory cytokines as interleukin-6 (IL-6), PDGF (Plateled-Derived-Growth-Factor) and TGFβ (Transforming-Growth-Factor-Beta), while the secretion The

TNF-α is stimulated by oxidized LDL. Some hypolipidemic (as probucol-a) and adrenergic beta blockers (as carvedylol) are able to inhibit or slow down this process (reduction of the production of MDA-malonyl Di aldehyde as peroxidation final product. Decrease of concentrations of LDL indirectly slows down the abovementioned process. In the patients with chronic dialysis peroxidation process of lipids is accerelated due to the decrease of antioxidant enzymes activity mainly *peroxide dismutase and gluthation reductase* .This phenomenon is also primarily due The deficit of vitamin "se" and tocopherol, which are highly dialyzable substances and early lost during dialysis. For this reason there is a need that after every dialysis session to be supplemented regularly . Exist documented facts about the deficit effects of selenium (Se) on the total reduction of antioxidant- status (Fisher et al.1992 (67). Use of not proper membranes continuously causes activated hydrogen superoxide production in neutrophils by formouar prerequisites for the excessive absorption of oxygen free radicals. (68,69,70). The use of biocompatible membranes early in treatment with dialysis is expected to reduce metabolic producing oxygen radicals and reduces the risk of oxidation of LDL-ch, namely to reduce the appearance of early accelerated atherosclerosis in uremic patients (atherosclerosis uraemica praecox). Uremic dyslipidemia in patients treated with HD always is associated with elevated serum concentrations of socalled- *particles stuck to chylomicrons (,, remmnant chylomicrons particls "* and IDL and the reduction of concentrations of ApoA-I. The atherogenic effect of dyslipidemia to uremic patients treated with HD is mentioned mostly as a result of increased concentrations of oxidized cholesterol (oxLDL-ch. There a large number of studies which show that the use of bioincompatible membranes increase the concentration of free radicals oxygen and chlorine from the activated phagocytes, exceeding the capacity of antioxidants in plasma system. Oxidative stress is the frequent occurrence of uremic patients and is important in appearance of accelerated atherosclerosis and atherosclerotic processes. Oxidative stress is estimated according enlarged concentrations of substances that react with thiobarbituric acid (TBARA), Malondialdehyde and oxidized LDL (LDLox). Free radicals oxidize plasma proteins and protein products oxidised form (AOPP), which are in correlation with the degree of activation of monocytes and are indicators of the reaction, as *neopterine and TNF-α* (71.72, 73.74) . According to basic disease that was analyzed (tab.nr.8-11) average values lipidic parameters and LPL of the group of patients manifested a significant difference with p <0.0001 compared with the results obtained from the group controller, results that are in line with other studies cited in the paper (183,75,76,77,79,80). Lower values of LPL in relation to the basic kidney diseases that have lead to dialysis are obtained in patients with: diabetes mellitus and diabetic nephropathy = 1.15, = 1.80 chronic glomerulonephropathy , HTA = 2.50, and patients with diseases without differentiation : 12.60u / L. From basic kidney diseases ,diabetes has shown a correlation and higher association with the hypertriglyceridemia (triglycridemia statistically higher compared to other diseases of the same basic patients). The pace of development and progress of accele-rated atherosclerosis are almost equally logged and affecting the deficit of HDL-ch and surplus LDL-ch to 38.3-42.0%.

5 CONCLUSIONS

There are documented facts that uremic hyperlipidemia persists in the early stages of chronic renal disease before starting treatment with hemodialysis and it is the main cause and risk factor of atherogenic processes and early atherosclerosis. Determination of lipid abnormalities and LPL concentrations examination of patients with CRI that in the initial stages can significantly contribute to the proposal and due treatment, with the aim of preventing and inhibiting the rapid progress of premature atherosclerosis and its impacts on artery coronary, cerebral and peripheral. Data obtained from literature on frequency of appearance that genetic variations and polymorphisms of genes and inhibiting effect of LPL in patients with CRI as well as the ordinary population (family hypercholestherolemia) on lipid

profile may help early diagnosis of hipertrigly-ceridemia and to take dietary measures and healing with obvious what will decrease the appearance of early atherosclerosis and its manifestations on the cardiovascular system, cerbrovascular and peripheral arterial disease. Examination of the lipid profile enables us to follow atheromathosis after dietary and medication treatment. The role of examinations of lipid profile and LPL means secure early diagnosis in evaluating visceral and peripheral atheromatosis.

LITERATURE

1. Ponticelli C, Barbie G, Cantallupi A, Donati C, ANNONI G, Brancaccio D. Maintenance lipid abnormalities in renal dialysis patients and transplant recipients. Kidney Int Suppl.1978; 8: S 72Chan MK, Varghese Z, Moorhead JF. Lipid abnormalities in uremia, dialysis and transplantation. Kidney Int. 1981; (19): 119- 625.
2. Miida T, et al. LCAT-dependent conversion of prey β1-HDL Into α-migrating HDL is severely delayed in Haemodialysis patients. *J Am Soc Nephrol. 2003; 14: 732-8.*
3. Varghese Z, Moorhead JF. Lipid abnormalities in uremia, dialysis and transplantation. Kidney Int. 1981; (19): 119- 625.
4. JB Somer, Aitken JM, Abbott LK, Charlesworth JA, McDonald G, Black RB. Lipoprotein lipids in Chronic renal failure and hemodialysis: the influence of etiology and implication for atherogenesis
. Atherosclerosis 1979; 34: 353.
5. Tsumura M, Kinouchi T, Ono S, Nakajima T, T. Komoda Serum lipid metabolism abnormalities and Change in lipoprotein contents in patients with Advanced-Stage Renal Disease Clin Chimica Acta 2001; 314 (1-2): 27-37.
6. SALAND JM, Ginsberg HN. Lipoprotein metabolism in Chronic renal insufficiency Pediatrics Nephrol 2007; 22 (8): 1095-112.
7. JD Baghdad, Albers JJ. Plasma high density lipoprotein concentrations in Chronic hemodialysis and renal transplantation patients. N Engl J Med . 1977; 296: 1436.
8. Mahley RW, Angelin B. Type III hyperlipo-proteinemia: Recent Insight Into Genetic defect of familial dysbetalipoproteinemia. Adv Int Med. 1984; 29: 385.
9. Mahley RW. Atherogenic hyperlipoproteine-mia. Med Clin North Am. 1982; 66: 375.
10. Brunzell JD, Albers JJ, Hass LB, Goldberg AP Agadoa L, Sherrard DJ. The prevalence of serum lipid abnormalities in Chronic hemodialysis. Metabolism. 1977; 26: 903.
11. PJ NESTEL, Fidge NH, Tan MH. Remnant Lipo-protein Increased formation in Chronic renal failure. N Engl Med. 1982; 307: 329.
12. Shoji T, Nishizawa Y. Plasma lipoprotein abno-rmalities in hemodialysis patients, clinical and therapeutic implications guidelines. Dial Apher Ther 2006; 10 (4): 305-15.
13. Lumpaopong A, AV Mathew, John E, et al. Early coronary calcification in Children and young adults with end-stage Renal Disease. Transplant Proc 2007; 39 (1): 37-9.
14. Vaziri ND. Dyslipidemia of Chronic renal failure: the nature, Mechanisms, and Potential consequences Am J Physiol Renal Physiol 2006; 290 (2): F262-72.
15. Gonzalez AI, Schreier L, Elbert A, et al. Lipo-protein alterations in hemodialysis: Differences Between diabetic and nondiabetic patients Metabo-lism 2003; 52 (1): 116-21.
16. Salinelli S, Lo JY, Mims MP, Zsigmond E, LC Smith, Chan L. Structure-function relationship of lipoprotein lipase-mediated enchancement of very low density lipoprotein binding and catabolism by the low density lipoprotein receptor. Functional importance of a properly folded loop Surface Covering the catalytic center. J Biol Chem. 1996; 271: 21906-13.).
17. Vaziri ND, Deng G, Liang K. hepatic HDL receptor SR-B1 and Or AI expression in Chronic renal failure. Nephrol Dial Transplant. 1999; 14: 1462-6.).
18. Morena M, et al. Protective Effects of high-density lipoprotein Against oxidative stress in Haemodialysis patients are impaired. Nephrol Dial Transplant. 2000; 15: 389-95.
19. Wanner C, Krane V, Metzger T, Quaschning T. Lipid Changes and statins in Chronic renal insuffi-ciency and dialysis. J Nephrol. 2001; 14 (S 4): S76-80.).
20. Ziozenkova O, Sevanian A. oxidative modification of low-density lipoprotein in Haemodialysis patients: role in electronegative LDL formation. Blood Purif. 2000; 18: 169-76.
21. Di Giulio S, LACOUR B, NK Man, Martinez-NATER F, Faguer P, Drueke T, Funck-Brentano Jl.

Post heparin lipolytic Activity in uremic patients Treated by hemofiltration.Contrib Nephrol. 1982; 29: 143.
22. Ibels LS, MF Reardon, PJ NESTEL. Post-heparin plasma lipolytic Activity and triglycerides clearance in uremic and hemodialysis patients and renal allograft recipients. J Lab Clin Med. 1976; 87: 648.
23. JK Huttenen, Pastemack A Snttinen T, Ehnholm C, Nikkilä EA. Lipoprotein metabolism in patients with Chronic uremia. Acta Med SCANDIA. 1978; 204: 208.
24. Leschke M, RUMPF KW, Eisenhauer T, Fuchs C, Becker K, Flip It, Scheler F. quantitative Assessment of camitine loss up during hemodialysis and hemofiltration. Kidney Int Suppl. 1983; 16: S143.
25. Hahn PF. Abolishment of alimentary lipemia following injection of heparin. Science 1943; 98: 19-20.
26. Afinsen CF, B Boyle, Brown RK. The role of heparin in lipoprotein lipase metabolism. Science 1952; 115: 583-6.
27. Borensztajn J. Lipoprotein lipase. Chicago: Evener Publishers, Inc., 1987.
28. Scanu A. Serum high-density lipoprotein: Effect of Change in structureon Activity of chicken adipose tissue lipase. Science 1966; 153: 640-1.
29. Nomenclature Committee of the International Union of Biochemistry andMolecular Biology. London: Enzyme Nomenclature (NC-IUBMB).
30. Van Tilbeurgh H, Roussel A Lalouel JM, Cambillau C. Lipoprotein lipase. Molecular model based on the pancreatic lipase x-ray structure:
consequences for heparin binding and catalysis. J Biol Chem 1994; 269 (6): 4626-33.
31. Winkler K, D'Arcy A Hunzicker W. Structure of human pancreatic lipase. Nature 1990; 343: 771.
32. JR Mead, Irvine SA, Ramji DP. Lipoprotein lipase: structure, function, Regulation, and roles in Disease. J Mol Med 2002; 80 (12): 753-69.
33. Staels B, Auwerx J. Perturbation of DEVELOPMENTAL INRA liver gene expression by fibric acid derivatives, lipoprotein lipase and alpha-fetoprotein or models.Development 1992; 115 (4): 1035-1043.
34. Merkel M, Eckel RH, Goldberg IJ. Lipoprotein lipase: Genetics, lipid uptake, and Regulation. J Lipid Res 2002; 43 (12): 1997-2006
35. Goldberg IJ. Lipoprotein lipase and lipolysis: Roles plant in lipoprotein
metabolism and atherogenesis. J Lipid Res 1996; 37 (4): 693-707.
36. Mayes PA. Lipid transport and storage. U: Murray RK, Granner DK,Mayes PA, Rodwel VW, ur. Harper's Biochemistry. New York: Mc-Grawe Hill; 2000, str. 268-84.
37. Patsch JR, Prasad S, GottoAMJr, Patsch W. High density lipoprotein2. Relationship of the plasma levels of this lipoprotein species to Its composition,
to the magnitude of postprandial lipemia, and to the Activities of lipoprotein lipase and hepatic lipase. J Clin Invest 1987; 80 (2): 341-7.
38. JC Mamputu, L Levesque, G. Renier proliferative effect of lipoprotein lipase on human vascular smooth muscle cells. Arterioscler Thromb Vasca Biol 2000; 20: 2212-9.
39. Murthy V, Julien P, Gagne C. Molecular pathobiology of the human lipoprotein lipasae gene . Pharmacol Ther 1996; 70 (2): 101-35.
40. Cohen JC. Chylomicron triglycerides clearance: Comparison of three METHODS Assessment. Am J Clin Nutr 1989; 49 (2): 306-13.
41 Fredrickson DS, Levy RI, RS Lees. Fat transport in lipoproteins - an Integrated Approach to Mechanisms and Disorders. N Engl J Med 1967; 276 (1): 34-42.
42. Brunzell JD. Familial lipoprotein lipase Deficiency and Other Causes chylomicronemia ofthe syndrome. U: Scriver CR, Beaudet AL, Sly WS, Valle D, ur. The Metabolic Basis of Inherited Dise-ase. New York: McGraw Hill; 2001 str. 2789-816.
43. N. Kirchs Zölner EB. Fotometriska-oboena methods. Ges Exp Med. 1962; 135: 545.
44. Bucola G, David H. quantitative determination of serum triglycerides by use of enzymes. Clin Chem. 1973; 19: 476-82.
45. Friedewald WT, Levy RJ, Fredrickson DS . Estimation of Concentration of low density lipoprotein cholesterol without the use of the preparations ultracentrifuge. Clin Chem.1972; 18: 499-502.
46. Allain CC, Poon LS, CS Chan, Richmond W. Enzymatic determination of total serum cholesterol. Clin Chem. 1974; 20: 470-5.
47. Wamick G, Benderson J, Allbers J. quantitation of high density lipoprotein subclasses After Separation by dextran sulfate and Mg + precipitation. Clin Chem. 1982; 28: 1574-61.
48. Tietze NW, Fiereck EA. A specific method for serum lipase determination. Clin Chim Act.1966; 13: 352.
49. Steinberg WM, Goldstein SS, Davies ND, et al. Diagnostic assays in acute pancreatitis. Ann Intern Med. 1985; 102: 576-80.
50. Leybold A W. Junge Importance of colipase for the measurment of serum lipase activity. Clin Adv Enzymol. 1986; 4: 60-7.
51. JD Baghdad, Porte D Jr., Bierman EL. Hypetreglyceridemia: a metabolic consequence of Chronic renal failure. N Engl J Med. 1968; 279 (4): 181-5.
52. Burt RK, Gupta S Burt, Saki WN, BARCENAS CG, JJ Ferguson, Van Buren CT. Reversal of left

ventricular dysfunction After renal transplantation. Ann Intern Med. 1989;111: 635-40.
53. JD Baghdad, Albers JJ. High-density lipoprotein Plasma Concentration in Chronic hemodialysis and renal transplantation patients. N Engl J Med. 1977; 296: 1436-9.
54.Pasternack 54. A Vanttinen T, Solakivi T, Kunsi T, T. Korte Normalization of lipoprotein lipase and hepatic lipase by gemfibrozil results in correction of lipoprotein abnormalities in Chronic renal failure. Clin Nephrol. 1987; 27: 163-8.
55. Attman 55. Yes, Alaupovic P. lipid abnormalities in Chronic renal insufficiency. Kidney Int. 1991; 39: 16.
56. DW Garber 56, GOTLIEB BA, JB Marsh, Sparks CE. Catabolism of very low density lipoproteins in experimental nephrosis. J Clin Invest. 1984; 74: 1375-83.
57. Kaysen GA, Pan XM, Couser WG, Staprans I. defective lipolysis persists in hearts of rats with Heymann nephritis in the Absence of nephrotic plasma. Am J Kidney Dis.1993; 22: 128-34.
58. George A, Kaysen, GM Monique De Sain-van der Velden. New Insights Into the lipid metabolism in the nephrotic syndrome. Kidney Int Suppl. 1999; 7: S18-21).
59. LZ Rosello, AR Echevarría, Perez-Oliva J, et al. Perfil de lipdos Serico apoproteinas AI y B y en a trataimento hemodialitico sometodos patient. Rev Cubana Invest Biomed 1997; 16 (2): 116-23.)
60. Attman 60. Yes, Alaupovic P, M Tavella, Knight-Gibson C. abnormal lipid and apolipoprotein composition of major density lipoprotein classes in patients with Chronic renal failure. Nephrol Dial Transplant. 1996; 11: 63-9.
61. Oi K, Hirano T, Sakai S, Kawaguchi Y, T. Hosoya Role of hepatic lipase in intermediate-density lipoprotein and small, low-density lipoprotein Dens formation in hemodialysis patients. Kidney Int Suppl. 1999; 71: S227-8.
62. Shoji T, Nishizawa Y, Kawagishi T, Tanaka M, Kawasaki K, Tabata T, Inoue T, atherogenic lipoprotein Morii H. Changes in the Absence of hyperlipidemia Treated with Chronic renal failure by hemodialysis. Atherosclerosis. 1997; 131: 229-36.).
63. Tetsuya G, Hiroko S, Toshio T, Akefumi M, Masatoshi M, SusumuY. Erythropoetin supplement increases plasma lipoprotein lipase and hepatic lipase triglycerides levels in hemodialysis patients. Kidney Int Suppl. 1999; 71: S213-5.
64. Tanaka A, Ejiri N, Y Fujinuma, Yui K, Tamura M, Nakajima K, Morohoshi M, Fujisawa K, Uchimura I Numano F. Remnant particles and restenosis of coronary artery After PTCA. Atherosclerosis. 1995; 748: 595-8.
65. Waner C, Zimmermann J, Quaschning T, Galle J. inflammation, dyslipidemia and vascular risk Factors in hemodialysis patients. Kidney Int Suppl. 1997; 62: S53-5.
66. Allegra V, L Martinbianco Vasile lipid and apolipoprotein A. Patterns erythropoietin therapy: Roles of erythropoietin, Route of Administration, and diet. Nephrol Dial Transp. 1997; 12: 924-32.
67. Fischer M, et al. Anti-oxidant status in Chronic hemodialysis patients; Impact of selenium supplementation. Kidney Int. 1992; 3: 364.
68. K. Cakalaroski 68. The importance of oxidative stress and antioxidative medicaments in medicine. Mak Med Pregled. 2001; 55 (S49): 138-45.
69. Dasgupta A, et al. Increased lipid peroxidation in patients on hemodialysis Maintenance. Nephron. 1992; 60:56.
70. Fiorillo C, et al. Oxidative stress and antioxidative defenses in the receiving Regular Haemodialysis renal patients. Clin Chem Lab Med. 1988; 36: 149-53.
71. Maggi E, Bellazzi R, Falaschi F et al. Enhanced LDL oxidation in uremic patients: an Additional Mechanism for accelerated atherosclerosis? Kidney Int.1994; 45: 876-83.
72. Paul JL, Sali ND, Sonny T, et al. Abnormalities in lipid peroxidation hemodialyzed patients. Nephron. 1993; 64: 106-9.
73. WH Sutherland, RJ Walker, Ball MJ, et al. Oxidation of low density lipoproteins from patients with renal failure or renal transplants. Kidney Int. 1995; 48: 227-36.
74. Witko-SARS V, Friedländer M, Nguyen-Khoa, Jungers P, et al. Advanced oxidation protein or a novel molecular Products Basis of oxidative stress in uremia. Nephrol Dial Transpl. 1999; 14: 76 ..
75. Kimak E, J Solski, Janick L, Ksaziek A, K. Janicki. Concentration of Lp (a) and other lipoproteins in predialysis, hemodialysis, peritoneal dialysis and ambulatory Chronic post-transplant patients. Clin Chem Lab Med. 2000; 38 (5): 421-5).
76. Kandoussi AM, Huguet V, Parra HJ, Dracon M, Fruchart JC, Tacquet H, et al. Apolipoprotein AI and apolipoprotein B Containing Particle Analysis in normolipidemic hemodialyzed patients: evidence of free apolipoprotein E. Am J Nephrol. 1996; 16: 287-98.
77. Kandoussi AM, Huge V, Cachera C, Hazzan M, Dracon M, Tacquet A, et al. Or (a) phenotypes and Lp (a) Concentration in renal transplant patients. Nephron. 1998; 80: 183-7.
78. G. Samsioe 78. The Effects of estrogen and progesterone on the lipid and lipoprotein

metabolism. Cardiovascular Effects of hormone replacement therapy, Novo Nordisk, Copenhagen. 1991. pp. 23-32.
79. Bao W, Srinivasan SR, Berenson GS. Tracking of serum apolipoprotein AI and B in Children and young adults. The BOGALUSA heart study. J Clin Epidemiol. 1993; 46: 609-16.
80. Lutfi Zylbeari. Aberatoin of Apolipoprotein and Dislipidemija in Patients Threated with Chronical Hemo-dialysis. racii so patient Lekuvani Povtoruvani Repeated . Doktorska Disertacija, Skopje 2009, the University ,, Sv.Kiril of Methodius"Maacedonija

Address of the author :
Prof. Dr. LNasir Behxheti
Faculty of Medical Sciences-SUT-Tetovo
E-mail: nasir.behxheti@unite.edu