DISTURBANCE OF LIPOPROTEIN LIPASEAE (LPL) IN PATIENTS WITH GLOMERULONEPHRITIS CHRONICA

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Abstract. Glomerulonephritis is a group of diseases that injure the part of the kidney that filters blood (called glomeruli). Other terms you may hear used are nephritis and nephrotic syndrome. When the kidney is injured, it cannot get rid of wastes and extra fluid in the body. If the illness continues, the kidneys may stop working completely, resulting in kidney failure. There are two types of glomerulonephritis—acute and chronic. The acute form develops suddenly. You may get it after an infection in your throat or on your skin. Sometimes, you may get better on your own. Other times, your kidneys may stop working unless the right treatment is started quickly. What causes chronic glomerulonephritis?Sometimes, the disease runs in the family. This kind often shows up in young men who may also have hearing loss and vision loss. Some forms are caused by changes in the immune system. However, in many cases, the cause is not known. Sometimes, you will have one acute attack of the disease and develop the chronic form years later.There are documented facts that uremic patients present clinical picture of dyslipidemia 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. 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 cytokineus 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. Disorders of lipid meta-bolism in patients with terminal chronic renal insufficiency (TCRI) are first documented in 1827 by Dr. Bright (1).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.

Term Index: Glomerulonephrits Chronica, Lipoprotein Lipasae (LPL), Uremia, Lipids profiles

1 INTRODUCTION

Glomerulonephritis (GN), also known as glomerular nephritis, is a term used to refer to several kidney diseases (usually affecting both kidneys). Many of the diseases are characterised by inflam-mation either of the glomeruli or of

the small blood vessels in the kidneys, hence the name, but not all diseases necessarily have an inflammatory component.As it is not strictly a single disease, its presentation depends on the specific disease entity: it may present with isolated hematuriaand/or proteinuria (blood or protein in the urine); or as a nephrotic syndrome, a nephritic syndrome, acute kidney injury, or chronic kidney disease.
They are categorized into several different pathological patterns, which are broadly grouped into non-proliferative or proliferative types. Diagnosing the pattern of GN is important because the outcome and treatment differs in different types. Primary causes are intrinsic to the kidney. Secondary causes are associated with certain infections (bacterial, viral or parasitic pathogens), drugs, systemic disorders (SLE, vasculitis), or diabetes.Patients with terminal chronic renal failure (TCRF) most often suffer from hyperlipopro-teinemia of type IV of secondary hyperlipoproteinemia (accor-ding to Frederickson's classi-fication) 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 chan-ged catabolism of the Pre β1HDL-ch (3) . 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 compo-sition 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 . Concen-trations Apo B_{48} / B_{100} are increased in the comp-osition 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 utilisa-tion 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-Atheroscle-rsosis-Infla-matio) which factors are frequent in uremic patients counted as activity (24) .

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 confir-med 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 antico-agulant 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 solu-tion to dyslipidemia in this group of patients. (17). The uremic patients hipetregli-ceridemia in parallel is associated with increased concentrations of V sub-class composed of LDL-ch . Of uremic patients treated with hemodialysis proathe-rogenic 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 lipo-protein 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 electro-negative charged subfraction of LDL (LDL^{-}) (18,19,20).The regular application of heparin during hemodi-alysis intraveno-usly *(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 there-fore in cases where the concentration is redu-ced then is a lot easier to justify inverse corre-lation which is found between hypertriglyceri-demia and low concentrations of HDL ch. It is assumed that the uremic patients treated with HD exist circula-ting inhibitors of lipases (22). The application of heparin (during dialysis) further reduces the activity of LPL, howe-ver attempts of leadership in HD 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 chro-nic renal insufficiency compared to patients with TCRI treated with HD, which means that the very TCRI (because of silent inflammation) may affect the reduction of LPL.

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 measu-rements 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 %)
Female	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	± SD
260	58.20	13:40

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

Gender	Number	Average	± SD
Men	145	57.40	14:50
Women	115	59.50	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 .. (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-para-metric tests were used the tests: Mann-Whitney and Wilcoxon's test. Statistically significant The differences between the Group of patients and control group obta-ined 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 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 the form of processed diagrams made with standard statistical program (Statistic for Windows, version 6.0 A, Stat.softincTulsa, OK USA.

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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	± SD
LPL	115	24:30	16:00
TL	115	10.8	1.80
TG	115	20.5	0.80
TCH	115	9.7	8.1
HDL-ch	115	1.4	0.60
LDL-ch	115	4.95	0.90

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

Parameters	Number	Average	± SD
LPL	145	19:35	13:00
TL	145	6.12	10.2
TG	145	2.80	0.70
TCH	145	7.5	1.50
HDL-ch	145	2.0	2.30
LDL-ch	145	4.70	0.85

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 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 number11: 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.9-11: 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 12: 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	2:32
HDL-ch	1165.00	2:50	2:20
LDL-ch	1240.50	00:55	00:30

From table 12 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 13: 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

DISCUSSION

Glomerulonephritis refers to an inflammation of the glomerulus, which is the unit involved in filtration in the kidney. This inflammation typically results in one or both of the nephrotic or nephritic syndromes.Nephrotic syndrome:The nephrotic syndrome is characterised by the finding of edema in a person with increased protein in the urine and decreased protein in the blood, with increased fat in the blood. Inflammation that affects the cells surrounding the glomerulus, podocytes, increases the permeability to proteins, resulting in an increase in excreted proteins. When the amount of proteins excreted in the urine exceeds the liver's ability to compensate, fewer proteins are detected in the blood - in particular albumin, which makes up the majority of circulating proteins. With decreased proteins in the blood, there is a decrease in the oncotic pressure of the blood. This results in edema, as the oncotic pressure in tissue remains the same. It should be noted here that although decreased intravascular oncotic (i.e. osmotic) pressure partially explains the patient's edema, more recent studies have shown that extensive sodium retention in the distal nephron (collecting duct) is the predominant cause of water retention and edema in the nephrotic syndrome. This is worsened by the secretion of the hormonealdosterone by the adrenal gland, which is secreted in response to the decrease in circulating blood and causes sodium and waterretention. Hyper-lipidemia is thought to be a result of the increased

activity of the liver . Nephritic syndrome: The nephritic syndrome is characterised by blood in the urine (especially Red blood cell casts with dysmorphic red blood cells) and adecrease in the amount of urine in the presence of hypertension. In this syndrome, inflamematory damage to cells lining the glomerulus are thought to result in destruction of the epithelial barrier, leading to blood being found in the urine. At the same time, reactive changes may result in a decrease in kidney blood flow, resulting in a decrease in the production of urine. The renin-angiotensin system may be subsequently activated, because of the decrease in perfusion of juxtaglomerular apparatus, which may result in hypertension.Minimal change disease is characterised as a cause of nephrotic syndrome without visible changes in the glomerulus on microscopy.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, hypercholesterolemia), 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 meta-bolism of lipoprotein and cholesterol transpo-rtation. 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 hyperlipoproteine-mias under Fredricksonit due to lack of syntesis of LPL or lack of Apo-C2 is introduced the hyper-lipoproteinemia 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-gly-ceridemia. Apearance of* hypertreglyceridemia 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 carbo-hydrates 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 apopro-tein. 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 abnor-malities 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 Lipopro-tein-Particles," -RLP)* and "Remnant" lipoproteinic particles of triglycerides (RLPs-TG) of patients with HD, with increasing concentrations of LPL and triglyceride Hepatale lipase (TGHL). Lipopr-oteinic 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 supple-mentary 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 athero-sclerosis 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, gene-rating and secondary dystrophy of calcium and forming of atheromatic tablets . Oxidized chole-sterol (LDLox) enables local manufacturing of chemoattrctant protein monocytes (MCP-1: Mono-cyte-Chemoat-tractant-Protein) and the granulo-cyte 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 macro-phages .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 hydro-lysis. 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 continu-ously 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 (atheroscle-rosis uraemica prae-cox). Uremic dyslipidemia in patients treated with HD always is associated with elevated serum concentrations of socalled- *particles stuck to chylomicrons (,, remmnant chy-lomicrons 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 accord-ing enlarged concentrations of substances that react with

thiobarbituric acid (TBARA), Malon-dialdehyde 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) . Accor-ding 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 glomerulonephro-pathy , HTA = 2.50, and patients with diseases without differ-rentiation : 12.60u / L. From basic kidney diseases ,diabetes has shown a correlation and higher association with the hypertriglyceridemia (triglyc-ridemia 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%.Minimal change disease typically presents with edema, an increase in proteins passed from urine and decrease in blood protein levels, and an increase in circulating lipids (i.e., nephrotic syndrome) and is the most common cause of the nephrotic syndrome in children. Although no changes may be visible by light microscopy, changes on electron microscopy within the glomerules may show a fusion of the foot processes of the podocytes (cells lining the basement membrane of the capillaries of glomerulus). It is typically managed with corticosteroids and does not progress to chronic kidney disease.Focal segmental glomerulosclerosis is characterised by a sclerosis of segments of some glomerules. It is likely to present as a nephrotic syndrome. This form of glomerulonephritis may be associated with conditions such as HIV and heroin abuse, or inherited as Alport syndrome. The cause of about 20–30% of focal-segmental glomerulosclerosis is unknown. On microscopy, affected glomerules may show an increase in hyalin, a pink and homogenous material, fat cells, an increase in the mesangial matrix and collagen. Treatment may involve corticosteroids, but up to half of people with focal segmental glomerulonephritis continue to have progressive deterioration of kidney function, ending in kidney failure. Membranous glomerulonephritis may cause either nephrotic or a nephritic picture. About two-thirds are associated with auto-antibodies to phospholipase A2 receptor, but other associations include cancers of the lung and bowel, infections such as hepatitis B and malaria, drugs including penicillamine, and connective tissue diseases such as systemic lupus erythematosus. Individuals with cerebral shunts are at risk of developing shunt nephritis, which frequently produces MGN.Microscopically, MGN is characterized by a thickened glomerular basement membrane without a hyperproliferation of the glomerular cells. Immunofluorescence demonstrates diffuse granular uptake of IgG. The basement membrane may completely surround the granular deposits, forming a "spike and dome" pattern. Tubules also display the symptoms of a typical Type III hypersensitivity reaction, which causes the endothelial cells to proliferate, which can be seen under a light microscope with a PAS stain. Prognosis follows the rule of thirds: one-third remain with MGN indefinitely, one-third remit, and one-third progress to end-stage kidney failure. As the glomerulonephritis progresses, the tubules of the kidney become infected, leading to atrophy and hyalinisation. The kidney appears to shrink. Treatment with corticosteroids is attempted if the disease progresses.In extremely rare cases, the disease has been known to run in families, usually passed down through the females. This condition, similarly, is called Familial Membranous Glomerulonephritis. There have only been about nine documented cases in the world.Thin basement membrane disease is an autosomal dominant inherited disease characterized by thin glomerular basement membranes on electron microscopy. It is a benign condition that causes persistent microscopic hematuria. This also may cause proteinuria which is usually mild and overall prognosis is excellent Proliferative glomerulonephritis is characterised by an increased number of cells in the glomerulus. These forms usually present with a triad of blood in the urine, decreased urine production, and hypertension, the nephritic syndrome. These forms usually progress to end-stage kidney failure (ESKF) over weeks to years (depending on type).IgA nephropathy, also known as *Berger's disease*, is the most common type of glomerulonephritis, and generally presents with isolated visible or occult hematuria, occasionally combined with low grade proteinuria, and rarely causes a nephritic syndro-me characterised by protein in the urine, and visible blood in the urine. IgA nephropathy is classically described as a self-resolving form in young adults several days after a respiratory infection. It is characterised by deposits of IgA in the space between glomerular capillaries.Henoch–Schönlein purpura refers to a form of IgA nephropathy, typically affecting children, characterised by a rash of small bruises affecting the buttocks and lower legs, with abdominal pain.Post-infectious glomerulonephritis can occur after essentially any infection, but classically occurs after infection with the bacteria *Streptococcus pyogenes*. It typically occurs 1–4 weeks after a pharyngeal infection with this bacterium, and is likely to present with malaise, a slight fever, nausea and a mild nephritic syndrome of moderately increased blood pressure, gross haematuria, and smoky-brown urine. Circulating immune comp-lexes that deposit in the glomerules may lead to an inflammatory reaction.Diagnosis may be made on clinical findings or through antistreptolysin ,,O'' antibodies found in the blood. A biopsy is seldom done, and the disease is likely to self-resolve in children in 1–4 weeks, with a poorer prognosis if adults are affected.Membranoproliferative GN (MPGN), also known as *mesangiocapillary glomerulonephritis,* is characterised by an increase in the number of cells in the glomerulus, and alterations in the glomerular basement membrane. These forms present with the nephritic syndrome, hypocomplementemia, and have a poor prognosis. Two primary subtypes exist:Type 1 MPGN ,and Type 2 MPGN, also known as *Dense Deposit Disease*, is characterised by an excessive activation of the complement system. The C3 Nephritic Factor autoantibody stabilizesC3-convertase, which may lead to an excessive activation of complement. Cres-centic glomerulonephritisinduced by infective endo-carditis onPAS staining and immunofluores-cence. PAS staining (left) demonstrated circumferential and cellular crescent formation with interstitial nephritis. Immunof-luorescence (right) demonstrated C3 positive staining inmesangial area.Rapidly progressive glomerulo-nephritis, also known as *crescentic GN*, is characterised by a rapid, progressive deterioration in kidney function.

People with rapidly progressive glomerulonephritis may present with a nephritic syndrome. In manage-ment, steroid therapy is sometimes used, although the prognosis remains poor. Type 1 is Goodpasture syndrome, an autoimmune disease also affecting the lung. In Goodpasture syndrome , IgG antibodies directed against the glomerular base-ment mem-brane trigger an inflammatory reaction, causing a nephritic syndrome and the coughing up of blood. High dose immunosuppression is required (intrave—asmaph-eresis. Immunohistochemistry staining of tissue speci-mens shows linear IgG deposits.Type 2 is characterised by immune-complex-mediated damage, and may be associated with systemic lupus erythe-matosus, post-infective glomerulonephritis, IgA nephro-pathy, and IgA vasculitis.Type 3 rapidly progressive glomerulonephritis, also called *pauciimmune type*, is associated with causes of vascular inflammati-onin-cluding granulomatosis with polyangiitis (GPA) and microscopic polyangiitis. No immune deposits can be seen on staining, however blood tests may be positive for the ANCA antibody.

CONCLUSIONS

The exact cause of CKD in patients with chronic glomerulonephritis may never be known in some patients. Therefore, it has generally been accepted that the diagnosis of CKD can be made without knowledge of the specific cause.There are documented facts that uremic hyperlipi-demia persists in the early stages of chronic renal disease before starting treatment with hemodialysis and it is the main cause and risk factor of athe-rogenic processes and early atherosclerosis. Determination of lipid abnormalities and LPL conce-ntrations examination of patients with CRI that in the initial stages can significantly contribute to the proposal and due treatment, with the aim of preve-nting 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. Nearly all forms of acute glomerulonephritis have a tendency to progress to chronic glomerulonephritis. The condition is characterized by irreversible and progressive glomerular and tubulointerstitial fibrosis, ultimately leading to a reduction in the glomerular filtration rate (GFR) and retention of uremic toxins. If disease progression is not halted with therapy, the net results are chronic kidney disease(CKD), end-stage renal dise-ase (ESRD), and cardiovascular disease. Chronic glomeru-lonephritis is the third leading cause and accounts for about 10% of all causes of CKD.

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