CARDIOVASCULAR RISK CALCULATED ON A GROUP OF PATIENTS WITH TYPE 1 DM DIAGNOSED AT LEAST 10 YEARS AGO

Mihaela Vladu [1]***, Diana Clenciu, Sigina Gîrgavu*** [2]***, Adina Mitrea*** [1]***, N.M. Panduru*** [3]***, Mihaela Bîcu*** [2]***, Maria Moţa*** [1]***, Eugen Moţa*** [4]***, Orlando Dell'unto*** [5]

[1] University of Medicine and Pharmacy Craiova – Department of Diabetes, Nutrition, Metabolic Diseases
[2] Emergency County Clinical Hospital of Craiova – Clinic of Diabetes, Nutrition, Metabolic Diseases
[3] „Carol Davila ” University of Medicine and Pharmacy Bucharest
[4] University of Medicine and Pharmacy Craiova – Department of Nephrology
[5] „S. Giuseppe di Marino” Hospital – Cardiology, Italy

Abstract

Diabetic nephropathy is the most common worldwide cause of renal chronic disease in terminal stage requiring a renal substitution therapy. Microalbuminuria is an independent risk factor for developing diabetic renal disease, for the decrease of glomerular filtrate as well as for cardiovascular morbidity and mortality. Micro and macroalbuminuria are important predictors for mortality increase of any cause in DM. Microalbuminuria is a predictor for periferal and coronary cardiovascular disease. In type 1 DM, the factors of cardiovascular risk are usually interpreted according to the presence or absence of nephropathy. Diabetes mellitus involves a high cardiovascular risk, especially if there is any diabetic nephropathy present as a microvascular complication.

key words*: diabetic nephropathy, type 1 DM, microvascular complication, renal chronic disease in terminal stage*

Introduction

Diabetic nephropathy is the most common worldwide cause of renal chronic disease in terminal stage requiring a renal substitution therapy. Renal and cardiovascular diseases represent public health problems [1], and they seem to share a complex relationship [2, 3, 4, 5]. The prevalence of traditional cardiovascular risk factors is high in patients with renal affection, these risk factors predicting the emergence of a renal disease [6].

Microalbuminuria was arbitrarily established between 20 and 200 μg/min, a value that is equivalent to 30-300mg/day and has a high risk of progression to macroalbuminuria (values higher than 200 μg/min or 300mg/day) and terminal renal disease.

Microalbuminuria is an independent risk factor for developing diabetic renal disease, for the decrease of glomerular filtrate as well as for cardiovascular morbidity and mortality.

Micro and macroalbuminuria are important predictors for mortality increase of any cause in DM. Microalbuminuria is a predictor for periferal and coronary cardiovascular disease.

Study Purpose

Evaluation of cardiovascular risk in a group of patients with type 1 DM diagnosed at least 10 years ago.

Material and Method

The studied group comprised 106 patients with type 1 DM diagnosed at least 10 years ago, recorded within the Clinical Center of Diabetes, Nutrition, Metabolic Diseases in Craiova. There were analyzed the following data:

- anamnestic data: age, sex, DM duration, lifestyle (smoker/non-smoker),
- clinical data: blood pressure,
- paraclinical data: total cholesterol and its fractions (HDL, LDL), triglycerides, albuminuria.

The cardiovascular risk was evaluated using the Framingham Algorythm.

For data processing there were used the software packs **EPI 2000**, distribuited by OMS, **SPSS 17**, specialized in scientifical statistical calculations, produced by SPSS Company and the Data Analysis Module of **MICROSOFT EXCEL**, together with XLSTAT for MS Excel. The recording with the EXCEL program of the patients data represented the initial data base from where the significant aspects for this study were taken.

The processing itself was performed with the Pivot Tables, Functions-Statistical, Chart commands, Data Analysis Module in MS Excel and with the commands in the XLSTAT Module for the performance of Chi Square and Cramer Tests. The Chi Square Test usually shows if there is any connection (reciprocal influence) between two factors. The Cramer Test checks up the power of association between two nominal factors.

Results

The studied group was made up of 106 patients out of which 39.62% (42) were females and 60.37% (64) were males (fig. 1).

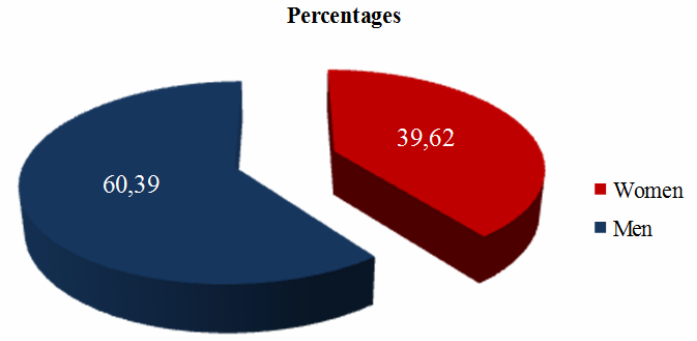

Fig. 1. Sex Distribution of the Patients in the Study

The patients in the study were distributed according to the following age decades (table 1):

Table 1. Age Decades of Patients

Age	Under 30 years-old	31 - 40 years-old	41 – 50 years-old	Over 50 years-old
Patients (%)	11.32 %	21.69 %	37.73 %	29.24 %

Regarding the duration of diabetes mellitus, 51.88% (55) of the patients had a DM duration between 10 and 20 years, 37.73% (40) of the patients between 21 and 30 years, 7.54% (8) of the patients between 31 and 40 years and 2.83% (3) of them over 40 years (fig. 2).

The 106 patients within our study group were distributed in 4 subgroups: normal, micro, macroalbuminuric, patients in the end stage of diabetic chronic renal disease. Thus, 32.07% (34) of the patients were in a normoalbuminuric stage, 14.15% (15) of the patients in a microalbuminuric stage, 49.05 (52) of the patients in a macroalbuminuric stage, while 4.71% (5) of the patients in the end stage of diabetic chronic renal disease (fig. 3).

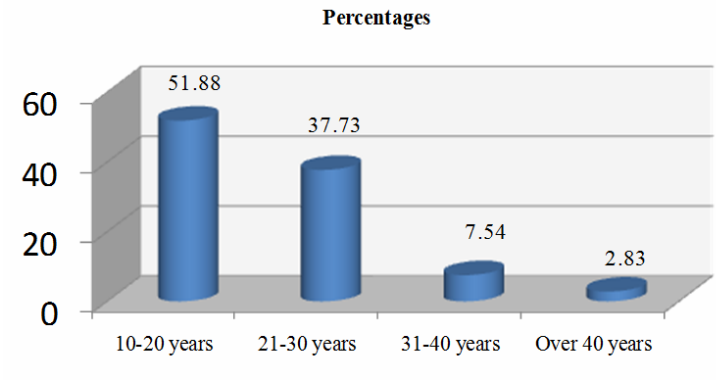

Fig. 2. Duration of DM Type 1 in the Studied Patients.

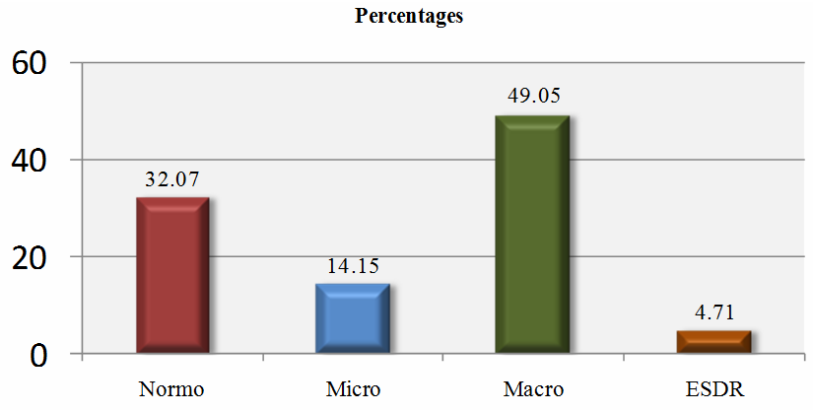

Fig. 3. Group Distribution of Studied Patients.

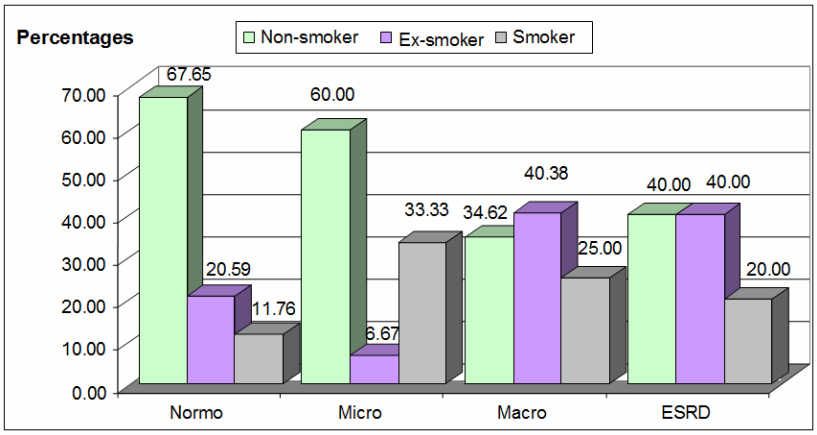

Fig. 4. Smoking Incidence in the Studied Patients.

We analyzed the manner in which the parameters used for calculating the Framingham score contributed to the influence of cardiovascular risk.

Smoking Status

In the subgroup of ***normoalbuminuric*** patients 67.65% (23) of them were non-smokers, 20.59% (7) of the patients were ex-smokers, while 11.76% (4) of the patients were current smokers. Within the subgroup of ***microalbuminuric*** patients (stage 3 diabetic nephropathy), 60% (9) of the patients were non-smokers, 6.67% (1) a patient was an ex-smoker, 33.33% (5) of them were smokers. In the subgroup of ***macroalbuminuric*** patients (stage 4 diabetic nephropathy), 34.62% (18) of the patients were non-smokers, 40.38% (21) of the patients were ex-smokers, while 25% (13) of them were current smokers. In the subgroup of the patients in the ***end stage of diabetic chronic renal disease*** (ESRD) 40% (2) of the patients were non-smokers, 40% (2) of the patients were ex-smokers, while 20% (1) a patient was a current smoker.

There is noted the influence of smoking in the emergence of albuminuria, a fact that is marked out by the value of p=0.033 (p <0.05), which indicates that the patients with different levels of albuminuria are in various percentages smokers or non-smokers, a statistically significant difference. The value calculated by the Cramer Test for checking up the power of association between albuminuria and smoking status is of 0.254, which indicates a (not very strong) association between a certain level of proteinuria and a certain smoking status (those with normoalbuminuria/microalbuminuria are more prone to be non-smokers, while the ones with macroalbuminuria are probable to be smokers or ex-smokers).

High Blood Pressure

High blood pressure (HBP) was found in 44.12% (15) of the ***normoalbuminuric*** patients, in 46.67% (7) of the ***microalbuminuric*** patients, in 71.15% (37) of the ***macroalbuminuric*** ones, while in the subgroup of patients in the ***end stage of diabetic chronic renal disease*** (ESRD) it was found in a percentage of 80%.

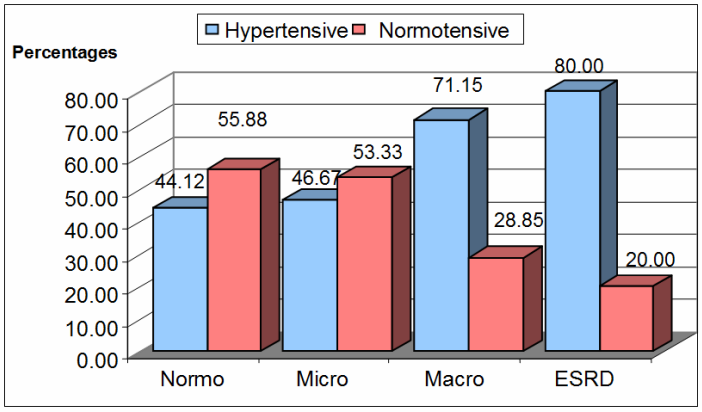

Fig. 5. HBP Prevalence in the Studied Patients

The relationship between high blood pressure and renal albumin release is proven by the value of p = 0.042 (p < 0.05), which indicates that the patients with different levels of albuminuria are either normal or hypertensive, a statistically significant difference.

The value calculated with the Cramer Test of the power association between present albuminuria and HBP is 0.277, which indicates a (not very strong) association

between a certain level of proteinuria and the presence or absence of high blood pressure.

Dyslipidaemia

In the subgroup of ***normoalbuminuric*** patients, dyslipidaemia was recorded in 64.71% (22) of the patients. In the ***microalbuminuric*** patients, dyslipidaemia was evidentiated in 40% (6) of the patients, in the subgroup of ***macroalbuminuric*** patients in 82.69% of them, while in the subgroup of the patients in the ***end stage of diabetic chronic renal disease*** (ESRD) in 60% of the patients.

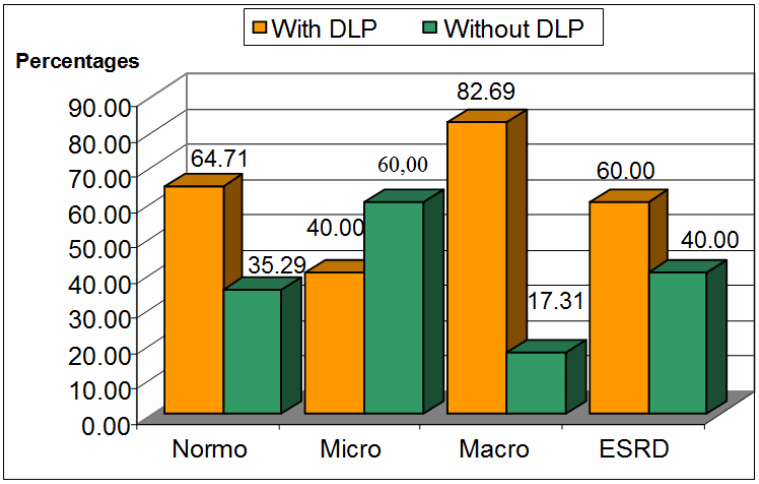

Fig. 6. DLP Incidence in the Studied Patients

By applying the Chi Square Test to show the influence between the two factors, dyslipidaemia and albuminuria, we obtain p = 0.011 (p <0.05), indicating that the patients with various levels of albuminuria are either normal or dyslipidaemic, a statistically significant difference.

The value calculated with the Cramer Test to check the power of the association between the two factors is 0.323, which indicates a (not very strong) association between a certain level of proteinuria and the presence or absence of dyslipidaemia (the ones with macroalbuminuria are more prone to have dyslipidaemia).

Regarding the cardiovascular risk, by applying the Framingham Score in the 4 subgroups, there was obtained the data in the following table (table 2):

Table 2. Cardiovascular Risk Calculated with the Framingham Score

		Normal albuminuria	Micro albuminuria	Macro albuminuria	ESRD
Low	**< 10 %**	76.47%	53.33%	40.38%	80%
Moderate	**10-20 %**	23.53%	33.33%	42.31%	20%
High	**> 20 %**	-	13.33%	17.31%	-

The results of Chi Square Test show that the patients with different levels of albuminuria are in different percentages of low, moderate or high cardiovascular risk, a statistically significant diference, evidentiated by the value of p=0.025 (p <0.05).

The value calculated with the Cramer Test for checking the power of the association between the two factors is 0.260, which indicates a (not very strong) association between a certain level of proteinuria and a certain level of cardiovascular risk (the patients with macroalbuminuria are more prone to develop a medium or a high risk).

The cardiovascular risk is influenced by the patients' age (Table 3), the result of the Chi Square Test (34.5) showing that the patients from different age classes are affected in various proportions by a low, moderate or high cardiovascular risk, evidentiated by the value of p~0 (p <0.001).

The value calculated with the Cramer Test for checking the power of the association between the two factors is 0.403, which indicates a strong association between the age class and a certain level of the cardiovascular risk. We may conclude that we have a statistical assurance for the affirmation that the cardiovascular risk is influenced by the patients' age.

Table 3. Cardiovascular Risk Calculated on Age Decades

CV RISK	AGE			
	Under 30 years old	31 – 40 years old	41 – 50 years old	Over 50 years old
Under 10 %	100 %	91.30 %	65 %	25.80 %
10 – 20 %	-	4.34 %	30 %	54.83 %
Over 20 %	-	4.34 %	5 %	19.36 %

Table 4. Cardiovascular Risk Compared to the Duration of Diabetes Mellitus

CARDIOVASCULAR RISK	DM DURATION			
	10-20 years	21-30 years	31-40 years	> 40 years
< 10%	63.63%	70%	37.5%	-
10-20%	27.27%	27.5%	50%	100%
> 20%	9.09%	2.5%	12.5%	-

Comparing the cardiovascular risk to the duration of diabetes mellitus (Table 4), the result of Chi Square Test (11.13) does not show that the patients with different durations of DM are affected differently by a low, moderate or high cardiovascular risk, the difference not being statistically significant, evidentiated by the value of p=0.0844 (p > 0.05).

The value calculated with the Cramer Test for checking the power of the association between the two factors is 0.229, which indicates a weak association between the DM duration and a certain level of cardiovascular risk. We cannot state that the DM duration significantly affects the cardiovascular risk from a statistical point of view.

Conclusions

In type 1 DM, the factors of cardiovascular risk are usually interpreted according to the presence or absence of nephropathy.

The calculated cardiovascular risk was found in a higher percentage in macroalbuminuric patients, followed by the microalbuminuric ones. In end stage of diabetic chronic renal disease, the calculation of the cardiovascular risk is no longer eloquent. The explanation could be associated with the decrease of proteinuria and albuminuria during this stage. This does not mean that the end stage of diabetic chronic renal disease is not accompanied by any cardiovascular risk. The patients with renal affection also have an associated cardiovascular disease and a high risk for developing a major cardiovascular event. Dr Galle said that the patients die on their way to renal substitution therapy from a different cause than the renal one, probably a cardiovascular one. Only some of them benefit from their substitution therapy. Therefore, those who reach dialysis are the survivors [5]. The present study is also limited by the small number of patients in the end stage of diabetic chronic renal disease.

Diabetes mellitus involves a high cardiovascular risk, especially if there is any diabetic nephropathy present as a microvascular complication.

This work was partially suported by project CNCSIS–PNCDI–II–RU–ID–1194/2009 and by project POSDRU/89/1.5/S/64109

REFERENCES

1. US Renal Data System (USRDS). USRDS 2008 annual data report: atlas of end-stage renal disease in the United States. Bethesda, MD: *National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases* 2008.

2. Elsayed EF, Tighiouart H, Griffith J, Kurth T, Levey AS, Salem D, et al. Cardiovascular disease and subsequent kidney disease. Arch Intern Med 167(11): 1130-6, 2007.

3. Kurth T, Jong PED, Cook NR, Buring JE, Ridker PM. Kidney function and risk of cardiovascular disease and mortality in women: a prospective cohort study. BMJ 338: b2392, 2009.

4. Hemmelgarn BR, Manns BJ, Lloyd A, James MT, Klarenbach S, Quinn RR, et al. Relation between kidney function, proteinuria, and adverse outcomes. JAMA 303: 423-9. 2010.

5. Matsushita K, Astor BC, Woodward M, Levey AS, de Jong PE, et al. Chronic Kidney Disease Prognosis ConsortiumAssociation of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet 375: 2073-81, 2010.

6. Gelber RP, Kurth T, Kausz AT, Manson JE, Buring JE, Levey AS, et al. Association between body mass index and chronic kidney disease in apparently healthy men. Am J Kidney Dis 46: 871-80, 2005.

Correspondence Data:
Vladu Mihaela
University of Medicine and Pharmacy Craiova
Department of Diabetes, Nutrition, Metabolic Diseases
Email: mihmitzu@yahoo.com