New Considerations Regarding Chronic Kidney Disease, Cardiovascular Disease and Dyslipidemia in Diabetic Patients

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The aim of the present study is to investigate the prevalance of chronic kidney disease (CKD), of cardiovascular disease (CVD) and dyslipidemia in patients with diabetes mellitus (DM). We conducted a prospective, controlled study involving 420 diabetic patients (120 T1DM, 300 T2DM) and investigate the following aspects: the presence of vascular complications (stroke, coronary artery disease, peripheral artery disease), lipid profile (total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides), kidney function (glomerular filtration rate, albuminuria), blood pressure, HbA1C. The results that in diabetic patients with CKD there is an increased prevalence of CVD and of dislipidemia. Also we noticed a negative correlation between total cholesterol level and decease in eGFR in all patients, with or without CKD.

Keywords: diabetes mellitus, chronic kidney disease, cardiovascular disease, dyslipidemia

Diabetes mellitus (DM) it is a major problem of health all over the world – it is a problem affecting millions of persons especially by the micro and macrovascular complications strongly related to the increased oxidative stress generated at the vascular level [1-6]. In the context of DM, one of the most complication is the chronic impairment of the kidney function-chronic kidney disease (CKD)[7, 8]. The prevalence of CKD in diabetic patients (named diabetic kidney disease - DKD) has an increased prevalence all over the word. Is characterized by high urine albumin excretion and reduction of glomerular filtration rate (eGFR), accompanied by the elevation of arterial blood pressure. In the evolution process of DKD almost 50 % of diabetic patients will present microalbuminuria (30-300 mg/day, moderate albuminuria) and around 30% will develov proteinuria (>300 mg/day, severe albuminuria) being at increased risk to develop end-stage-renal-disease (ESRD)[8, 9]. In the same time, patients with DKD have higher risk to develop the vascular complication of DM[10-12]. Classicaly, the risk of CVD become increased as albuminuria increases and eGFR decreases. The factors responsible for the negative evolution of DKD are: poor glycemic control, high blood pressure, albuminuria level [13-15].

In the evolution of DKD the most severe complication it is represented by the renal failure. The evolution time necessarily to develop renal failure from the apparition of moderate albuminuria is around 9 years. In conditions of optimal glycemic and blood pressure control this time duration can be doubled [16-18].

In US CKD is present in 40% of patients with type 2 DM (Fourth National Health and Nutrition Examination Survey). There is a powerfull correlation between renal and cardiac pathophysiology in type 2 diabetes, this aspect being expressed by the *cardio-renal* risk factors: type 2 DM, obesity, smoking, dyslipidemia, hypertension, genetic factors, etc. Regarding the association between DM with dyslipidemia and hypertension, approximately 50% of people with DM present simultaneously both dyslipidemia and hypertension [8, 9, 19].

The aim of this study is to investigate the prevalance of CKD, CVD and dyslipidemia in patients with DM from an outpatient diabetes survey unit from western Romania.

Experimental part
Material and methods
In this study were included 420 diabetic patients, 120 with type 1 and 300 with type 2. The characteristics of the groups are presented in table 1.

Clinical and paraclinical investigations
Based on estimate glomerular filtration rate (eGFR) patients were divided in two groups: with and without chronic kidney disease (CKD). Diagnosis of CKD was established using K/DOQI criteria (2002). Estimated glomerular filtration rate (eGFR) was calculated with MDRD 4 (Modification of Diet in Renal Disease) formula.

In all the patients we investigate the following parameters:

Characteristics	Type 1 DM	Type 2 DM
Number	120	300
Sex (F/B):	F: 231(55%)	
	M: 189 (45%)	
Age (years)	57 ± 12	
Duration of diabetes (years)	11 ± 4	

Table 1
CHARACTERISTICS OF THE GROUPS

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-Blood pressure
-Presence of cardiovascular disease (CVD): congestive heart failure (CHF), coronary artery disease (CAD), history of stroke, peripheral vascular disease;
-HbA1c;
-Lipid profile: Total cholesterol, LDL cholesterol, HDL cholesterol, Triglycerides.

Statistical analyses

Two-group comparisons were performed using the t-test and the Fisher test; correlation has been evaluated with Pearson test. Statistical significance was considered if $p < 0.05$.

Results and discussions

Our results showed that aprox. 35% of the patients with diabetes presented CKD. Regarding the prevalence of cardiovascular disease (stroke, coronary artery disease, cerebral vascular disease, peripheral vascular disease) the percent was 50%. Dyslipidemia (hypercholesterolemia, hypertriglyceridemia or mixted dyslipidemia) was present in 60% of diabetic patients. In diabetic patients with CKD the prevalence of stroke, CVD or stroke was significantly higher then in patients with diabetes without CKD (table 2).

In a second part of the study based on the lipid profile result we split the patients in four groups: withthout dyslipidemia, with hyper-cholesterolemia, with hyper-trygliceridemia and with mixed dyslipidemia. Of note, the highest prevalence of CKD was in the mixed dyslipidemia patients and the highest prevalence of stroke, CAD and PVD were in the hypercholesterolemia group (table 3).

In the third part of the study we performed some correlation of the biological parameters obtained from the patients. The most important aspect is that in the group of diabetic patients without CKD eGFR was correlated negatively with age and cholesterol level. In the group of CKD diabetic patients eGFR was correlated negatively with age, cholesterolemia and proteinuria (table 4).

Dyslipidemia (including high levels of total cholesterol, triglycerides, LDLc and low levels of HDLc) is one of the factors responsible for the increased cardiovascular risk associated with CKD and also with progression of kidney injury. In this context, in diabetic patients, optimal management of dyslipidemia should lead to cardiovascular and renal benefits.

It is well known that statins (inhibitors of 3-hydroxy-3-methylglutaryl-CoA - HMG-CoA reductase) are reducing serum cholesterol levels and reduce the cardiovascular morbidity and mortality [8, 9, 16, 19-21]. Also, it is well established that patients with CKD, even those in the early phases of the disease have an high risk to develop cardiovascular disease. Some non-traditional factors, like oxidative stress and inflammation are associated with CKD and systemic atherosclerosis, being also mediators which could explain the high proportion of CVD in CKD patients [11, 14].

Indeed, The National Kidney Foundation Kidney Disease Outcomes Quality (K / DOQI) and the National Cholesterol Education Program (NCEP) recognize CKD as a CVD risk

Table 2
SIGNIFICANTLY HIGHER PREVALENCE OF CVD IN DIABETIC PATIENTS WITH CKD

	CKD (+), n=147	CKD (-), n=273	*p*
Stroke	7.15%	3.15%	p<0.05
CAD	61.75%	42.15%	p<0.05
PVD	26.75%	15.17%	p<0.05

Table 3
PREVALENCE OF CKD, STROKE, CAD AND PVD IN DIABETIC PATIENTS WITH OR WITHOUT DISLIPIDEMIA

	No dyslipidemia n=82	Hyper-cholesterolemia n=118	Hyper-tryliceridemia n=98	Mixed dyslipidemia n=112
CKD	20.35%	25.24%	24.25%	30.16%
STROKE	15.65%	37.5%	26.5%	20.35%
CAD	12.15%	48.35%	25.17%	24.33%
PVD	18.38%	44.67%	16.05%	20.90%

Table 4
CORRELATION OF eGFR WITH AGE, CHOLESTEROLEMIA, BMI AND PROTEINURIA IN DIABETIC PATIENTS WITH AND WITHOUT CKD

	eGFR – CKD (-) n=273		eGFR – CKD (+) n=147	
	r	p	r	p
AGE	- 0.3214	0.001	- 0.3124	0.001
CHOLESTEROLEMIA	- 0.1945	0.001	- 0.1324	0.001
PROTEINURIA			- 0.2014	0.001

equivalent. Important to mention, CKD patients have a number of additional risk factors associated with CVD, including inflammation, increased oxidative stress, proteinuria, electrolyte imbalance, impairment of nitric oxide (NO) signaling cascade [12, 15, 18]. Micro-albuminuria is often found in association with hyperlipidemia, especially in patients with diabetes, and this may contribute to the development of cardiovascular disease in this patients. Of note, novel mechanism involving micro RNA are curently investigated regarding kidney impairment in context of diabetes [22] or other several pathological conditions [23].

Screening for diabetic nephropathy should be performed annually, by measuring albuminuria or urine albumin/creatinine ratio and estimated GFR (eGFR). Aggressive management of the cardiovascular risk factors reduces the incidence of cardiovascular events and of progression to nephropathy by around 60% [9, 10]. Also cumulative trial evidence about statin therapy among participants with albuminuria suggests that statins can reduce pathologic excretion even in the firts 6 months after initiation of therapy [12, 13, 20]. Our results strongly sustain the recommendations of statins use for both cardio and renoprotective purposes.

Conclusions

The prevalence of CKD amoung diabetic patients is extremely high. Also it is associated with a significantly higher prevalence of CVD compared to patients with DM without CKD. The prevalence of dyslipidaemia in patients with DM is also high. The glomerular filtration rate of the studied patients correlates inversely with the total cholesterol level, both in patients with BCR and without BCR. These results sugest intervention with statins for both cardioprotective and nephroprotective purposes.

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