DE GRUYTER OPEN

http://www.jrdiabet.ro
Rom J Diabetes Nutr Metab Dis. **21**(3):203-212
doi: 10.2478/rjdnmd-2014-0025

THE PROGNOSIS OF PATIENTS WITH CHRONIC KIDNEY DISEASE AND DIABETES MELLITUS

Mihaela Vladu [1,2,✉], ***Diana Clenciu*** [2], ***Mihaela Bîcu*** [2], ***Maria Moţa*** [1,3]

[1] University of Medicine and Pharmacy Craiova
[2] Clinical Philanthropy Hospital Craiova – Diabetes Nutrition and Metabolic Diseases Department
[3] Clinical County Emergency Hospital Craiova – Clinic of Diabetes Nutrition and Metabolic Diseases

received: August 23, 2014 *accepted*: September 01, 2014
available online: September 15, 2014

Abstract

Background and Aims: *Diabetes mellitus (DM) is a chronic disease which can evolve towards devastating micro and macro-vascular complications. Chronic kidney disease (CKD) is a worldwide public health problem, with adverse outcomes of kidney failure, cardiovascular disease (CVD) and premature death. The aim of our study was to evaluate the prognosis in patients with DM and CKD, depending on estimated glomerular filtration rate (eGFR) and albuminuria, according to the classification of Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease (KDIGO) from 2013* ***Materials and Methods:*** *The study was epidemiological, transversal, non interventional type, with 600 subjects unselected patients divided into three subgroups: 200 patients with T1DM, 200 patients with T2DM and 200 age matched subjects without DM. The recorded data have been analyzed using the Statistic Package for Social Sciences (SPSS), the 17.00 software (IBM Corporation, Armonk, NY, United States of America).* ***Results:****. We found a statistically significant difference among the three study groups ($p < 0.0001$) regarding the prognosis of CKD.* ***Conclusions:*** *DM represents an important risk factor for the appearance of CKD but also a negative prognosis factor for the patients with CKD.*

key words: *diabetes mellitus, chronic kidney disease, prognosis*

Background and Aims

Diabetes mellitus (DM) is a chronic disease which can evolve towards devastating micro and macro-vascular complications. DM is the most frequent cause of chronic kidney disease (CKD), representing worldwide 50% of all cases of end stage CKD (which involves renal substitution therapy), the majority of patients having type 2 DM. CKD in patients with DM is associated with a reserved prognosis. Meanwhile chronic kidney disease (CKD) is a worldwide public health problem, with adverse outcomes of kidney failure, cardiovascular disease (CVD) and premature death.

The diabetic chronic kidney disease (CKD) is a clinical syndrome characterized by persistent albuminuria (albumin/creatinine ratio in the spontaneous urine ≥ 30mg/g) and/or a sustained decline of the estimated glomerular filtration rate

✉ No. 40, Nicolae Titulescu Street, Tel: 0251307500; *corresponding author e-mail*: mihmitzu@yahoo.com

(eGFR) below 60 ml/min/1.72m^2. If at least one of these values is still maintained within these abnormal limits after 3 months from the first measurement, the diagnosis of diabetic CKD may be established [1,2]. The mortality in patients with type 1 diabetes mellitus (DM) is 3-4 times higher than in general population.

The presence and severity of CKD is a predictor for all-cause mortality in type 1 diabetes mellitus (T1DM) [3]. Data from the Finnish Diabetic Nephropathy (FinnDiane) study [3] have demonstrated that CKD is the main cause of this excess of mortality. The raised mortality has been observed in patients with CKD while those with a normal albuminuria haven't shown any excess of mortality.

In type 2 diabetes mellitus (T2DM), end stage reanl disease (ESRD) is associated with very high mortality and accelerated cardiovascular disease [4]. Several recent studies suggest that the risk for death is increased independently in individuals who have less severe impairment of kidney function and are not dialysis dependent, compared with those who have preserved kidney function [5,6].

The aim of our study was to evaluate the prognosis in patients with DM and CKD, depending on eGFR and albuminuria, according to the classification of Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease (KDIGO) from 2012 [2].

Materials and Methods

The study was conducted in a period of three years (2010-2013) and comprised patients with DM registered in the Clinical Centre of Diabetes, Nutrition and Metabolic Diseases of Dolj county and unselected control subjects without DM, recruited from the registration of general practitioners from Dolj county.

The study design was epidemiological, transversal, non interventional type, with unselected patients. Finally, the study group included 600 subjects divided into three subgroups, as it follows:

- Group 1 included 200 patients with type 1 DM
- Group 2 included 200 patients with type 2 DM
- Group 3 (control) included 200 age matched subjects without DM

Anamnestic data have been analyzed (age, sex, the duration of DM), as well as paraclinical data (urea, creatinine and urinary albumin-to-creatinine ratio). The estimated glomerular filtration rate (eGFR) has also been calculated according to the Modification of Diet in Renal Disease (MDRD) equation [7]. The CKD stage has been established according to KDIGO 2012 definition [2]. In predicting risk for outcome of CKD we used GFR and albuminuria category. GFR from 60 to 89 ml/min/1.73 m^2 is classified as CKD stage 2, from 45 to 59 ml/min/1.73 m^2 as CKD stage 3a, from 30 to 44 ml/min/1.73 m^2 is classified as CKD stage 3b, from 15 to 29 ml/min/1.73 m^2 is classified as CKD stage 4. Stage 1 is defined by GFR over 90 ml/min/1.73 m^2 and stage 5 by GFR under 15 ml/min/1.73 m^2. Albuminuria category were: A1 < 30mg/g (Normally to moderately risen), A2=30-300 mg/g (moderately risen), A3> 300 mg/g (severely risen).

Statistical analysis

The recorded data have been analyzed using the Statistic Package for Social Sciences (SPSS), the 17.00 software (IBM Corporation, Armonk, NY, the United States of America). We performed analysis of the entire study population and separate statistics for each of the 3 groups. The methods used were t-test, Mann-Whitney test, Chi-square test and Cramer test as

appropriate. We used the following interpretation of p values: $p < 0.05$, the difference between the two means is significant (S), $p < 0.01$, the difference between the two means is highly significant (HS), $p < 0.001$, difference between the two averages is very highly significant (VHS), $p > 0.05$, the difference between the two means is not significant (NS).

Results

The distribution according to sex of the subjects from the 3 study groups has been relatively balanced. Thus, patients from the study group 1 included 84 (42%) women and 116 (58%) men; in group 2 there were 101 (50%) women and 99 (50%) men while in the control group 104 (52%) women and 96 (48%) men as shown in Figure 1.

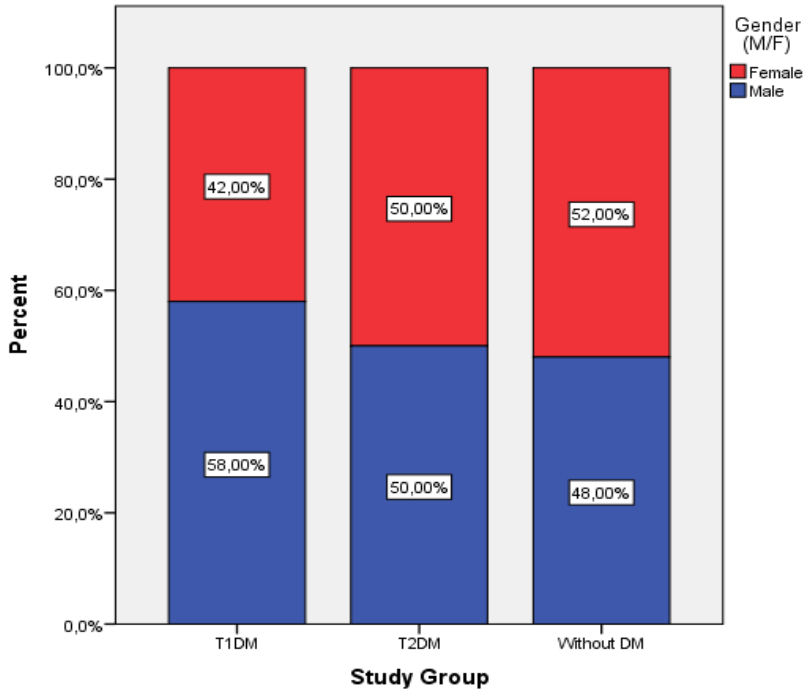

Figure 1. *The distribution of the 3 study group patients according to sex.*

Table 1. The distribution according to age of patients from the 3 study groups.

Age	Group 1	Group 2	Control group
0 - 19 years old	4 (2%)	-	-
20-39 years old	103 (51.5%)	3 (1.5%)	34 (17%)
40-59 years old	88 (44%)	60 (30%)	74 (37%)
60-79 years old	5 (2.5%)	134 (67%)	91 (45.5%)
Over 80 years old	-	3 (1.5%)	1 (0.5%)

Table 2. The duration of diabetes mellitus.

Duration	Group 1	Group 2
0-9 years	55 (27.5%)	131(65.5%)
10-19 years	84 (42%)	56 (28%)
20-29 years	48 (24%)	11(5.5%)
30-39 years	7 (3.5%)	2 (1%)
Over 40 years	6 (3%)	-

The analyzed subjects were distributed on age groups, as it is shown in Table 1. It may be observed that, as expected, the patients from the type 1 DM group had a younger age.

The distribution of diabetic patients according to disease duration is given in Table 2.

A longer duration of type 1 DM compared to type 2 DM could be observed as shown in Figures 2 and 3.

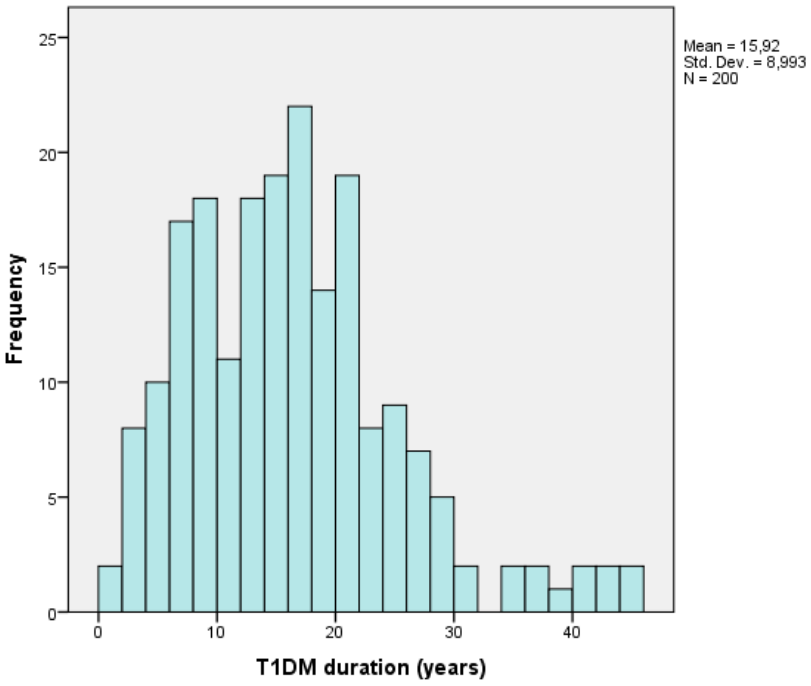

Figure 2. *The duration of diabetes in type 1DM patients*

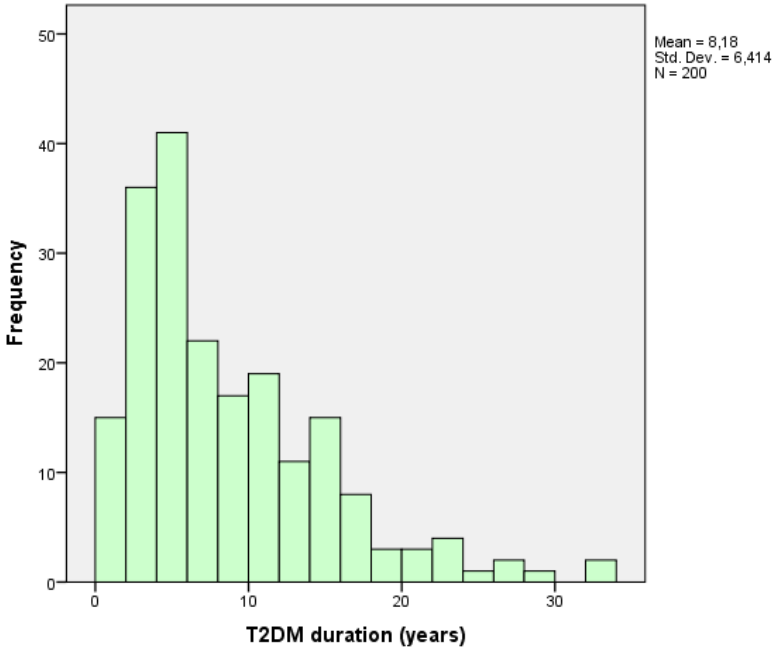

Figure 3. *The duration of diabetes in type 2 DM patients.*

Depending on eGFR, we classified CKD in its 5 stages. Figure 4 emphasizes the presence of CKD for each study group. Thus, in group 1, for patients with type 1 DM, the diabetic CKD was present in a percent of 44.5%; in group 2, for patients with type 2 DM, CKD was present in a percent of 53.5%, while in the control group the prevalence was of only 8% as shown in Figure 4.

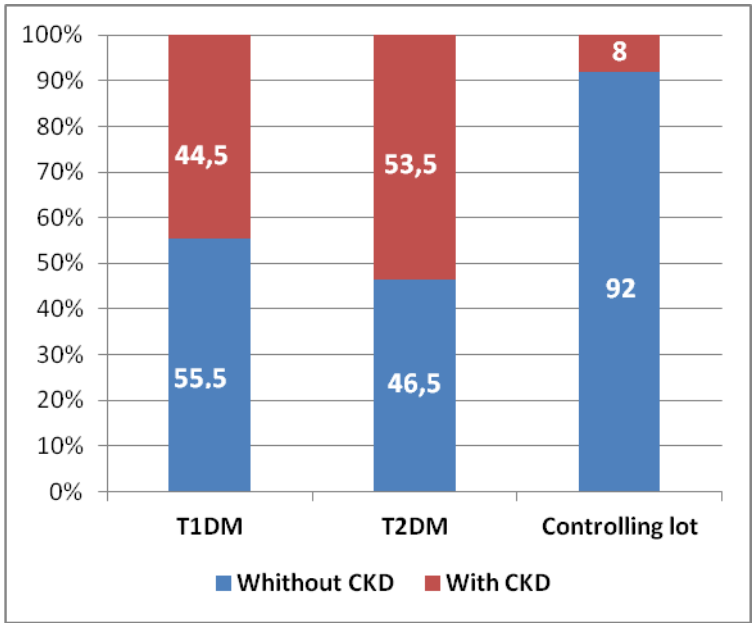

Figure 4. *The presence of diabetic CKD in the 3 groups (subjects with T1DM, T2DM and control group).*

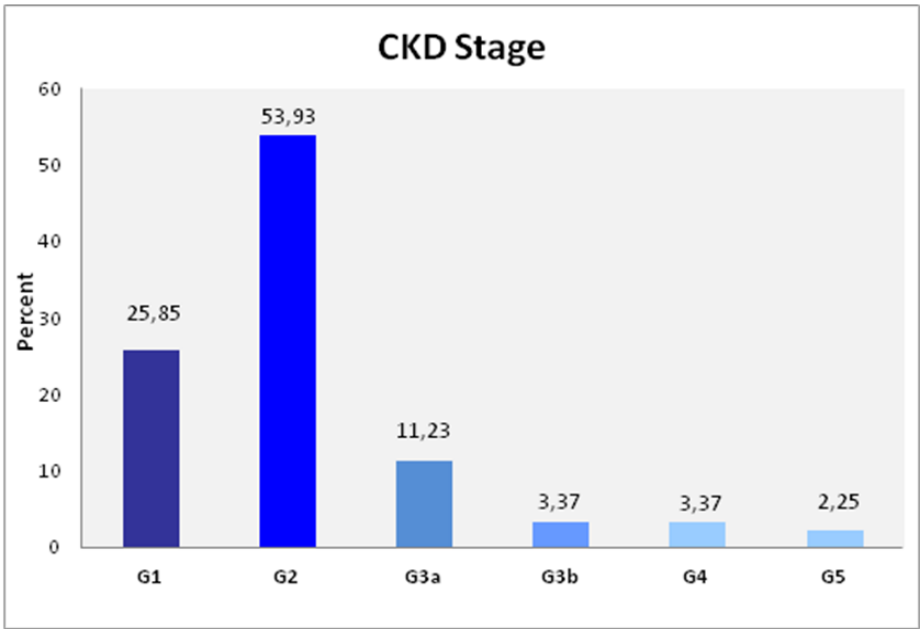

Figure 5. *The distribution of patients with type 1 DM according to the stage of CKD.*

We calculated the Phi and Cramer's V contingency coefficient, obtaining a value of 0.412. There is a statistically significant difference among the three study groups ($p < 0.0001$) regarding the presence of CKD, the highest percentage being emphasized in patients with type 2 DM, followed by patients with type 1 DM.

The analyzed patients were distributed in different stages of CKD according to the KDIGO 2012 classification. Thus, in group 1, most patients were in stage 2 of CKD (53.93%),

followed by stage 1 (25.85%), stage 3a (11.23%), stages stage 3b and 4 (3.37%), and stage 5 representing 2.25% each as shown in Figure 5.

In group 2, most patients were also in stage 2 of CKD (42.99%), followed by stage 3a (26.16%), then stage 1 (20.57%), stage 3b (7.48%), stage 4 (0.94%), and stage 5 (1.86%). (Figure 6).

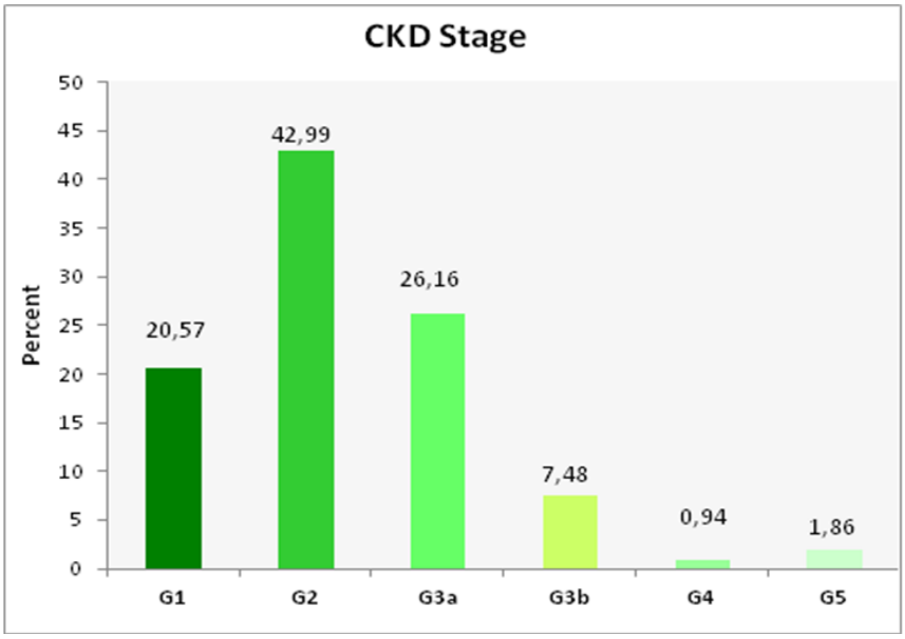

Figure 6. *The distribution of patients with type 2 DM according to the stage of CKD.*

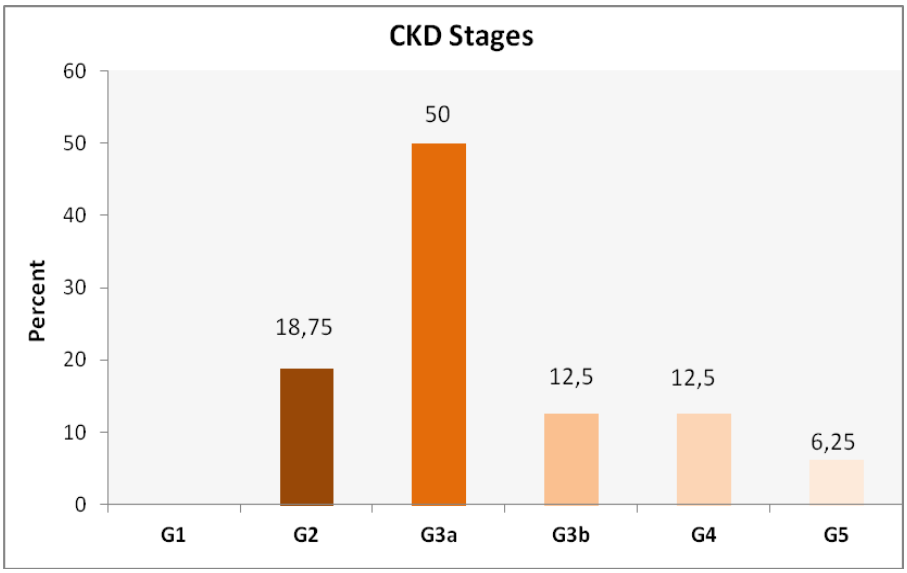

Figure 7. *The distribution of subjects from the control group according to the stage of CKD.*

In the control group, most patients were in stage 3a (50%), followed by stage 2 (18.75%), 3b and 4 each with a percentage of 12.5%, respectively stage 5 (6.25%) as shown in Figure 7.

We assessed the prognosis of CKD depending on eGFR and albuminuria, according to the KDIGO 2012 table that predicts the risk of general mortality, cardiovascular risk or progression to dialysis. The prognosis of CKD was showed by the following colours: green

represent low risk, yellow moderately increased risk, orange high risk and red represent very high risk.

In T1DM group (Table 3 and Figure 8) more than half patients (55.5%) had lower risk for evolution of CKD and for development of complications, 12,5% had moderately increased risk and 26% had high risk. Only 6% patients were at severely high risk.

Table 3. The number (percentage) of T1DM patients in each CKD risk group depending on eGFR and albuminuria (KDIGO 2012) [2]

				ALBUMINURIA		
				A1	A2	A3
				Normally to moderately risen	Moderately risen	Severely risen
				< 30mg/g	30-300 mg/g	> 300 mg/g
GFR (ml/min/1, 73 m^2)	G1	N/Risen	≥ 90	96 (48%)	7 (3.5%)	16 (8%)
	G2	Slightly reduced	60-89	15 (7.5%)	15 (7.5%)	33 (16.5%)
	G3a	Slightly to moderately reduced	45-59	3 (1.5%)	3 (1.5%)	4 (2%)
	G3b	Moderately to severely reduced	30-44	0 (0%)	0 (0%)	3 (1.5%)
	G4	Severely reduced	15-29	0 (0%)	1 (0.5%)	2 (1%)
	G5	Renal insufficiency	< 15	1 (0.5%)	0 (0%)	1 (0.5%)

Green - low risk, Yellow - moderately increased risk, Orange - high risk, Red - Severely high risk

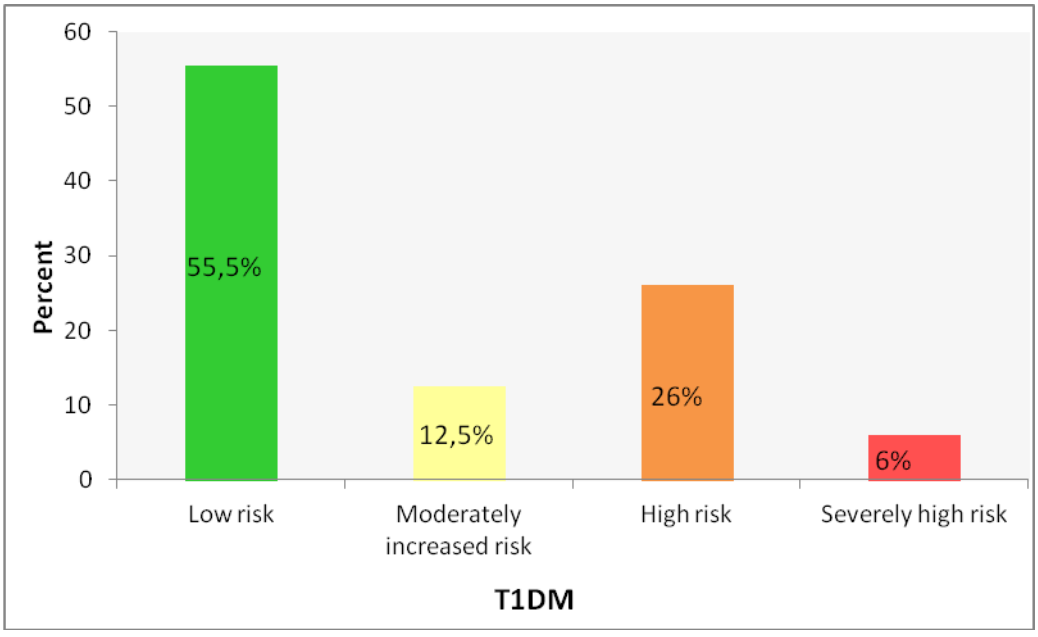

Figure 8. *The risk of patients with CKD and type 1 DM.*

In T2DM group (Table 4 and Figure 9), 46.5% of patients had lower risk for evolution of CKD and for development of complications, 34.5% had moderately increased risk and 19% had severely high risk. We had no patients with high risk in the T2DM group.

Table 4. The number (percentage) of T2DM patients in each CKD risk group depending on eGFR and albuminuria (KDIGO 2012) [2]

				ALBUMINURIA		
				A1	A2	A3
				Normally to moderately risen	Moderately risen	Severely risen
				< 30mg/g	30-300 mg/g	> 300 mg/g
GFR (ml/min/1, 73 m^2)	G1	N/Risen	≥ 90	50 (25%)	22 (11%)	0 (0%)
	G2	Slightly reduced	60-89	43 (21.5%)	46 (23%)	0 (0%)
	G3a	Slightly to moderately reduced	45-59	1 (0.5%)	0 (0%)	27 (13.5%)
	G3b	Moderately to severely reduced	30-44	0 (0%)	0 (0%)	8 (4%)
	G4	Severely reduced	15-29	0 (0%)	0 (0%)	1 (0.5%)
	G5	Renal insufficiency	< 15	2 (1%)	0 (0%)	0 (0%)

Green - low risk, Yellow - moderately increased risk, Orange - high risk, Red - Severely high risk

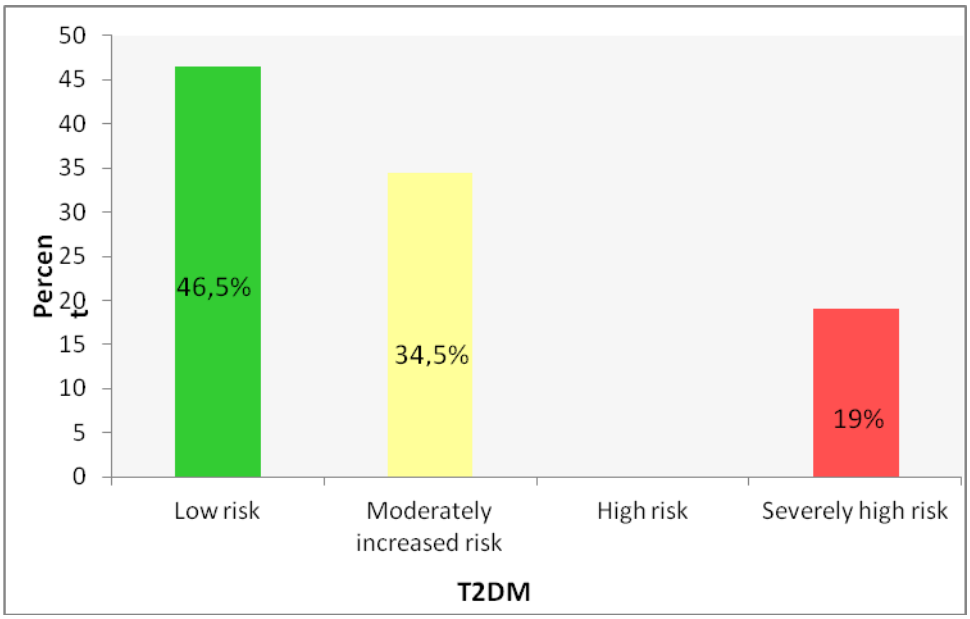

Figure 9. *The risk of patients with CKD and type 2 DM.*

In the control group (Table 5 and Figure 10), 92% patients were in low risk risk group. There were no patient at high risk and only 1.5% were in moderately increased risk and 6.5% were at severely high risk

The correlation tests have emphasized statistically significant differences ($p<0.0001$) of the risk in patients with type 1 DM versus control subjects, respectively in patients with type 2 DM versus control subjects ($p<0.0001$), proving the fact that DM is a negative prognosis factor for CKD. There were also statistically significant differences between the risk of patients with type 1 DM compared to patients with type 2 DM ($p<0.0001$), in type 2 DM the severely increased risk being present in a higher percentage.

Table 5. The number (percentage) of control subjects in each CKD risk group depending on eGFR and albuminuria (KDIGO 2012) [2]

				ALBUMINURIA		
				A1	A2	A3
				Normally to moderately risen	Moderately risen	Severely risen
				< 30mg/g	30-300 mg/g	> 300 mg/g
GFR (ml/min/ 1,73 m^2)	G1	N/Risen	≥ 90	100 (50%)	0 (0%)	0 (0%)
	G2	Slightly decreased	60-89	84 (42%)	3 (1.5%)	0% (0%)
	G3a	Slightly to moderately decreased	45-59	0% (0%)	0% (0%)	8 (4%)
	G3b	Moderately to secerely decreased	30-44	0% (0%)	0% (0%)	2 (1%)
	G4	Severely	15-29	0% (0%)	0% (0%)	2 (1%)
	G5	Renal insufficiency	< 15	0% (0%)	0 (0%)	1 (0.5%)

Green - low risk, Yellow - moderately increased risk, Orange - high risk, Red - Severely high risk

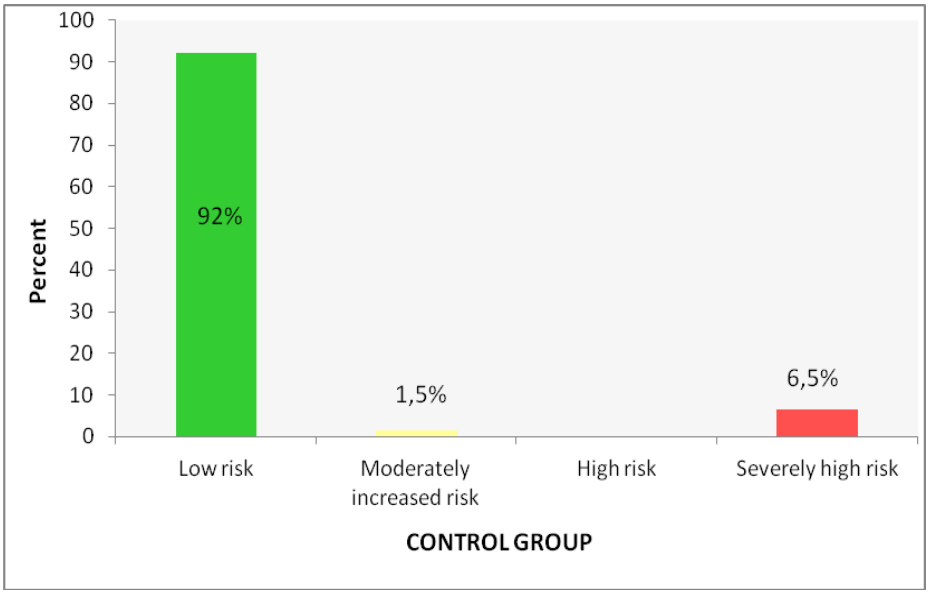

Figure 10. *The risk of patients with CKD from the control group.*

Discussions

There were differences in risk estimation of general mortality, cardiovascular risk or progression to dialysis associated CKD in T1DM and control group. T1DM represent an adjuvant factor for CKD progression and prognosis. This remark is available for T2DM and control group, too. There were also differences between T1DM and T2DM group. Dates were irregular distributed in the group with T2DM similar to some literature data where the magnitude of the increased risk had varied substantially for reasons that are unclear [8].

Our study has a limitation - the analysis was transversal, based on a single data collection, and we cannot exclude effects caused by changes over time that we were unable to assess. Finally, the observational nature does not allow interpretation of results in causal terms.

Conclusions

DM represents an important risk factor for the appearance of CKD but also a negative prognosis factor for the patients with CKD. The prognosis of patients with type 1 DM is somehow predictable, while in the case of type 2 DM the assessment of prognosis is more difficult and unpredictable.

REFERENCES

1. **National Kidney Foundation.** K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 39(2 Suppl. 1): S1–S266, 2002.

2. ******* KDIGO 2012 Guideline for Evaluation and Management of CKD. *Kidney Int Suppl* 3: 19–62, 2013. *Available at* http://www.kidney-international.org

3. **Groop PH, Thomas MC, Moran JL et al**. The presence and severity of chronic kidney disease predicts all-cause mortality in type 1 diabetes. Diabetes. 2009;58:1651-1658.

4. **Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY**. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 351*:* 1296*–1305,* 2004.

5. **Ruilope L, Antonio S, Jamerson K et al.** Renal function and intensive lowering of blood pressure in hypertensive participants of the hypertension optimal treatment (HOT) Study. *J Am Soc Nephrol* 12*:* 218*–225,* 2001.

6. **Culleton BF, Larson MG, Wilson PWF, Evan JC, Parfrey PS, Levy D**. Cardiovascular disease and morality in a community-based cohort with mild renal insufficiency. *Kidney Int* 56*:* 2214*–2219*, 1999.

7. **Levey AS, Stevens LA, Schmid CH et al.** A new equation to estimate glomerular filtration rate. *Ann Intern Med* 150: 604-612, 2009.

8. **Garg AX, Clark WF, Haynes RB, House AA**. Moderate renal insufficiency and the risk of cardiovascular mortality: Results from the NHANES I. *Kidney Int* 61: 1486*–1494,* 2002.