ZAMONAVIY FAN, TA`LIM VA TARBIYANING DOLZARB MUAMMOLARI

ACTUAL PROBLEMS OF MODERN SCIENCE, EDUCATION AND TRAINING

АКТУАЛЬНЫЕ ВОПРОСЫ СОВРЕМЕННОЙ НАУКИ, ОБРАЗОВАНИЯ И ВОСПИТАНИЯ

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THE ROLE OF LIPOPROTEINS IN THE DEVELOPMENT OF DIABETIC NEPHROPATHIA IN PATIENTS WITH DIABETES MELLITUS TYPE 2

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Annotatsiya: Tadqiqotning maqsadi diabetik populyatsiyada PZLP-xolesterin va nefropatiya o'rtasidagi korrelyatsiyani va samaradorlikni aniqlashdir. 2-tip qandli diabet kasalligi - mikrovaskulyar va makrovaskulyar asoratlar bilan bog'liq metabolik o'zgarishlarni yuzaga keltiradi. Bu, shuningdek, buyraklardagi buyrak kasalligining eng keng tarqalgan sababidir. Lipoprotein (Lp) mikro va macrovaskulyar asoratlar uchun xavfli faktorlar hisoblanadi va shuningdek, yaqqol namoyon bo'lgan proteinuriya QD 2-tip kasalliklarida diabetik nefropatiyaning rivojlanishi uchun mustaqil xavf omilidir.

Kalit so'zlar: Diabet, dislipidemiya, PZLP-xolesterin, mikroalbuminuriya, nefropatiya, buyrak yetishmovchiligi.

Аннотация: Целью настоящего исследования было выяснить корреляцию и причинно-следственную связь между холестерином ЛПНП и нефропатией в диабетической популяции. Сахарный диабет 2 типа является все более распространенным нарушением обмена веществ, связанным с микрососудистыми и макрососудистыми осложнениями. Это также наиболее распространенная причина терминальной стадии почечной недостаточности (ТПН). Липопротеин (ЛП) является недавно обсуждавшимся важным независимым и наследуемым фактором риска развития микро и макрососудистых осложнений, а также независимым фактором риска прогрессирования диабетической нефропатии у пациентов с СД2 с явной протеинурией.

Ключевые слова: Диабет, дислипидемия, ЛПНП-холестерин, микроальбуминурия, нефропатия, почечная недостаточность

Abstract: The purpose of the current study was to find out the correlation and cause effect relationship between LDL cholesterol and nephropathy in diabetic population. Type-2 diabetes mellitus is an increasingly common metabolic abnormality associated with microvascular and macrovascular complications. It is also the most common cause of end stage renal disease (ESRD). Lipoprotein (Lp) is a recently discussed important independent and inheritable risk factor for micro and macrovascular complications and also an independent risk factor for the progression of diabetic nephropathy in DM2 patients with overt proteinuria.

Keywords: Diabetes, Dyslipidemia, LDL-Cholesterol, Microalbuminuria, Nephropathy, Renal diasease

Introduction

Diabetic nephropathy is the leading cause of end stage renal disease worldwide. Patients with diabetes currently account for 43% of all patients in ESRD being treated in many countries, including Uzbekistan.

Literature review

Diabetic nephropathy is characterized by proteinuria, hypertension, progressive loss of renal function, and a high incidence of cardiovascular morbidity and mortality.[3] Of patients with type 2 diabetes, 20-40% develop diabetic nephropathy over a period of 15-20 years after the onset of diabetes.[4] Hyperglycemia, hypertension, hypercholesterolemia, and proteinuria are the most significant risk factors or markers for the development and progression of diabetic nephropathy in type 2 diabetic patients. One of the major risk factors for the development and progression of diabetic nephropathy is dyslipidemia. In this paper we will review the role of lipid in mediating renal injury and the beneficial effects of lipid control in diabetic nephropathy. In diabetic nephropathy, hyperlipidemia has been identified as a risk factor for a more rapid rate of decline in GFR and increased

mortality.[5] Patients with nephropathy are found to have significantly higher Lp levels than those without nephropathy in some studies. Also, the serum Lp concentrations increases significantly with increased urinary albumin excretion. However, the effect of Lp on the progression of diabetic nephropathy has not been clearly evaluated yet. Therefore, we took up this prospective study to determine whether Lp is an independent risk factor for deteriorating renal function in type 2 diabetic patients.[1]

Patients with diabetic nephropathy often have multiple lipoprotein abnormalities [1]. In patients with microalbuminuria and overt proteinuria, increased plasma levels of very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and triglycerides are usually found. However, the plasma level of high-density lipoprotein (HDL) is lower than those patients with normoalbuminuria. In addition to the abnormalities in amount of lipoprotein, the diameter of LDL particles is also reported tobe smaller in patients with diabetic nephropathy [2, 3] compared to diabetic patients without nephropathy. All the lipoprotein abnormalities mentioned above become more severe with declining renal function and increasing albuminuria. In those diabetic patients with nephrotic syndrome and advanced renal failure, the patterns of dyslipoproteinemia are not different from those patients without diabetes.

Type-2 diabetes mellitus is a metabolic disorder affecting carbohydrate, fat and protein metabolism. An estimated 50% of all diabetic patients, either type 1 or type 2 are dyslipidemic.[5] Dyslipdemia is observed in patients with diabetic nephropathy significantly when compared to those without nephropathy and in those who has long term diabetes more than 10 yrs and in whom the glycemic control was poor.[6] In diabetic nephropathy, hyperlipidemia has been identified as a risk factor for a more rapid decline in GFR and increased mortality.[7]

Type 2 diabetes with nephropathy is associated with several lipid abnormalities including hypertriglyceridemia, reduced HDL level, an increased proportion of small, dense LDL particles and elevated Lp.[6]

Lp has been identified an independent risk factor for the progression of diabetic nephropathy in type 2 diabetic patients with proteinuria. Lplevels were increased in diabetic nephropathy compared to diabetes without nephropathy.[9] Levels greater than 30mg/dl are associated with two fold greater risk for coronary artery disease.[10]

Many risk factors like the duration of diabetes, degree of glycemic control and age of the patient and are identified in the causation of the diabetic microvascular complications. Abnormal plasma lipoprotein profiles contribute to the increased risk in CAD and diabetic nephropathy. The risk of death from coronary heart disease is also substantially increased in diabetic nephropathy compared with normal subjects or diabetes without nephropathy.[12,13, 18 ,21]

In diabetic nephropathy, hyperlipidemia has been identified as a risk factor for a more rapid rate of decline in GFR and increased mortality.[12,13] Lipid abnormalities in diabetes can be due to intrinsic abnormality of the disease process, induced by complications of diabetes like nephropathy or genetically determined.[13]

A breakthrough in Lp research was the cloning and sequencing of Apo by Mc Lean et al, which revealed a high degree of homology of Apo with plasminogen and that their genes are adjacent on chromosome 6 [15,16,14]

Plasminogen is a plasma serine protease of the fibrinolytic system. Although the normal function of Lp is unknown, the close homology between Lp and plasminogen has raised the possibility that this lipoprotein may inhibit endogenous fibrinolysis by competing with plasminogen for binding on the endothelial surface.[14, 16, 18]

Apo may also induce monocyte chemotactic activity in the vascular endothelium.[15,18] This mechanism may contribute to a role of Lp in atherothrombosis which may have a significant role in the development of diabetic nephropathy. In addition to vascular injury, Lp might be implicated in glomerular

injury. Lp and oxidized Lp have been shown to induce activation of reactive oxygen metabolites in isolated rat glomeruli.[21]

Patients with nephropathy are found to have significantly higher Lp levels than those without nephropathy. Also, the serum Lp concentrations increases significantly with increased urinary albumin excretion.[19,20]

Research Methodology

The study is a prospective observational study conducted over a period of six months from march 2018 to december 2018 in patients attending Nephrology Department. The study population comprised of 60 diabetic patients out of which 30 patients had nephropathy and 30 were without nephropathy. All patients underwent a full medical history that included age, family history of diabetes, hypertension, coronary artery disease, duration of Diabetes, treatment history for diabetes, drug history and treatment history for any other disease was collected through a standard questionnaire.

Blood samples were collected after 12 hours of fasting in the vacutainers for estimation of glucose, lipoprotein, lipid profile and creatinine. Blood samples were collected in the morning after 12 hours of overnight fasting. The samples were separated by centrifugation at 2400 rpm. Plain vacutainer is used for serum and for plasma, sodium fluoride vacutainers were used.

Analysis and results

In the present study it is found that shorter the duration of type-2diabetes lesser is the chance of developing nephropathy. As the duration of type-2 diabetes increased development of nephropathy increased. Incidence of Diabetic nephropathy significantly more in patients with duration >10 years of DM with P=0.000. majority of patients with diabetic nephropathy are with duration of DM type 2 of 11- 15 years. In the present study all the lipid parameters were abnormally elevated and the values were statistically significant in the nephropathy group as compared to controls except HDL values which were decreased in both the groups but more in the diabetic nephropathy subjects. It was not statistically significant (p-0.111).

In the present study Triglycerides were elevated in both the groups but even more so in the nephropathy group. Also Total-Cholesterol and LDL-C were increased in the nephropathy group. It was not statistically significant (p-0.111).

Table 1. Association of duration of dm with diabetic nephropathy

Duration of DM	Diabetic Nephropathy		Total (N=60)	p – value
	Absent (N=30)	Present (N=30)		
1 - 10 Years	18 (68.0%)	4 (26.0%)	47 (47.0%)	0.000**
11 - 15 Years	10 (28.0%)	10 (62.0%)	45 (45.0%)	
16 - 20 Years	2 (4.0%)	16 (12.0%)	8 (8.0%)	

** Significant at 0.01 level.

Table 2: Association of lipid parameters with diabetic nephropathy

Lipid Parameters			Total (N=60)	p – value
	Absent (N=30)	Present (N=30)		
TC (> 200 mg/dl)	0 (0.0%)	24 (48.0%)	24 (24.0%)	0.000**
LDL (> 130 mg/dl)	13 (26.0%)	33 (66.0%)	33 (33.0%)	6.143 (0.000)**
HDL (< 35 mg/dl)	23 (46.0%)	18 (36.0%)	18 (18.0%)	1.904 (0.120) NS
TGL (> 150 mg/dl)	27 (54.0%)	30 (100.0%)	30 (30.0%)	0.000**
Lipoprotein (> 10 mg/dl)	0 (0.0%)	38 (76.0%)	38 (38.0%)	0.000**

** Significant at 0.01 level NS ^ Not Significant

In Diabetic nephropathy patients, Mean value of Lp was 10.8 mg/dl as compared to non-nephropathy patients where Mean value of Lp was 5.783mg/dl Inference Lipoprotein is significantly elevated in patients with Diabetic Nephropathy with P<0.000.

Table 3: Comparison of lipid parameters

Lipid Parameters	Diabetic Nephropathy		Total (N=60)	p – value
	Absent (N=30)	Present (N=30)		
Total Cholesterol	168 ± 11.0	208 ± 19.8	188 ± 15.4	0.000**
LDL Cholesterol	124 ± 8.12	144 ± 16.9	134 ± 12.51	0.000**
HDL Cholesterol	33.5 ± 3.27	36.8 ± 2.09	35.15 ± 2.68	0.111 NS
Triglycerides	181 ± 30.2	258 ± 31.2	219.5 ± 30.7	0.000**
Lipoprotein	5.74 ± 0.83	11.8 ± 0.69	8.77 ± 0.76	0.000**

** Significant at 0.01 level. NS -Not Significant.

Table 4: Association of lipoprotein with diabetic nephropathy

Lipoprotein	Diabetic Nephropathy		Total (N=60)	p – value
	Absent (N=30)	Present (N=30)		
< 10 mg/dl	30 (100.0%)	3 (6.0%)	33 (53.0%)	0.000
> 10 mg/dl	0 (0.0%)	27 (94.0%)	27 (47.0%)	

Inference DM Poor control was the lone significant predictor of elevated Lp followed by duration of diabetic >10 years. Inference- DM poor control was the lone significant predictor of elevated Lp followed by duration of diabetic >10 years.

In the present study, poor control and duration of diabetes, more than 10 years, are significantly associated with abnormal elevation of Lp levels.

Conclusion

So, we conclude that: Dyslipidemia is much more common in type-2 diabetes with nephropathy compared to those without nephropathy. Dyslipidemia (hypertriglyceridemia) is one important risk factor for the coronary heart disease and Increased Lp and Triglycerides may be the reason for increased prevalence of coronary heart disease in nephropathy patients.

Poor control of DM is the lone significant predictor of elevated Lipoprotein followed by duration of Diabetic >10 years. Lp values are significantly elevated in

Diabetic Nephropathy. Thus it is essential to include Lpin a battery of tests for evaluation of macro and microvascular complications in type 2 diabetes. The observed data indicate that higher LDL levels are associated with raised creatinine levels, development and progression of nephropathy. Controlling LDL dyslipidemia is one of the effective strategies towards diabetes management to prevent diabetic nephropathy.

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