POTENTIAL PREDICTORS OF DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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INTRODUCTION

- Diabetic nephropathy (DN) is a leading cause of ESRD worldwide
- DN is an independent risk factor of cardio-vascular mortality in diabetics
- The pathogenesis of DN is complex and multifactorial
- No affirmed biomarkers of its presence so far, except albuminuria
- Renal biopsy still stays the only method that confirms the diagnosis

AIM OF THE STUDY

- To reveal a relationship between particular biomarkers and development of DN in patients with type 2 Diabetes Mellitus.

MATERIAL AND METHODS

- **81 patients** (22-75 years old): male – 49 (60,5%) and female – 32 (39,5%) with CKD and histologically proven nephropathies.

➢48 of all (59,3%) are with Diabetes mellitus Type 2

➢33 (40,7%) – without Diabetes mellitus

3 groups:

I gr.- Type 2 DM with histology of DN (n=30);

male 22 (73,3%); female 8 (26,7%)

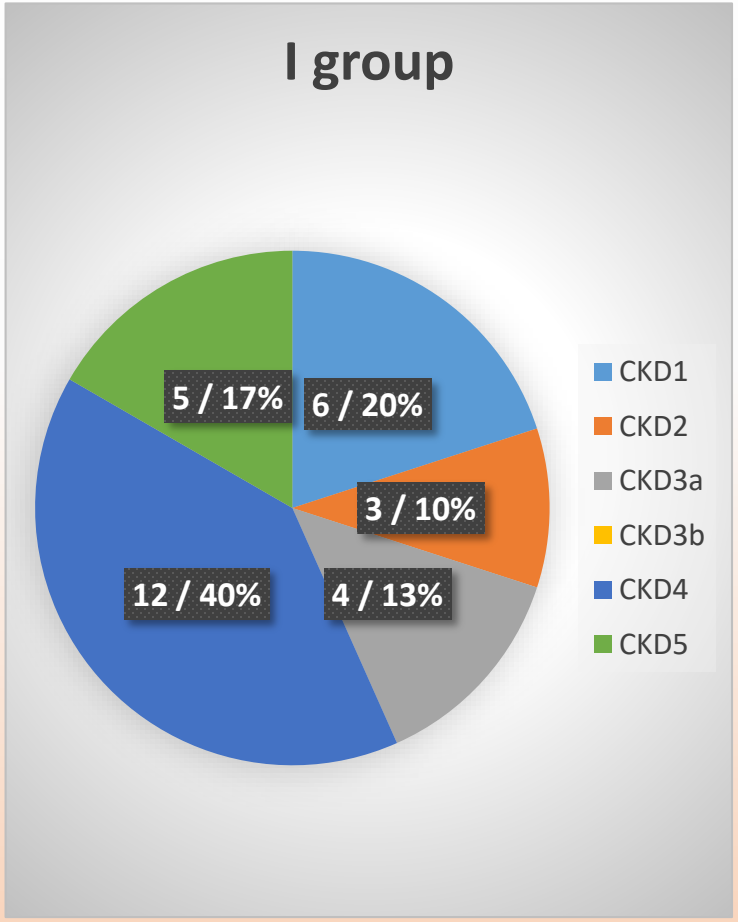
II gr. – Type 2 DM without DN in the biopsy (n=18)

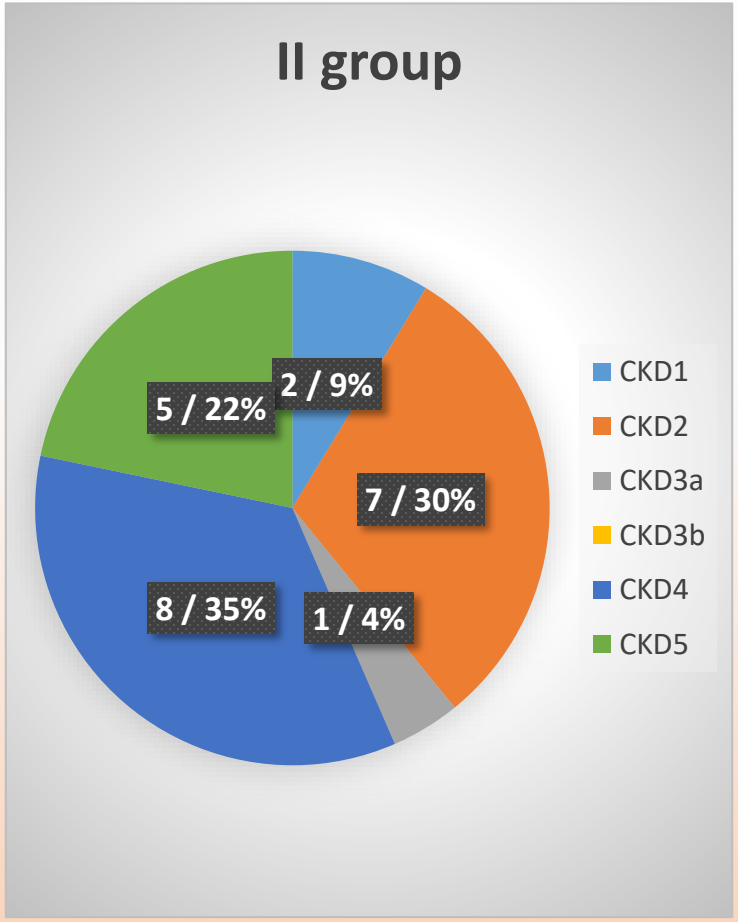
male 11 (61,1%); female 7 (38,9%)

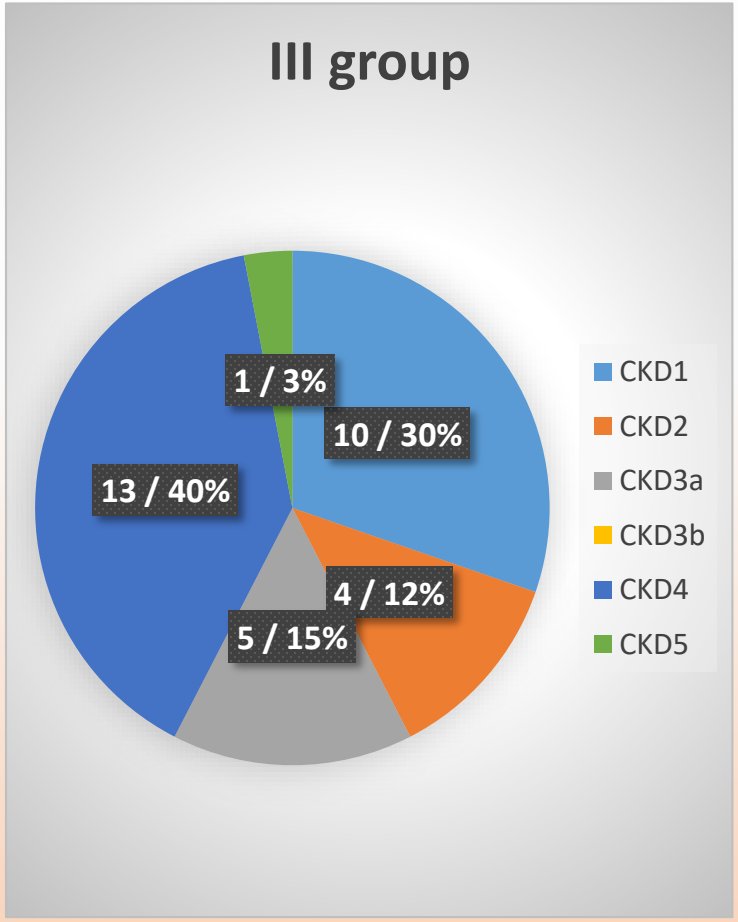
III gr. – Non Diabetics (n=33)

male 16 (48,5%); female 17 (51,5%)

Distribution of the patients according to stages of CKD (KDIGO Classification):







MATERIAL AND METHODS

- The patients are investigated for the following parameters:
  1. Complications of DM: Diabetic retinopathy; polyneuropathy, macroangiopathy
  2. BMI
  3. Arterial hypertension
  4. Lipid status (LDL, HDL, Triglycerides) and uric acid
  5. HbA1C
  6. Inflammatory markers: CRP, Il-6
  7. Indexes of blood clotting and vessel damage: Fibrinogen, D-dimer
  8. Homocysteine, folic acid
  9. Genetic factors: Methylenetetrahydrofolate reductase gene polymorphism (MTHFR A1289C and C677T)
  10. Thyroid function (TSH, FT4, TAT Ab, MAT Ab)

RESULTS

		I group – DM with DN	II group DM without DN	III group Non Diabetics	p group 1/2	p group 1/3	p group 2/3	p group (1+2)/3
Gender	Male	n=22 (73,3%)	n=11 (61,1%)	n=16 (48,5%)	0,376	0,044	0,388	0,067
	Female	n=8 (36,7%)	n=7 (38,9%)	n=17 (51,5%)				
Diabetic Retinopathy	Yes	n=15 (50,0%)	n=0 (0,0%)		<0,001			
	No	n=15 (50,0%)	n=18 (100,0%)					
Diabetic polyneuropathy	Yes	n=20 (66,7%)	n=10 (55,6%)		0,441			
	No	n=10 (33,3%)	n=8 (44,4%)					
Diabetic macroangiopathy	Yes	n=10 (33,3%)	n=7 (38,9%)		0,697			
	No	n=20 (66,7%)	n=11 (61,1%)					
Diabetic gangrene	Yes	n=2 (6,7%)	n=0 (0,0%)		0,263			
	No	n=28 (93,3%)	n=18 (100,0%)					
BMI	18,0-24,9	n=1 (3,3%)	n=1 (5,6%)	n=11 (33,3%)	0,747	<0,001	0,013	<0,001
	25,0-29,0	n=6 (20,0%)	n=5 (27,8%)	n=13 (39,4%)				
	>30,0	n=23 (76,7%)	n=12 (66,7%)	n=9 (27,3%)				
Arterial Hypertension	Yes	n=30 (100,0%)	n=18 (100,0%)	n=28 (84,8%)		0,054	0,148	0,009
	No	n=0 (0,0%)	n=0 (0,0%)	n=5 (15,0%)				

RESULTS

		I group – DM with DN	II group DM without DN	III group Non Diabetics	p group 1/2	p group 1/3	p group 2/3	p group (1+2)/3
LDL	Low	n=4 (14,3%)	n=5 (27,8%)	n=1 (3,3%)	0,307	0,322	0,024	0,092
	Normal	n=22 (78,6%)	n=13 (72,2%)	n=26 (86,7%)				
	High	n=2 (7,1%)	n=0 (0,0%)	n=3 (10,0%)				
HDL	Low	n=19 (67,9%)	n=11 (61,1%)	n=9 (30,0%)	0,639	0,013	0,093	0,007
	Normal	n=9 (32,1%)	n=7 (38,9%)	n=20 (66,7%)				
	High	n=0 (0,0%)	n=0 (0,0%)	n=1 (3,3%)				
Triglycerides	Normal	n=15 (50,0%)	n=10 (55,6%)	n=24 (72,7%)	0,709	0,064	0,214	0,062
	High	n=15 (50,0%)	n=8 (44,4%)	n=9 (27,3%)				
Uric acid	Normal	n=24 (80,0%)	n=11 (61,1%)	n=28 (84,8%)	0,154	0,613	0,085	0,204
	High	n=6 (20,0%)	n=7 (38,9%)	n=5 (15,2%)				
HBA1C	Normal	n=14 (46,7%)	n=9 (50,0%)	n=30 (100,0%)	0,823	<0,001	<0,001	<0,001
	>6,5%	n=16 (53,3%)	n=9 (50,0%)	n=0 (0,0%)				

RESULTS

		I group DM with DN	II group DM without DN	III group Non Diabetics	p group 1/2	p group 1/3	p group 2/3	p group (1+2)/3
CRP	Normal	n=17 (56,7%)	n=13 (72,2%)	n=26 (78,8%)	0,281	0,060	0,732	0,119
	High	n=13 (43,3%)	n=5 (27,8%)	n=7 (21,2%)				
IL-6	Normal	n=17 (56,7%)	n=14 (77,8%)	n=29 (87,9%)	0,139	0,005	0,430	0,019
	High	n=13 (43,3%)	n=4 (22,2%)	n=4 (12,1%)				
D-dimer	Normal	n=13 (43,3%)	n=10 (55,6%)	n=22 (66,7%)	0,412	0,063	0,433	0,095
	High	n=17 (56,7%)	n=8 (44,4%)	n=11 (33,3%)				
Fibrinogen	Low	n=1 (3,3%)	n=0 (0,0%)	n=0 (0,0%)	0,508	0,012	0,177	0,021
	Normal	n=14 (46,7%)	n=11 (61,1%)	n=27 (81,8%)				
	High	n=15 (50,0%)	n=7 (38,9%)	n=6 (18.2%)				

RESULTS

		I group DM with DN	II group DM without DN	III group Non Diabetics	p group 1/2	p group 1/3	p group 2/3	p group (1+2)/3
Homocysteine	Normal	n=9 (30,0%)	n=11 (61,1%)	n=11 (33,3%)	0,034	0,777	0,056	0,448
	High	n=21 (70,0%)	n=7 (38,9%)	n=22 (66,7%)				
Folic acid	Normal	n=20 (87,0%)	n=13 (100,0%)	n=27 (81,8%)	0,323	0,338	0,219	0,242
	Low	n=3 (13,0%)	n=0 (0,0%)	n=6 (18,2%)				
MTHFR A1289C	Homozygous AA normal	n=16 (53,5%)	n=10 (55,6%)	n=15 (45,5%)	0,982	0,794	0,785	0,721
	Heterozygous	n=12 (40,0%)	n=7 (38,9%)	n=16 (48,5%)				
	Homozygous CC mutation	n=2 (6,7%)	n=1 (5,6%)	n=2 (6,1%)				
MTHFR C677T	Homozygous CC normal	n=13 (43,3%)	n=6 (33,3%)	n=7 (21,2%)	0,770	0,094	0,300	0,084
	Heterozygous	n=12 (40,0%)	n=8 (44,4%)	n=22 (66,7%)				
	Homozygous TT mutation	n=5 (8,7%)	n=4 (22,2%)	n=4 (12,1%)				

RESULTS

		I group – DM with DN	II group DM without DN	III group Non Diabetics	p group 1/2	p group 1/3	p group 2/3	p group (1+2)/3
TSH	Low	n=1 (3,3%)	n=0 (0,0%)	n=3 (9,1%)	0,135	0,140	0,416	0,220
	Normal	n=29 (96,7%)	n=16 (88,9%)	n=27 (81,8%)				
	High	n=0 (0,0%)	n=2 (11,1%)	n=3 (9,1%)				
FT4	Low	n=2 (6,9%)	n=0 (0,0%)	n=1 (3,0%)	0,240	0,326	0,753	0,640
	Normal	n=27 (93,1%)	n=17 (94,4%)	n=30 (90,9%)				
	High	n=0 (0,0%)	n=1 (5,6%)	n=2 (6,1%)				
TAT	Normal	n=26 (86,7%)	n=15 (83,3%)	n=29 (87,9%)	0,999	0,885	0,686	0,751
	High	n=4 (13,3%)	n=3 (16,7%)	n=4 (12,1%)				
MAT	Normal	n=29 (96,7%)	n=15 (83,3%)	n=26 (78,8%)	0,142	0,033	0,999	0,096
	High	n=1 (3,3%)	n=3 (16,7%)	n=7 (21,2%)				

CONCLUSION

- There is no single biomarker that could be a predictor of Diabetic nephropathy
- A combination of biomarkers might be more reliable test and should be searched
- Larger studies are needed to determine the predictive value of the particular biomarkers for the development of DN