

Treatment And Dyslipidemia of Patients With Diabetes Mellitus (DM) and Cardiovascular Diseases

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Abstract: Cardiovascular disease (CVD) is a primary cause of morbidity and mortality among patients with hyperglycemia or type 2 diabetes mellitus (DM) despite the availability of effective therapies to treat major risk factors such as elevated blood pressure and cholesterol levels. The most common lipid pattern in patients with DM, hypertension, and/or the metabolic syndrome includes hypertriglyceridemia, increased concentrations of small dense low-density lipoprotein particles, low levels of high-density lipoprotein cholesterol (HDL-ch, increased remnant lipoproteins, and elevated apolipoprotein-B concentrations. This profile of mixed dyslipidemia significantly increases risk for all forms of atherosclerotic disease, including cardiovascular disease (CVD).The burgeoning prevalence of insulin resistance throughout the world is greatly increasing the incidence of mixed dyslipidemia. It is estimated that approximately 40% of patients with coronary artery disease have low-density lipoprotein cholesterol (LDL-ch) levels below 130 mg/dL yet these patients also have low levels of HDL-ch, with or without increased levels of triglycerides (TG). Observational studies indicate that low HDL-ch levels are strongly and independently associated with increased CVD risk. The results of the first major clinical trial specifically focusing on the treatment of low HDL-C demonstrated that lipid treatment that raised HDL-ch and lowered TG but had no effect on LDL-ch substantially reduced the incidence of major cardiac and cerebrovascular events. One of the major risk factors of early atherosclerosis and the introduction of thrombolytic processes and cardiovascular disease in patients with diabetes mellitus in addition to known factors (arterial hypertension, MIA syndrome, smoking, sedenterity, oxidative stress, psycho-stress, cytokines, etc ...) in recent years are counted also lipid abnormalities such as dyslipidemia or rather, are diabetic dyslipidemia. In patients with Diabetes Mellitus (DM type 1 and DM type 2) is proven and documented that there is a high positive correlation between hyperglycemia, glycosylated hemoglobin (HbA1c) and high lipid concentration values (LDL-ch and TG) and decrease in HDL-ch concentrations micro and macrovascular consequences, cardiovascular disease (CVD), retinopathy and diabetic nephropath(1) There are verifiable evidence that patients with insulin-dependent DM or treated with oral therapy are candidates with potential risk of cardiovascular diseases, peripheral vascular diseases, stroke compared with the healthy population. In the plasma of patients with DM were detected besides high concentrations of: blood glucose, glycosylated hemoglobin (HbA1c) were also detected high concentrations of LDL-ch and triglycerides and low concentrations of HDL-ch which further help the occurrence of cardiovascular disease (CVD) and coronary atherosclerosis complications (2). Aim of the paper work was to verify and document, role and correlation of lipid disorders (dyslipidemia) and hyperglycemia in the pace of progress and the appearance of cardiovascular diseases in patients with Diabetes Mellitus type.1 and the type 2 compared with healthy control individuals. The paper also aimed to influence positive effects of statins family in the treatment of hypercholesterolemia in patients with diabetes mellitus type 1 and type 2. In our patients treated with statins at the dose of 40 mg per day with duration of 3 months and reached a target of reducing the LDL cholesterol by 30-38%. The research was prospective cohort („, cross-section ") Totally are included N^o -240 examiners of whom 120 were patients of diabetes mellitus (DM 75 with tip1 while 45 were with DM type 2) while 120 individuals were healthy you served as group controllers.

Index Term: Cardiovascula disease(CVD), Diabetes Mellitus (DM), statins, glycosylated hemoglobin (HbA1c), Lipids profiles

1 INTRODUCTION

Despite the availability of treatment guidelines for dyslipidemia management and the abundance of clinical trial evidence highlighting the benefits of lipid-modifying therapy to reduce the risk for CHD and its clinical sequelae, treatment of DM patients with abnormal LDL-C, HDL-C, and TG levels continues to be suboptimal. In our patient population, 16% of patients with suboptimal lipid values and 21% of our mixed dyslipidemia group had DM. Our DM patient population had a high (> 50%) proportion of patients with abnormal HDL-C and TG levels. This is in line with the results of a recent study by Grant et al. (78), who also found a high prevalence of suboptimal HDL-C among

patients with type 2 diabetes, with nearly half (49.5%) of patients exhibiting low HDL-C. Another study, involving a high-risk population with documented CHD or CHD risk equivalents, also found a high prevalence of low HDL-C across various LDL-C levels, including among patients taking statins(78). In that study, low HDL-C was most prevalent in patients with LDL-C of 70 mg/dL or lower, and was equally and highly prevalent in patients taking statins (67%) and those not taking statins (64%). A large percentage of DM patients with suboptimal lipid levels in our study did not receive lipid-modifying therapy either prior to or after a suboptimal lipid value was obtained (53% and 42%,

respectively). While the percentage of patients receiving lipid-modifying therapy increased in the post-index period, a substantial number of DM patients with suboptimal lipid levels did not receive any lipid-modifying therapy in the post-index period irrespective of abnormal lipid parameter, or the degree of the abnormal value. At least 30% of DM patients with suboptimal lipid levels across all mixed dyslipidemic groups were not treated with any lipid-modifying medication for at least 6 months post-index. Although lipid treatment rates increased post-index in all mixed dyslipidemic groups, and even though treatment rates were correlated with the number of total risk factors, abnormal lipid parameters and more severe lipid value quartiles, the incremental use of lipid-modifying medication was not as substantial as would be expected, given the compelling association between multiple lipid abnormalities and cardiovascular risk in patients with DM. Of particular note is that in DM patients with low HDL-C and elevated TG, the most common post-index lipid therapy used was statin monotherapy (in 37% of patients), and only 17% received any niacin or fibrate therapy to target suboptimal HDL-C or TG. Grant et al.(78-81) described similar findings, with the vast majority of Diabetes is one of the most massive diseases in the modern world with a tendency to increase the size of large and mostly appears in the developed and developing world (3). Diabetes is counted as the fourth cause of mortality in developed countries. A large number of studies have verified that epidemiologic regulation and control of sugar concentrations significantly reduced the rate of incidence of cardiovascular diseases (CVD) cerebral-vascular insults therefore the American Association for Diabetes (AAD) always provides guidance and recommendations on control and regulation of high values of glycemia and examination of glycosylated hemoglobin(HgbA1c) in patients with DM with which measures also reduce the risk of CVD, myocardial infarction and mortality of this group of patients. The control of hyperglycemia and glycohemoglobine (HgbA1c-average value of glycemia within three months) represents one of the primary measures in pursuit of the pace of progress to diabetes, so regular controls tracking and balancing of diabetes with dyslipidemia in the early stages of the disease, obviously would influence the prevention of the appearance of early atherosclerotic processes in coronary, cerebral and peripheral arteries. We always control glycemia and HgbA1c in patients with diabetes mellitus respecting the recommendations of AAD.

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Recent years the incidence of unregulated diabetes and diabetic nephropathy and not only in the US and Europe but also the Balkans has an increase of 38% -42% which is due to: unregulated treatment of diabetes, psychostress, adiposity unrespected hygiene and dietary measures, excess consumption of fatty foods and disregard of ordinated therapy, smoking, physical inactivity, oxidative

their study patients receiving statin monotherapy and a very small percentage being prescribed treatment targeting the suboptimal HDL-C level.

These results are also consistent with those reported by Klingman and colleagues (81). who evaluated data from the 1999–2000 National Health and Nutrition Examination Survey to assess the state of dyslipidemia management in the US adult population and to determine whether treatment patterns were consistent with guideline recommendations. They demonstrated that 44% of treatment-eligible adults had never been told by a physician, or any other healthcare professional, that they had dyslipidemia. Among all treatment-eligible adults, only 30% were adopting therapeutic lifestyle changes (TLC) and only 10% were receiving lipid-modifying therapy. Very high percentages of treatment-eligible adults were receiving no treatment at all for dyslipidemia: 69% overall, 61% of high-risk adults, 70% of medium-risk adults, and 77% of low-risk adults. Unlike the present study, however, Klingman and colleagues focused on the achievement of LDL-C goals and did not evaluate HDL-C and TG levels.

stress etc. Therefore, in recent years doctors always suggests that measurement and monitoring of blood glucose and lipid control to be one of the goals and measures mandatory for doctors of primary and secondary practice to what will be considerably decreased the incidence of SKV. So in the initial stages of presentation of Diabetes (DM) have dyslipidaemia and dyslipoproteinemia disorders with increased concentrations of LDL-ch, TG and HDL-ch reduction compared with patients with other diseases, so early examination of these disorders can significantly affect the prevention of the appearance of cardiovascular diseases (CVD (6.7). There are documented facts that the disorders of blood glucose and HgbA1c everytime in patients with DM are also associated with disturbance of lipid and therefore we decide to make our paper examinations lipid profile (total Cholesterol (CHT), Triglycerides(TG) Total lipid (TL), HDL and LDL-ch)], glycemia (GI) and glycosylated hemoglobin (HbA1c) in patients with diabetes-insulin users and patients treated with oral therapy. Patients with Diabetes Mellitus (DM) are at higher risk for early atherosclerosis and its consequences to the cerebrovascular system, cardiovascular and peripheral artery atherosclerosis compared with healthy population (4,5). Besides lipid abnormalities patients with DM have the disturbance of apolipoproteins. Apolipoproteines are integral protein of lipoproteinemic macromolecule specific to each class of them (8). Are related to lipid molecule using hydrophobic properties of fatty acids from phospholipids and polar part of the polypeptide chain (the process of inter-ionic reaction between phospholipids couples and opposite-charged amino acid alpha-helix electric to apoproteine. As factors underlying the appearance of cardiovascular diseases, cerebrovascular and early atherosclerosis in patients with DM apolipoproteines have an important role in metabolic disorders (9-11). Genetic factors of cardiovascular diseases, cerebrovascular and sclerotic processes are counted: the disruption of reverse transport of HDL-ch, cumbersome expression of B-receptors compared with E-receptors, reducing the conversion of VLDL to IDL and LDL ch (12). The function of apolipoproteins is that they allow plasma lipid hydrosolubility in water (C_h, TG, FL) of macromolecular complex-forming hydrosolubile lipoprotein (apolipopro-proteins) that are transported by the blood. The exact pathogenesis of diabetic dyslipidemia is not yet known; however, a large number of evidence suggest that insulin resistance has a central role in the development of this pathological phenomenon. The main cause of diabetic dyslipidemia is the release of fatty acids by increasing

insulin-resistant fat and increased flux of free fatty acids in the liver in the presence of adequate stores of glycogen, which is still draining triglycerides encourages production, which in turn stimulates its secretion apolipoproteins-B (apo-B), Lp (a). and VLDL cholesterol. Diabetes mellitus – type 1 and generally well controlled rarely is associated with hyperlipidemia except diabetic ketoacidosis often associated with hypertriglyceridemia due to the increased release of tissue fatty acids (13-17). Pathological consequences of hypertriglyceridemia mostly appear to lipoprotein metabolism and early atherosclerotic manifestation. Anytime Diabetes is associated with high risk of cardiovascular disease (CVD) .Management of diabetic dyslipidemia is a key element in a multi-factorial approach to prevent the occurrence of CVD in patients with diabetes. Patients with diabetes have a higher absolute risk of coronary disease presenting as patients without diabetes equally but with coronary disease, acute myocardial infarction and congestive heart failure, high prevalence of mortality(18,19) Lipid disorders ie diabetic dyslipidemia (atherogenic dyslipidemia) are always manifested by increased levels of triglycerides and LDL cholesterol and reduced level of cholesterol proatherogen-HDL-ch. Diabetic dyslipidemia is often helped by insulinemic resistance and is present even before the diabetes. Small dense particles of LDL are more atherogenic due to their high sensitivity by increasing oxidative modification and the growth of taking the fat from the arterial wall. Overall, 30-40% of patients with diabetes suffer from diabetic dyslipidemia. All current

national guidelines (NCEP- National Cholesterol Education Program) on the treatment of diabetic dyslipidemia as main target values have reduced the TG and LDL-ch and they suggest for LDL-c values from 100 to 70 mg / dl (20,21,22) as the optimal value for preserving the risk of coronary disease. NCEP recommendations association 2005 for the start of treatment of diabetes dyslipidemia of hypercholesterolemia namely with statin should be started when the values of LDL-ch are > 100 mg / dl to gain target effects of treatment with decreases in LDL-ch of 30-40 %, no pre-Liner LDL cholesterol levels, thus the lower the degree of risk of CVD. Results of many studies on the treatment of diabetic dyslipidemia and verified results have proven very successful during treatment with statine. In the case treatment with statin did not give proper effect to then preferably combined therapy, statin and niacin or statin with holestipol or holestiramin or fibrates with but any means combination niacin and fibrates between statins family due to the harmful effects of myositis or rhabdomyolysis consequences (23-27). Improvement and regulation of blood glucose values regardless of the type of dyslipidemia treatment has shown positive effects in improving lipid values. Beneficial effects in improving lipid abrevations in tip2 diabetic patients with oral therapy have shown metformin and rapaglinid treatments. There is documented evidence of these drug's influence on the improvement of diabetes and lipid disorders is closely linked with reduced levels of triglycerides and increased HDL-ch values (28,29,30)

2 Material and Methods Used

The research was prospective cohort (, cross-section ") Totally are included N^o = 240 examiners of whom 120 were patients of diabetes mellitus (DM 75 with tip1 while 45 were with DM type 2) while 120 individuals were healthy you served as group controllers. For examination was used 5+ (5) ml of venous blood taken from the vein in the patient lying position in order to avoid possible variations and the influence of the position of patients on lipid fraction values (9- 12%) which occur if the blood of patients is taken from the horizontal position. Of the patients with DM (120) -54 (45%) of them were girls with an average age: 59.50± 10.00 but- 66 (55%) were male, with an average age: 58.70± 12:50 years. Group controller sound examination (voluntary blood donors) also were 54 (45%) women and 66 (55%) men with an average age identical: 15:00 ± 58.60 years. Of the total number of patients-N^o - 120with Type-1 diabetes mellitus (DM Tip1 th insulin dependent) were 75 while 45 were

patients with Type-II diabetes mellitus (DM type 2 th treated with oral hypoglycemic), table nr-1. Patients who were insulin dependent are counted as Type-1 while patients independent of insulin but with oral therapy, count as type-2 DM. So together with examination of concentrations of lipid profile, glycemia and the glycosylated hemoglobin (HbA1c) we made the determination of BMIx (Body Mass Index- tabel . no. 3). In all patients and the control group were analyzed lipid values of blood glucose and hemoglobin that is glycosylated within 3 months. The methods of determining the concentrations of lipid profile, blood glucose (GI) and HbA1c are identified in the table of number 2. As a reference value for GI and HbA1c values were taken according to criteria proposed by the World Health Organization-GI = 3.5-6.5 mmol / l, (HbA1c%-4.4-- 6.6%.

Table number 1: Presentation of diabetes patients under therapy-oral and insulin

Tot. patients- 120	DM type 2 (oral hypoglycemic)	DM type 1 (insulin-dependent)
	45	75

Table number 2: Distribution of patients by sex and age average

Gender	Number	The average age
Men	66 (55%)	58.70± 12:50
Women	54 (45%)	59.50± 10.00

Table number 3: Distribution of the control group average by gender and age

Gender	Number	The average age
Men	66 (55%)	57.80 ± 11.50
Women	54 (45%)	58.50 ± 12:80

The average age of patients was male gender = 56.40 ± 12.80, while female sex was = 59.50 ± 14:50, the average age difference between male and female according to statistics is nonsignificant $p = 0.0005$, which indicates a homogeneous groups (tab. 2)

3 Statistical processing of material examined

Values obtained of the blood glucose, HbA1c% and lipids (Kol.Total, TG, HDL-ch, LDL-ch) and control group are presented with mean values and standard deviation $X \pm SD$. In the results were also calculated correlation coefficient "r" statistical value of p, " less that 1% ($p < 0.0001$). Statistics comparative lipid parameters between the two groups were analyzed to test the so-called

Studentov „ t "while for examples dependent or independent and non-parametric tests were used tests: Mann-Whitney-U. significant statistics differences between the group of patients and control group obtained values of the parameters of lipids, glycemia and HbA1c% were analyzed to test the so-called „ Anonova Two-Factor "statistical Worth „ p 'lesser of 5 %, namely $p < 0.0005$.

4 Results obtained:

The results obtained from the examination of blood glucose, HbA1c, lipid, (Kol.Total, TG, HDL-ch, LDL-ch) and the results obtained from the control group are presented in tables.2 and 3. Tables itself noted that the two groups of patients (DM Type-1 and DM-type 2) are verified high concentrations of lipids and HbA1% with significant statistical difference for $p < 0.0001$, compared with control group. Between values obtained of patients (with DM Type-1 and Type-2 DM) did not notice any significant difference facts that are consistent with many other studies (31,32). Lipid parameters presented a significant increase of the concentrations of: LDL-ch and TG and low concentrations of HDL-ch of the two groups of patients with DM compared with the results from acquired by the group controller.

Table number 4: Presentation of the average Values of the Parameters analyzed to Examine patients with type 1 DM - the insulin-dependent $N^0 = 75$ before treatment with hypopolypemic therapy.

Parameters	Number of patients	Average ± SD
HbA1c%	76	10.80±5.60
Glycemia	75	9.60±3.40
TL	75	7.50±2.50
TG	75	3.70±0.70
TCH	75	5.60±2,10
HDL-ch	75	1:00±0.80

LDL-ch	75	4.60±0.70
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Table nr.5: Presentation of the average Values of the Parameters analyzed to Examine patients with type 2 DM dependent N^o = 45 (oral hypoglycemic) -Before hippolypemic therapy treatment

Parameter s	Number of patients	Average	Minimum	Maximum	± SD
HbA1c%	45	8.10	6.90	8.90	1.20
Glycemia	45	7.80	6:40	9:00	0.80
TL	45	7:50	5:40	12:50	3:60
TG	45	3:50	2:50	4.60	0.70
TCH	45	5.80	5.00	7.90	2.40
HDL-ch	45	1.15	0.80	2.30	0.80
LDL-ch	45	4.90	3.90	6.80	0.60

Table number 6: Presentation of the Mann-Whitney U-test for the Difference of the Values of the Parameters analyzed patients with DM type 1 and type 2 DM

Parameters	U	Z	p-level
Glycemia	6750.000	0.46878	0.860358
HbA1c%	8280.000	0.48300	0.006860
LT	1145.000	-0.13778	0.890410
TG	68.95200	-3.25748	0.001120
Cholesterol	1080.700	0.39693	0.691420
HDL-ch	687500	-3.42614	0.001260
LDL-ch	8170.000	-3.456500	0.001470

Was Recorded qual Difference Between the average seething of patients with DM type 1 and type 2 DM is josinjifikant for p <0.005, Significant Difference Was Recorded only at: TG (p = 0.00112, HDL-ch (p = 0.001260) and LDL -CH (p = 0.001470)

Table number 7: Presentation of the average Values of the Parameters Examined in patients with DM Type 1, Type 2 DM and control group

	Patients with - DM Type 1 and Type 2 DM					Controls Group		
	Number	Average	Minimum	Ma ximum	± SD	Average	± SD	p
T L	1 20	7. 80	2. 40	12.60	2.8 0	6. 40	0.60	0 .0001
TG	1 20	3.85	2. 50	4. 80	0. 80	1. 28	0.63	0.0001
T Ch	1 20	5. 80	4. 60	7. 40	0.9 2	4.9 0	1.2 4	00:025
HDL-ch	1 20	1:03	0. 50	1. 15	0. 82	1.60	0. 60	0.0001
LDL-ch	1 20	4.20	3:40	5.4 0	0.9 5	3 .50	1.0 2	0.0001
Glycemia	1 20	8. 60	4.90	9.80	4.6 5	5. 60	2. 10	0.0001
HbA1c%	1 20	8. 60	5. 80	12. 40	3. 90	7.20	3. 80	0.0001

Table 7: shows significant differences-p between the parameters examined between the patients with Diabetes mellitus (type 1 and type 2) and the control group. The difference which appears between the average values of the examined parameters of the two groups is significant statistic except total cholesterol values differ with $p > 0.0005$). The values of the parameters examined LT, TG and LDL-ch, are higher of patients with DM-1 and DM-Tip Tip 2 with $p < 0.0001$, compared with control group. Lower values of patients with DM type 1 and type 2 DM compared with the control group were recorded only in HDL-ch for $P < 0.0001$.

Table number 8: Indicates significant differences between the examined parameters of patients with diabetes mellitus (type 1 and type 2) and the control group after 3 months after treatment with statins.

Parameters	Number of patients	Average	Minimum	Maximum	± SD	Controls group	± SD
Glycemia	120	8.60	6.40	8.90	1.20	6:30	0.50
HbA1c%	120	7.50	7.00	8.60	0.80	1.20	0.60
LT	120	7.40	5:20	7.50	1:40	4.60	1.20
TG	120	2780	2.40	2.90	0.80	1.70	0.60
TCh	120	5.90	4:00	5.40	1.20	3:60	1:00
HDL-ch	120	1.10	0.70	2.80	2:00	52.60	2.00
LDL-ch	120	4:30	3.50	4.00.	0.80	7020	3.50

From the table itself noted that the total lipid, triglycerides, total cholesterol and LDL-ch after treatment with statins doses of 12 weeks 1 tablet of 40 mg in the evening have significant reduction of their concentrations with $p = 0.0001$ while the HDL fraction ch noticed a remodeling to increase its concentration, which testifies to the positive effects of statin for a double effect and the regulation of LDL hypercholesterolemia but also in increasing proatherogen HDL-ch concentration

4 DISCUSSION:

Hypertriglyceridemia should be addressed with dietary and lifestyle changes. Severe hypertriglyceridemia ($>1,000$ mg/dL) may warrant immediate pharmacological therapy (fibrates or fish oil) to reduce the risk of acute pancreatitis. If severe hypertriglyceridemia is absent, then therapy targeting HDL cholesterol or triglycerides lacks the strong evidence base of statin therapy. If HDL cholesterol is <40 mg/dL and LDL cholesterol is between 100 and 129

mg/dL, a fibrate or niacin might be used, especially if a patient is intolerant to statins. Low levels of HDL cholesterol, often associated with elevated triglyceride levels, are the most prevalent pattern of dyslipidemia in persons with type 2 diabetes. However, the evidence base for drugs that target these lipid fractions is significantly less robust than that for statin therapy. In a large trial specific to diabetic patients, fenofibrate failed to reduce overall cardiovascular outcome.

Treatment of diabetic dyslipidemia recent years often by the Americanthat dyslipidemia and concentrations of elevated TG, LDL-ch and Diabetes Association (ADA American Diabetes Association) has beenreduced concentrations of HDL-ch are at high positive correlation and the topic of discussion by proposing dietary and therapeutic measuresindependent predictor of CVD risk (33). In recent study by group of on managing of dyslipidemia in patients with diabetes. There arepatients 5963 from ages > 40 years with dyslipidemia and diabetes documented facts that the patients with diabetes from lipid fractionstreated with statins its verified a reduction and a decrease in LDL-ch most often manifest hypertriglyceridemia (concentration increase offer 22% and significant reduction in symptoms of CVD triglycerides-TG) and hypercholesterolemia-increased concentrationsappearances (34). Observational studies of ADA American Diabetes of LDL-ch with decreased cholesterol values of proatherogen (HDL-Association together with friends Medical Nutrition Therapy -MNT-ch). In particular, patients with diabetes tend to have a significanthave verified that patients who have used more healthy diet and increase of oxidized cholesterol (LDLox) and a higher percentage ofincreased physical activity (normal body weight) had decreased the particles ,, foam cells "which are highly susceptible to oxidation attriglycerides and LDL-ch to increase levels of HDL cholesterol and high risk consequences of submitting the Cardiovascular diseaseshave had less symptoms of CVD (35,36,37). A large number of clinical (CVD, acute myocardial infarction, angina pectoris stable and unstablestudies for effects of treatment of diabetic dyslipidemia targeting the coronary insufficiency ...). A large number of cohort studies suggestscope of medication therapy (statins, fibrates, niacin holestipol,

holestiramin) as target values for effective treatment have been treated with fibric acid derivatives (gemfibrozil or fenofibrates) or proposed: LDL-ch are <2.60 mmol / l in HDL cholesterol are $= 1.02$ niacin .
mmol / l), and triglycerides levels are 1.7 mmol / l). The females HDL- the result of unregulated diabetes we have manifestations of the ch levels may be higher due to estrogens. Recommendations for disturbances in micro and macrovascular levels (39). There are documented treatment of dyslipidemia are always followed on the basis of facts that a large number of patients with DM are potential candidates for recommendations and consensus proposed by the ADA and NCEP-more comorbid conditions ranging from cardiovascular disease (ischemic National Cholesterol Education Program (38) . Hypertriglyceridemia heart disease, acute stroke infarction, angina pectoris unstable, left may be a risk factor for CVD in people with initial diabetes .Initial ventricular hypertrophy, congestive heart weakening, stroke, peripheral hypertriglyceridemia therapy is consisted of dietary preventive vascular disease, vascular complexity diabetic, diabetic retinopathy, diabetic measures such as: changes of way of life, weight loss, increased nephropathy, etc. All of the aforementioned diseases are the main cause of physical activity, limited consumption of saturated fats, reducing frequent and morbidity and mortality of patients with unregulated carbohydrates consumption , and reducing alcohol consumption, diabetes (40-45) therefore the American Association of Diabetes always balancing diabetes (oral therapy or insulinemic) and then if this suggests the maintenance and regulation of normal glycemia aforementioned measures do not show proper effects to then start values. Irregular checks and not balancing the glycemia is counted as one of therapy with medication Group of fibrates (gemfibrozil, fenofibrat, risk factors for cardiovascular diseases and rapid progression of chronic Clofibrat etc.) or in the cases of high hypertriglyceridemia fibrates may renal damage in patients with diabetes whether they are insulin users or be combined with Niacin (<2 g / day. Often the clinicians presented they have oral hypoglycemic therapy (46-52). Numerous epidemiological studies question of when and in which value of Tg should start treating and the American Association for Diabetes (AAD) have verified and hypertriglyceridemia? Decision to initiate pharmacological therapy documented that the regulation and regular check of glycemia decrease the depends on the judgment of the clinician - it must begin between risk of cardiovascular disease and myocardial infarction and their triglyceride levels from $2:30$ to $4:50$ mmol / l). The therapeutic complications with which is reduced the rate of mortality of diabetic patients combination of statins family and fibrates is prohibited due to the. Concentration of the hemoglobin that is glycosylated HgbA1c (which extremely high side effects of myositis and rhabdomyolysis. In case of represents the average value of glycemia within three months) is calculated high dyslipidemia these combinations are preferred therapy, statins as above standard risk assessment of CVD in patients with with nicotinic acid, statins with holestiramin or holestipol, fibrates with DM (53,54,55). American Association for diabetes (ADA American nicotinic acid, fibrates with holestiramin and holestipol, nicotinic acid Diabetes Association) always calls and suggests for mandatory screening of with holestiramin or Holestipol. Choosing statins family should depend hemoglobin glycosylated values in order to appropriately make decisions for mainly on lowering LDL necessary to achieve the goal of LDL-ch value treatment of diabetes in order to reduce further diabetic of <100 mg / dL [2.60 mmol / l]). The use of statin therapy with high complications [56 57]. The results of the acquired from lipid profile showed a dose (eg 80 mg) to treat dyslipidemia in patients with high levels of high disorder for both groups of patients examined (also those with Type 1 LDL- ch and TG also shall be limited to because of side effects DM also those with DM-Tip.2) that complies with all studies on disorders (increased transaminases and pain muscle) and therefore to these profiles of lipoproteins in patients with DM. In the presentation of the CVD patients therapy should be started with the dose of 40 mg once a day and mortality rates in diabetic patients except increased sugar level also and be accessed and then normalized target values after dosage effect many other factors such as: metabolic imbalance lipoapoprotein Apo-B laboratory examination shall be reduced to 20 mg per day. Patients and Lp (a), disordered metabolism of carbohydrates, disorder of coagulation with type 1 diabetes who are in good controlled glycemia tend to have factors, arterial hypertension, smoking, secondary hyperparathyroidism, normal levels of lipoprotein, unless they are overweight. Contained sedentary, oxidative stress etc. (58). Chronic hyperglycemia combined with lipoprotein may be abnormal, but the effects of these anomalies in dyslipidemia and hyperapolipoproteinemia increase the risk of morbidity and relation to CVD are unknown. Aggressive treatment of diabetic mortality from cardiovascular diseases in uremic patients with diabetes dyslipidemia decreases significantly the risk of CVD in patients with treated with terminal chronic hemodialysis. Besides disorder of carbohydrate diabetes. The main purpose of therapy is to reduce the concentrations metabolism diabetes as a chronic metabolic disorder impairs and other of LDL-ch to ≤ 100 mg / dL [2.60 mmol / l]. Initial pharmacological substances . Thus during diabetes predominates unraveling protein therapy consists and should be with the use of statins family. In case of metabolism that is expressed by decreases in total protein level in the blood, submission of an intolerance to statins family then preferably be and its special ingredients, such as: Albumins and globulins and all globulins combined therapy also with other hypolipemics (such as niacin, ingredients such as: alpha globulins, especially gamma beta globulins which holestipol, holestiramin, etc). Treatment of high levels of triglycerids are protective antibodies for the organism (59,60.61, 62).). Protein breakup

is clinically manifested with curbing of body growing. In diabetics there physical activity (normal body weight) had decreased the triglycerides and sensitive turbulences of lipids values .As we know the main lipids LDL-ch to increase levels of HDL ch and have had less symptoms of cholesterol, triglycerides, phospholipids and free fatty acids . These lipids in (67,68,69). A large number of clinical studies for effects of treatment of blood are not free but circulate with other substances as lipoproteins different dyslipidemia targeting the scope of medication therapy (statins, disorder of fatty metabolism in diabetes is the increasing of lipoproteins, niacin holoestipol, holestiramin) as target values for effective process (melting of fats) that occurs during the gluconeogenesis. treatment have been proposed: LDL-ch are <2.60 mmol / l in HDL causes the increase in blood of free fatty acids which serve as the starting point for excess production of some biochemical substances which are called females HDL-ch levels may be higher due to ketone bodies and therefore for the emergence of diabetes ketoacidosis. Recommendations for treatment of dyslipidemia are always During diabetes by activation of many metabolic pathways, emerges followed on the basis of recommendations and consensus proposed by the increase of the cholesterol and hypercholesterolemia ADA and NCEP-National Cholesterol Education Program (70.71) . Initial hypertriglyceridemia . On the other side for genetic reasons yet not hypertriglyceridemia therapy is consisted of dietary preventive measures clarified blood level rise occurs for some lipoproteins such as increased as: changes of way of life, weight loss, increased physical activity, LDL (which carries blood cholesterol) of VLDL (which carries in blood consumption of saturated fats, reducing carbohydrates consumption , endogenous triglycerides) and decrease of HDL (lipoproteins that remove cholesterol from the blood, also referred to as " clearing factor ") Increased (ischemic) and then if the aforementioned measures do not show proper cholesterol, endogenous triglyceride LDL and VLDL and HDL reduction effects to then start therapy with medication Group of fibrates (gemfibrozil, separately or combined between them form the phatobiochemical fibrat, Clofibrat etc.) or in the cases of high hypertriglyceridemia fibrates pathophysiologic basis of birth and acceleration of the atherosclerosis may be combined with Niacin (<2 g / day. Often the clinicians presented the process that damages mostly large caliber medium caliber arteries question of when and in which value of TG should start treating clinical practice known as atherosclerosis (63). Treatment of hypertriglyceridemia? Decision to initiate pharmacological therapy depends dyslipidemia recent years often by the American Diabetes Association the judgment of the clinician - it must begin between triglyceride levels (ADA American Diabetes Association) has been the topic of discussion from 2:30 to 4:50 mmol / l). The therapeutic combination of statins family and proposing dietary and therapeutic measures on the management fibrates is prohibited due to the extremely high side effects of myositis and dyslipidemia in patients with diabetes mellitus. Patients with type 2 diabetes myolysis. In case of high dyslipidemia these combinations are are potential candidates to four fold risk of cardiovascular diseases preferred therapy, statins with nicotinic acid, statins with holestiramin or presentation (CVD) compared with the population which suffers from holoestipol, fibrates with nicotinic acid, fibrates with holestiramin and diseases. There are documented facts that the patients with diabetes holestipol, nicotinic acid with holestiramine or Holestipol. Choosing statins lipid fractions most often manifest hypertriglyceridemia (concentration family should depend mainly on lowering LDL necessary to achieve the goal increase of triglycerides-TG) and hypercholesterolemia-increased HDL-ch value of <100 mg / dL [2.60 mmol / l]). The use of statin therapy concentrations of LDL-ch with decreased cholesterol values in high dose (eg 80 mg) to treat dyslipidemia in patients with high levels of proatherogen (HDL-ch). In particular, patients with diabetes tend to have HDL-ch and TG also shall be limited to because of side effects (increased significant increase of oxidized cholesterol (LDLox) and a higher percentage triglyceridases and pain muscle) and therefore to these patients therapy of particles ,, foam cells "which are highly susceptible to oxidation as should be started with the dose of 40 mg once a day and be accessed and risk consequences of submitting the Cardiovascular diseases (CVD, then normalized target values after dosage laboratory examination shall be myocardial infarction, angina pectoris stable and unstable coronary reduced to 20 mg per day. Patients with type 1 diabetes who are in good insufficiency ...). A large number of cohort studies suggest that dyslipidemia led glycemia tend to have normal levels of lipoprotein, unless they are and concentrations of elevated TG, LDL-ch and reduced concentrations over weight. Contained lipoprotein may be abnormal, but the effects of these HDL-ch are at high positive correlation and independent predictor of CVD families in relation to CVD are unknown (72.73). Aggressive treatment of risk(64) In recent study by group of patients 5963 from ages> 40 years diabetic dyslipidemia decreases significantly the risk of CVD in patients with dyslipidemia and diabetes treated with statins its verified a reduction diabetes Some studies have verified that controls and normalization of decrease in LDL-ch for 22% and significant reduction in symptoms of CVD may be even more important and effective in patients with type 1 appearances (65.66) . Observational studies of ADA American Diabetes mellitus compared with patients with type 2 diabetes in reducing the Association together with friends Medical Nutrition Therapy -MNT- appearance of aggressive CVD. verified that patients who have used more healthy diet and increased

5 Conclusion:

In conclusion we can say that the knowledge of mechanisms, etiopathogenesis, function and abnormalities on polymorphism and the negative impact of lipids (hypertriglyceridemia and hypercholesterolemia) and unbalanced glycemia of patients with diabetes mellitus (regardless of the type of diabetes) are among risky factors and independent in presentation CVD and premature atherosclerosis. Treatment and normalization of their highest values at the initial stages of the disease is of paramount importance and can significantly affect the prevention and deterrence pace of progress to early atherosclerotic processes and cardiovascular disease in these patients. Patients with diabetes (regardless of their type- insulin dependent diabetes mellitus or treated with oral hypoglycemic) are at same and high risk from the early appearance of atherosclerosis and cardiovascular disease. Therefore, improvement, balancing and regular checkups of diabetes and lipids with medicament therapy (statins, fibrates, niacin, Holestipol, Holestiramina are the first step (per primam) ATPIII recommends adjunctive therapy with niacin or fibrates (to achieve non-HDL goal) for dyslipidemic patients with multiple CVD risk factors who have low HDL-C and/or high TG, after the LDL-C goal has been achieved with statin monotherapy. Our study results suggest that the majority of patients with DM receiving lipid-modifying treatment are being treated with statin monotherapy. Although it is well documented that the different classes of lipid-modifying medications have different (complementary) effects on lipid parameters ,

in prevention and pace of progress and incidence of CVD and atherosclerotic processes . In treatment of uremic dyslipidemia in recent years a large number of studies have verified extremely high positive effects during treatment with statins (the dose of 40 mg) with what it seems is also contained and reduced the incidence of CVD presentation of diabetic patients and was also verified in our paper where we noticed a decrease in concentration of LDL-ch for 37% and 28-30% TG for facts that are consistent with other studies. We propose, based on preferences and consensus proposed by the American Association for Diabetes on the control of blood glucose, glycosylated hemoglobin (HgbA1c) that treatment of diabetic dyslipidemia should be started in the initial stages of diabetes, no matter what type of diabetes what will be prevented visible appearances atherosclerotic phenomena (early atherosclerosis) in cardiovascular system, brain and peripheral arteries.

Statin monotherapy continued to be prescribed to 81% of patients with more than 1 suboptimal lipid value who received treatment during the post-index period of our study, even though many patients with multiple lipid abnormalities – i.e., those with suboptimal HDL-Ch and TG levels – may have gained greater benefit from adjunctive treatment with either niacin, a drug with the greatest capacity to increase HDL-Ch, or fibrates, which have the most pronounced capacity to decrease elevations in serum TG.

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