# DIABETES AND INFLUENCE IN PROGRESS CHRONIC KIDNEY FAILURE

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**Abstract:** Diabetes mellitus with thee remains a serious health problem with a high prevalence in developed countries and developing countries, and is the main cause of failure chronic renal insufficiency, chronic renal terminals of manifsetuar with increased high rate of mortality due kardiovaskulaer disease (CVD). Diabetes is calculated as the fourth cause of mortality in developed countries. (1). Nephropathy diabetic (DN) is typically defined by macroalbuminuria-that is, a urinary albumin excretion above 300 mg in the urins 24-hour meeting, or mikroalbuminuri. In the United States and Western countries with ND diabetes, counted as the main cause of ESRD. A large number of epidemiological studies have shown that 1/3 of patients treated with hemodialysis (HD) with chronic diabetes are type 2 (2,3,4) . Clinically, diabetic nephropathy is characterized by a progressive increase of proteinuria, hypertension and decline of glomerular filtration (GFR-glomerular filtration Rate) and a higher risk of mortality from cardiovascular diseases (CVD) and cerebrovaskualar disease.**The aim of the paper:** the purpose of this paper was to verify and document the impact of diabetes unbalanced, hyperglycemia and risk factors in the progress of progress in ESRD, and the correlation between hyperglycemia with CVD disease and arteriosclerosis early that manifested in patients with uremia treated with hemodialysis, compared with the control group of healthy individuals. **Material and methods of work** In this prospective cohort research (,, cross-section ") are included 360 examiners of whom 180 were patients with DN and ESRD treated with HD (80 (45%) of them were women with an average age of 56.80 ± 9:50 while 100 (55%) were men, with an average age: 57.90 ± 10:00 years) and 180 were healthy individuals who served as a control group, of whom 100 were male with average age of 57.20±11:00, while 80 (45%) were female with an average age of 58.00 ± .50 = year. Of the total number of patients treated ($N^{O}$=180), 100 were patients with diabetes mellitus of the insulin dependent (addicted -insuline Tip1 DM), while 80 were patients with diabetes mellitus treated with oral hypoglycemic and diabetes as they computed mellitus type-2 (DM type 2) table number 1. the two groups of patients and control group were analyzed within 12 months -once every three months, with 4 total measurement of glycemic profile, hemoglobin glycosylated (HbA1c) , lipid profile. The patients treated with HD we made the measurement of body mass index - BMIx (Body Mass Index) Numerous studies have verified that the check and normalization of hyperglycemia and HbA1c, normalization of arterial hypertension, and regulation of profile lipid visible impact in preventing rapid progress of renal injuries presenting to ESRD and micro /macralbuminur events with micro/macrova-sculare and cardiovascular disease (CVD).

**Index terms:** Diabetic Nephropathi, Diabetes Mellitus (DM),ESRD, blood glucose (Gl), HbA1c , lipids profile.

# 1 INTRODUCTION

Terminal chronic renal failure represents ireveryibil progressive reduction of renal function and glomerular filtration. When glomerular filtration rate (GFR-glomerular Filtration Rate) reduced <30ml / min / 1.73 m2 and serum creatinine concentrations begin to rise above 240-280 μmol / l, the progress of kidney failure begins with the fastest growing (5) . For chronic renal impairment should be considered when starting when life begins GFR <90 ml / min, with a duration over 3 months. Diabetic nephropathy (DNP) is associated with an increased risk of progression to chronic terminal renal failure (ESRD) and cardiovascular mortality (6,7).

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Diabetic nephropathy (ND) is the leading cause of ESRD in many countries and its incidence is in rrititje in recent decades (8,9) .About 25% of patients with diabetes type-1 (DT-1) develop ND (10,11).As a marker and warning an ancient and powerful that in the early stages of diabetic nephropathy counted mikroalbumiruia which leads to ESRD appear other factors including No regulation of blood glucose, hyperlipidemia, arterial hypertension, smoking, psikostres, physical inactivity, as well as genetic and environmental factors (12-15). Most of these data were reported from developed countries. The situation regarding the progress of diabetic nephropathy may not be quite the same in developing countries, where socio-economic conditions pose a real obstacle for the medical management of patients with diabetes. Diabetes today is a very big problem socio-economic, due to the high cost of material that pe-environmentally friendly manner. Factors most shpsësht that increase the risk and progress quickly damages chronic renal counted the loss of excess protein in urine, micro/macroalbuminuria, proteinuria disorders, diabetic disorders of lipid syndrome MIA, essential hypertension with nefroloarteriosklerosis etc. for early detection of injuries renal must first create the conditions and doctrine on diagnos stikimin early basic disease, stages of damage renal by level of filtration glomrular (GFR-glomerular filtartion Rate), defined renal disease fundamental discovery manifestations and complications of renal damage and detection of secondary factors in influencing riskant progress and performance of kidney damage and cardiovascular damage (table number1)

Under the proposal of K / DOQI and NKF (National Kidney Foundation), the levels of renal damage are determined according to GFR. (Table 1).

| Phases | Description of renal damage | GFR* ml/min/1.73m$^2$ |
|---|---|---|
| **1** | Mild renal impairment with normal filtering | ≥ 90 |
| **2** | The slight decrease in renal function | 60-89 |
| **3** | The average reduction in renal function | 30-59 |
| **4** | Severe damage in renal function | 15-29 |
| **5** | **Renal failure** | **< 15 (dialysis)** |

*** GFR-Glomerul Filtration Rate**

At the table number 2 are identified normal and pathological values of proteinuria and albuminuria. (M=Males,F=Females)

| Values | Microalbuminuria | Proteinuria |
|---|---|---|
| F < 25 mg/L | F= 25- 355 mg/L | F= 355mg/L |
| M= 17-250 mg/L | M= < 17mg/L | M > 250mg/L |

Patients with chronic kidney disease (CKD) and diabetes are obliged to obey the rules of the consumption of protein (when cleaning the endo-genes creatinine is <50-40 ml / min / 1.73m2) they should consume 0.6-0.8 g / kg / PT / day or 30-35 kcal / kg / day. Clinical results from the study by MDRD-Modification of Diet in Renal Disease (modification of diet in renal disease) proved that if arterial pressure is of the order of: 125/75 mmHg and protein consumption is 0.6- 0.8g / kg / PT a day, it can significantly affect the performance of the fast of kidney damage. As parameters for determining the nutritional status should be taken into account: the concentration of albumin, and body mass index (BMIx)

At the table number 3 we presented the definition of progress, remission and regression of chronic nephropathy manifested by proteinuria

| Parameters | Progression | Remission | Regression |
|---|---|---|---|
| Proteinuria | >1.0 g/24 h | < 1.0 g/24 h | < 0.3 g/24 h |
| Levels of FG | FG diminished | FG stable | FG increased |
| The structure of the kidney | FG exacerbated | FG stable | FG improved |

Increased protein in the urine can be reduced if the patient was referred to the councils of the following: the use of low doses of ACE blockers, restriction salt s, the use of beta blokerëve, angiotensin II receptor antagonist (when the value of K is <5.0 mmol / l) statin use, normalizing hypertension, balancing the blood glucose. A good blood glucose control when the HbA1c level is <7.0%, significantly slows the progression of diabetic nephropathy. Uremik patients treated with HD, HbA1c values should be brought <8.0% (16,17,18). A multicenter study on diabetes has verified that intensive treatment of diabetes and high values normalize blood glucose, reduced the risk by 16 -21% of acute myocardial infarction, and peripheral vascular disease incidence was reduced by 35-39 % etc. any reduction in glycosylated hemoglobin of 1%, is the highest positive correlation with decreased risk for microvascular complications 37% and 21% of CVD. Therefore, control of glycemia and HbA1c, the primary obligation should be on early detection of diabetic nephropathy. recent years because of the smooth functioning of dispensaries to diabettit is evident that patients with type 2 diabetes with proteinuria have nfropati and relatively good prognosis of cardiovascular events. There are documented facts in numerous studies that patients with IRK levels of proinsulin and C-peptide were increased (19,20,21), and the C-peptide clearance by the kidney is higher compared to insulin clearance therefore these patients have the appearance of values lower-false glycemia, therefore examine the concentration of C-peptide (as a warning before the secretion of insulin), due to hipoperfuzionit renal result of increased half-life insulin, and general requirements for insulin even more are reduced more than necessary for patients with diabetes and nephropathy, diabetic should be as the primary responsibility of doctors of primary, secondary and tertiary This phenomenon compensator decrease filtration insulin more evident is at the stage when GFR is <20-30 ml /min/1.73m2. (22-26).

## 2 MATERIAL AND METHODES

In this prospective cohort research (,, cross-section ") are included 360 examiners of whom 180 were patients with DN and ESRD treated with HD (80 (45%) of them were women with an average age of 56.80 ± 9:50 while 100 (55%) were men, with an average age: 57.90 ± 10:00 years) and 180 were healthy individuals who served as a control group, of whom 100 were male with average age of 57.20±11:00, while 80 (45%) were female with an average age of 58.00 ± .50 = year. Of the total number of patients treated ($N^{O}$=180), 100 were patients with diabetes mellitus of the insulin dependent (addicted -insuline Tip1 DM), while 80 were patients with diabetes mellitus treated with oral hypogly-cemic and diabetes as they computed mellitus type-2 (DM type 2) table number 1. the two groups of patients and control group were analyzed within 12 12 months -once every three months, with 4 total measurement of glycemic profile, hemoglobin glycosylated (HbA1c) , lipid profile. The patients treated with HD we made the measurement of body mass index - BMIx (Body Mass Index) Numerous studies have verified that the

check and normalization of hyperglycemia and HbA1c, normalization of arterial hypertension, and regulation of profile lipid visible impact in preventing rapid progress of renal injuries presenting to ESRD and micro /macralbuminur events with micro/macrova-sculare and cardiovascular disease (CVD). Methods of determining the concentrations of lipids, glycaemia (Gl) and HbA1c are presented below. Reference value for glycaemia and HbA1c were taken according to the criteria proposed by the World Health Organization (WHO)-for glycaemia=5-6.5 mmol/l and HbA1c %=4.4% -6.6 %. All analyzes provided by the study protocol, were defined at the Institute of Clinical Laboratory at the University Clinical Centre of Skopje.

Table no. 4: reference values and methods by authors whose concentrations are determined a blood glucose, HbA1c and lipid profiles are presented in Table 4.

| Parameters examined | Reference values | Authors |
|---|---|---|
| LT | 4-10 g/l | Zollner & Kirsch [27] |
| TG | 0,68-l,70 mmol/l | G. Buccola & H. David [28] |
| TCh | 3,l-5,2 mmol/l | CC. Allain et al [29] |
| LDL-ch | <3,4mmol/l, danger at adults > 4,1 mmol/1 | Friedewalde & Fredrickson [30] |
| HDL-ch | >1,6mmol/1, danger at adults < 0,9 mmol/1 | G. Warnick et al [31] |
| Glicemia (Gl) | 3.5-6.5 mmol/L | Turbidimetric, Aparat Cobas-Integra 400 |
| HbA1 c % | 4.4-6.6 % | Turbidimetric, Aparat Cobas-Integra 400 |

Table number 5. Presentation of diabetes patients under therapy

| Tot. Pacients | D.M Tip 1 (insulin-dependent ) | D.M Tip 2 (oral hypoglicemic) |
|---|---|---|
| N°=180 | 100 | 80 |

Table number. 6: Distribution of patients by sex and age average

| Gender | Number | The average age |
|---|---|---|
| Men | 100 ( 55%) | 57.90 ± 10.00 |
| Women | 80 ( 45%) | 56.80± 9.50 |

**Table number 7: Distribution of control group average by gender and age**

| Gender | Number | The average age |
|---|---|---|
| Men | 100 (55%) | 57.20±11.00 |
| Women | 80 (45%) | 58.00±10.50 |

Table. 8: Distribution of patients according BMIx: male=100 and female =80

| BMIx | Women=80 | Men=100 |
|---|---|---|
| Poor feeding | 18 | 30 |
| Normal feed | 30 | 42 |
| More feed | 26 | 18 |
| Obesity instance II-a | 6 | 10 |

From the total number of examinated patients – 180 (100% ) by BMIx, with the highest percentage of 32.0% were patients that belong to the group that were normal feeded, than follows the group of patients fed highly with 45.0 %, then the group fed poor 13.0%, and finally the group with second-degree obesity –a (II-a) with 10.0%, under the table and graph number 8. The difference between patients according to statistics is not significant with p<0.0005, and shows that this is homogeneous groups of patients.



## Statistical processing of material examined

Values obtained of blood glucose, HbA1c% and lipids (Total chol., TG, HDL-ch, LDL-ch) and control group are presented with average values and standard deviation X ±_ SD. We tested the association between obtained variables, with linear regression analysis (y=Bx+A) where it was estimated the correlation coefficient ,,r" with statistical value for,,p" less than 1%, p<0.0001 . Comparative statistics of the parameters of blood glucose and HbA1c % between the two groups, was analyzed with test calledstudentov,,t", while for dependent and independent exa-mples, as well as non-parametric tests, we used Mann-Whitney-U test. Statistically signifi-cant differences between the group of patients and control group for obtained values of the examined parameters, were analyzed with the test so-called ,,Anova Two-Factor" with statistical value for ,,p " less than 5%, respectively <0.0005.

## GAIEND RESULTS:

Results ( glycaemia, HbA1c, lipids,-tot.chol.,TG, HDL, LDL) obtained from patients group and control group are presented in tabular form. From these tables we can observe that at the two gruops of patients ( DM Type-1 and DM Type- 2 ), are verified high concentrations of lipids and HbA1c with significant statistical differences for p<0.0001, compared with control group. Between obtained values of patients ( DM Type-1 and DM Type-2 ), was not noticed any significant difference, facts that are consistent with many other studies. Lipid parameters presented a significant increase of the concentrations of: LDL-ch and TG, while low concentrations of HDL-ch at two group of patients with ESRD and DM, compared with the results from the control group. Values obtained the total cholesterol (TC-h) from the group of patients with DM and ESRD, compared with control group did not show any statistical significance.

Table nr.9. Presentation of the average values of the parameters analyzed to examine patients with DM type 1 - the Insulin-Dependent $N^0$=100) and DM type 2 (with oral hypoglycemic-$N^0$=80)

| Parameters | Number | Average | Minimum | Maximum | ± SD |
|---|---|---|---|---|---|
| **Patients with Diabetes Mellitus, Type 1 (insulin-dependent $N^0$ = 75 )** | | | | | |
| HbA1c % | 100 | 9.60 | 6.80 | 13.50 | 6.70 |
| Glycaemia | 100 | 10.18 | 7.50 | 11.40 | 3.80 |
| LT | 100 | 7.40 | 2.80 | 12.60 | 2.00 |
| TG | 100 | 3.60 | 1.90 | 4.60 | 1.30 |
| Cholesterol | 100 | 5.80 | 2.80 | 7.20 | 3.50 |
| HDL-ch | 100 | 1.10 | 0.50 | 3.80 | 0.90 |
| LDL-ch | 100 | 4.80 | 3,20 | 5.80 | 1.20 |
| **Patients with type 2 D. Melltus tip 2 ( oral hypoglycemic - $N^0$ = 45)** | | | | | |
| Glycaemia | 80 | 7.50 | 4.00 | 9.00 | 3.80 |
| HbA1c % | 80 | 8.10 | 5.80 | 8.50 | 3.50 |
| LT | 80 | 7.40 | 5.80 | 10.40 | 4.60 |
| TG | 80 | 3.80 | 2.60 | 4.20 | 0.90 |
| Cholesterol | 80 | 5.20 | 3.60 | 6.20 | 2.80 |
| HDL-ch | 80 | 1.04 | 0.90 | 2.40 | 0.90 |
| LDL-ch | 80 | 4.80 | 3.10 | 5.90 | 1.50 |



Table number 10. The average values of the analyzed paramaters for urea, creatinin and uric acid (serume values) and GFR defined under formula from Cocroft&Gault in ml / min in examined patients with DM Type 1 (insuline dependent) N0 = 100 at the beginning of the study

| Parameters | Average values | ± SD |
|---|---|---|
| Potassium (mmol/l) | 4.60 | 0.50 |
| Urea(mmol/l) | 16.50 | 4.80 |

| | | |
|---|---|---|
| **Creatinin(mmol/l)** | **350.00** | **20.00** |
| **Uric acid(μmol/l)** | **380.00** | **40.60** |
| **GFR ( by Cocroft&Gault)** | **54.00 ml/min** | **8.50** |

Table number 11. The average values of the analyzed paramaters for urea, creatinin and uric acid (serume values) and GFR defined under formula from Cocroft&Gault in ml / min in examined patients with DM Type 1 (insuline dependent) N0 = 100 after 12 months

| Parameters | Average values | ± SD |
|---|---|---|
| **Potassium (mmol/l)** | **5.0** | **0.60** |
| **Urea (mmol/l)** | **18.40** | **3.90** |
| **Creatinin ( mmol/l)** | **390.00** | **24.00** |
| **Uric acid(μmol/l)** | **410.00** | **38.50** |
| **GFR (by Cocroft&Gault)** | **60.00 ml/min** | **8.40** |

Table number12. The average values of the analyzed paramaters for urea, creatinin and uric acid (serume values) and GFR defined under formula from Cocroft&Gault in ml / min in examined patients with DM Type 2 (treated with oral hypoglycemic) N0 = 80 at the beginning of the study



| Parameters | Average values | ± SD |
|---|---|---|
| **Potassium (mmol/l)** | **4.50** | **0.80** |
| **Urea (mmol/l)** | **14.00** | **2.20** |
| **Creatinin ( mmol/l)** | **320.00** | **10.00** |
| **Uric acid (μmol/l)** | **346.00** | **23.00** |
| **GFR (by Cocroft&Gault)** | **60 ml/min** | **5.20** |

Table number 13. The average values of the analyzed paramaters for urea, creatinin and uric acid (serume values) and GFR defined under formula from Cocroft&Gault in ml / min in examined patients with DM Type 2 (treated with oral hypoglycemic) N0 = 80 after 12 months

| Parameters | Average values | ± SD |
|---|---|---|
| **Potassium (mmol/l)** | **5.00** | **0.50** |
| **Urea (mmol/l)** | **16.00** | **2.90** |
| **Creatinin ( mmol/l)** | **390.00** | **14.00** |
| **Uric acid (μmol/l)** | **420.00** | **10.00** |

| | | |
|---|---|---|
| **GFR (by Cocroft&Gault)** | **54.00 ml/min** | **6.80** |

In the tables we can notice that between the parameters of the two groups of patients with DM (Insulin dependent patients and patients that are treated with oral hypoglycemic) there is no significant difference, except a slight increase of urea, kreatinin, uric acid and a mild decration of gromerular filtration (but on a significant decration) that shows the stabilization of diabetes takes place, and the rate of the renal insufficiency will slow down.

Table number 14. Presentation of the Mann-Whitney U-test for the difference of the analyzed parameters values at patients with DM type 1 and DM type 2.

| Parameters | U | Z | *p-level* |
|---|---|---|---|
| Glicemi | 6850.000 | 0.57595 | 0.950250 |
| HbA1c % | 8565.000 | 0.49340 | 0.007520 |
| LT | 1170.000 | -0.124584 | 0.900570 |
| TG | 648.500 | -3.25700 | 0.001130 |
| Cholesterol | 1068.400 | 0.42690 | 0.601380 |
| HDL-ch | 1086.400 | 0.52610 | 0.60500 |
| LDL-ch | 1649.400 | -0.08540 | 0.864620 |

The difference which was recorded between the average values of patients with DM type 1 and type 2 DM was nonsignificant, for p <0.005. Significant difference was recorded only at: TG (p = 0.001130)



# 4 DISCUSSION

There are documented facts that a large number of patients with DM and ESRD are potential candidate of a large number of diseases: cardiovascular, unstable angina pectoris, ischemic heart disease, acute myocardial infarction, left ventricular hypertrophy, congestive heart weakening , brain stroke, macrovascular complication, peripheral vascular diseases, diabetic vascular complications, diabetic retinopathy etc. All the above mentioned diseases are frequent and the main causes of morbidity and mortality of uremic and diabetic patients treated with HD (32-36). Among the risk factors that in recent years have been given special attention, are higher concentration of lipoproteins and hyperglycemia. Therefore the American Association of Diabetes always suggests the maintenance and regulation of normal values of glycemia. Irregular checks and bad control of glycemia, are calculated as a indipedent risky factors rapid progression in ESRD (regardless of the type of diabetes). Patients with chronic renal failure have disturbed metabolism of glucose and insulin sensititvity. The basic mechanisms of disruption of glucose metabolism at diabetic patients with ESRD are not well known, but it is assumed that in this mechanism are involved and influencing: increase of gluconeogenesis in liver, reduced hepatal and skeletal absorption of glucose from muscles helped by an impairment of intracellular metabolism of glucose , due to the reduced oxidation of glucose in carbon dioxide and water , or as a consequence of the reduced synthesis of glucagon. The exact mechanism of insulin resistance of diabetic patients with ESRD is unclear, although some experts in their clinical studies have verified that during uraemia

glucose production and glucose absorption from liver are normal, however skeletal muscles are the principal place of insulin resistance, while the oxidation of glucose is relatively normal (37,38,39). Other factors that contribute to insulin resistance at uremic patients with diabetes are: accumulation of uremic toxins (proinflammatory cytokines, Interleucin,, MIA syndrome , secondary hyperparathyroidism , increase of PTH, renal anaemia, metabolic acidosis , iron deficiency, intravenously suppleme-ntation therapy with calcitriol (40,41,42).The need for insulin in patients with DM and ESRD showa a biphasic requirement. At the beginning control (where GFR> 50 mL / min) and balance of glycemia is deteriorating due to insulin resistance. Therefore to achieve normalization of glucose are needed higher doses of insulin. With advanced kidney failure and reduction of GFR <50 ml / min, insulin needs are smaller, and for normalization of glycemia are needed lower doses of insulin, even in some extreme cases may be necessary to stop with insulin. The need for insulin is also reduced due to reduced calorie intake of uremic patients with diabetes (43,44). The measurement of HbA1c should be the most accurate method to assess glycemic control at patients with diabetes and ESRD, and uremic patients treated with HD(45-48) . Management of diabetic patients with advanced kidney disease, involves the use of low protein diet and limited sugary foods. In patients with type 1 diabetes (insulin therapy) food and insulin should be taken at certain time, and also attention should be paid to body weight, physical activity etc. Therefore, patients with diabetes and chronic renal failure should be advised to consume food with a limited amount of protein and to compensate the losses of calories from carbohydrates. This group of patients should avoid oral hypoglycemic, because of risk from hypoglycemia, with the exception of Glipizide or repaglinide. It is proven and documented that there is a high correlation between renal damage (micro / makroalbuminurise and proteinurise) and high values of glycaemia and HbA1c, with the rapid pace of progress of esrd, associated with diabetic nephro-pathy, and retinopathy (49,50). A large number of studies on the role and effect of diabetes, have verified that patients with diabetes have pace and higher frequency of chronic renal damage progression. During blood laboratory examinations of patients with DM (regardless of the type of diabetes) is always present hypertrigly-ceridemia and high values of C-Reactive Protein (PCR), that also shows the presence of a silent inflammation in patients with diabetes mellitus (DM) and chronic renal failure. A large number of epidemiological studies have verified that with regulation and control of hyperglycemia, significantly is reduced the incidence rate of renal disease, therefore the American Association for Diabetes annually provides recommendations on control and regulation of hypergly-cemia and elevated HbA1c values of patients with ESRD and Diabetes Mellitus, which recommendations signify-cantly slows down the pace of progress of the ESRD and the risk of CVD. In recent years the incidence of ESRD as a result of unregulated diabetes and diabetic nephropathy not only in the US and Europe, but also in the Balkans, has an increase of 33% -40%, which arises from the failure to treat the diabetes. Therefore recent years nephrologists always suggest and propose that the measurement and monitoring of blood glucose, HbA1c, arterial pressure and lipid control, to be one of the manda-tory measures for doctors at primary and second-dary practice, which evidently will reduce the rapid pace of diabetes. Patients with diabetes mellitus are at higher risk for early atherosclerosis compared with healthy population, as well as its consequences on the cardiovascular system. According to contemporary thoughts diabetes is a multi-factorial disease etiology, and its main characteristic is hyperglycemia accompanied by metabolic disorders of sugars, fats, and proteins, which are manifested by disturbances in the secretion of insulin, insulin resistance, or by interaction all the aforementioned mechanisms. As the underlying factors of appearance of cardiovascular and cerebrovascular disease, and early atherosclerosis in patients with DM, disorders on metabolism of lipids have an important role (51,52,53). Function of apolipoproteins is that they enable the hydrosolubility in water of undigested primary plasma lipids (Ch, TG, FL) by forming hydrosoluble macromolecular complexes of lipoproteins who are transported through the blood. Disorders of apoproteins are genetically determined and their function is defined in the basic way for any apolipoprotein in particular. ApoB-$_{100}$ provides the absorption of cholesterol from hepatic and extrahepatic tissue by binding to receptors B/E enabling the extraction of triglycerides from the liver. Increased concentrations of ApoB-$_{100}$ except in patients with Diabetes Mellitus (DM) are also recorded in other diseases as hyperproteinemia: Type II-A, II-B, Type-IV, Type-V, the period of pregnancy, nephrotic syndrome, hiperapo-ß lipoproteinemia, hepatic duct obstruction, smoking, use of diuretic, excessive use of ß-inhibitor therapy with corticosteroids, therapy with ciclosporin (CSA) and in patients with chronic renal failure. Small lipoprotein-A (Lp/a/) antigen (Apolipoprotein/a/; Apo/a/) is synthesized in the liver and in intracellular way via

disulfide links is connected with ApoB-$_{100}$. Lp(a) for the first time discovered Berger in 1963 (54). And is assumed that is a variation of LDL-cholesterol (LDL-ch) and quantitative marker for the risk of atheromatous [Lp(a)-atheromathosis]. Lp(a) reacting with fibrinolysis by enforcing thrombogenesis and formation of atherosclerotic plaque. Lp(a) in plasma circulates together with ApoB-$_{100}$ as the protein basis of lipoproteins (Lp) rich with esterified cholesterol. Lipoprotein(a) can be calculated as the reactant in the acute phase of injury. A large number of studies have documented that between CVD and high value HgbA1c there is a high positive correlation with IRKT patients and D. mellitus (55,56.57). Numerous epidemiological studies and the American Association for diabetes (aad) have verified and documented that the regulation and regular check of glycemia decreases the risk of cardiovascular disease (CVD) and their complications wich reduces the mortality rate in uremic patients treated with hemodialysis (HD) ( 58). Concentration of glycated hemoglobin (HgbA1c) (which represents the average value of glycemia within three months) is calculated as the gold standard in the assessment of the risk of CVD in patients with ESRD treated DM and HD. American Association for diabetes (AAD)- always calls and suggests examination of glycated hemoglobin in order to behave adequate treatment decisions and treatment of diabetes in patients with ESRD in order to reduced the complications of diabetic nephropathy (59,60) and slow the pace of progress of the ESRD. This happens by the lack of consensus on HgBA1C testing of patients with ESRD and diabetes type 1 and type 2 that in the initial stages of the disease, especially in those patients who are treated with EPO therapy prior to treatment with HD. In the pace of disease progression in patients with diabetes and ESRD affect many factors: the pharmacodynamic effects uremic acid, the perocedures dialysis itself, influence of insulin pharmacokinetics on carbohydrate metabolism and oral hypoglycemics, oxidative stress, lipidic peroxi-dasis, MIA syndrome, arterial hypertension, dyslipidemia, hypertriglyceridemia, shortened erythrocyte life, renal anemia etc. ESRD and DM patients, due to the appearance of anemia in the initial stages should be treated with Eritropoetin (rHuEpo) because eritropo-etina increases the percentage of reticulocyte and stimulates the production of new red blood cells (61). Some authors have verified a high correlation between high concentrations of ApoB-100 and Lp (a), and proteinuria in patients with diabetes mellitus. The above phenomena are justified by the fact that proteinuria results with increased protein synthesis in the liver, which increased synthesis, stimulates more the synthesis of apoproteins with origin from liver, and in particulary increases the concentration of apoliporoteins (a), a constituent of lipoproteins (a). A number of authors have verified early atherosclerosis in patients with DM-Tip1 and those with DM-Tip2 measured with the the scale of the occlusion of peripheral arteries, which is in high correlation with high concentrations of Lp (a). Results obtained from lipid profile showed a high disorder for both groups of exami-ned patients ( those with Type 1 DM and those with DM-Tip.2), which is consistent with all studies about disorders of lipid profile at patients with diabetes. A significant number of patients with DM compared with control groups of healthy individuals present high concentrations of ApoB-100, HbA1c% and Lp (a). This high correlation many authors correlate with the first symptoms of kidney damage from diabetes (the presence of macro- and micro- proteinuria) at those patients. A number of approxi-mately 40% of patients with diabetes and esrd a year before starting treat-ment with HD, have not check the value of HbA1c. According to recent reports from the Association of American nephrologists have there are evidences for increased use of insulin and oral hypoglycemic, which tells us about aggressive access in the treatment of patients with ESRD and diabetes. In the presentation of cardiovas-cular diseases and mortality rates at uremic and diabetic patients treated with HD, in addition to increased sugar level, also affect many other factors such as: disorder of lipid metabolism, hyperapo-lipoproteinemia, pharmacodynamic effects of uremia, uremic toxins, hemodialysis as medical procedure, effects of insulin, disorders of carbohy-drate metabolism, disorders of coagulation factors, arterial hypertension, smoking, secondary hyperpara-thyro-idism, hyperhomocysteinemia, thrombotic factors, Oxidative stress etc.There are documented facts that the number and the life of erithrocytes at patients with ESRD are reduced, so is expected the decrease of concetration of HbA1c. Eritropoetin therapy of uremic patients with diabetes treated with hemodialysis, is proved that increases the percentage of new red blood cells in circulation, with the smallest exposure of glycemia during the process of glycolysis. HbA1c measurement is required every three months, but there are a group of patients with large discrepancy of values of glycaemia, so measurements of HbA1c at that group of patients should be more frequent. ( 62). Chronic hyperglycemia combined with dyslipidemia and hiperapolipoproteinemi even further increase the risk of morbidity and mortality from cardiovascular disease in

uremic patients with diabetes treated with chronic hemodialysis terminals.About 30% -60% of patients with DT-1 have developed microalbuminuri within 10-20 years after the onset of diabetes (63,64) with chronic kidney damage. Chronic renal failure generally occurs 15-20 years after the start of the presentation that microalbuminurise, and ESRD occurs in 50% of patients with mikroalbuminuri within ten years and 75% within 15 years. Thus, regardless of model, microalbuminuria appears to play a fundamental role in the initial development of the DNP, and macroalbuminuria is a factor the DNP(Diabetic Nephropaty-DNP in the progression and evolution of ESRD evolution. This will be a reason to target the reduction of urinary excretion of albumin in the treatment of DNP. pathogenesis exact NDP is complex and not fully known. This complicates even further the NDP and the medical management requires a multidisciplinary approach aiming to control all the factors that affect its progress. optimal control of blood glucose, hemoglobin that glikolizuar with insulin therapy remains a fundamental objective in the management of patients with type-1 diabetes. Antihypertensive therapy with ACE blocker and statin,fibrat, niacin,cholestyramine also recommended to these patients when arterial pressure and lipid profiles and eshet under normal lipid profile

# 5 CONCLUSION:

Treatment and normalization of their values at the initial stages of the disease is of big importance, and can significantly affect the prevention and can prevent premature progression rate of ESRD and atherosclerotic processes in coronary, cerebral and peripheral arteries. For conclusion we can say that the knowledge of mechanisms, etiopathogenesiss, function and abnormalities on polymorphism and the negative impact of hyperglycemia and dyslipidemia are among the indipendent and risky factors of CVD and premature atherosclerosis, in patients with ESRD and diabetes.. Uremic and diabetic patients treated with HD (regardless of the type of diabetes) are at high risk of early atherosclerosis appearance. Hyperglycemia and dyslipidemia are among the most dangerous factors of progress of ESRD. Therefore, improvement, balancing and regular control of diabetes and lipid, are the first step in preventing the pace of progress and the incidence of ESRD, early atherosclerosis and CVD. Are needed to further studies on the occurrence of CVd in uremic patients with diabetes treated with HD, in order to propose on tcocontrol of blood glucose and HbA1c based onthe facts at the early stages of the disease.



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