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RENAL VASCULAR LESIONS IN PATIENTS WITH DIABETES MELLITUS

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Abstract

Background and Aims. *Patients with diabetes mellitus, especially type 2 diabetes, have often a multifactorial renal impairment. The aim of this study was to correlate renal vascular lesions occurring in patients with diabetes mellitus with clinical and laboratory parameters.* ***Material and method****. We performed a retrospective study on a sample of 127 patients with diabetes mellitus, who died in hospital. Data from necropsies were correlated with the clinical and laboratory data collected from the medical records of these patients.* ***Results.*** *Renal vascular lesions were frequently found in patients from the study group. The most common were nephroangiosclerosis lesions, which correlated with age, diabetes duration, systolic blood pressure and mean fasting glucose.* ***Conclusions****. Most patients in the study group had multiple cardiovascular risk factors (advanced age, dyslipidemia, hypertension) that explain the high prevalence of renal vascular lesions.*

key words: *diabetes mellitus, renal vascular lesions, nephroangiosclerosis.*

Background and Aims

Diabetes mellitus is a disease whose prevalence is increasing. One of the diabetes complications with a high socio-economical impact is diabetic renal disease. Patients with diabetes, especially those with type 2 diabetes (T2DM), may have also nondiabetic renal lesions, favored by a number of conditions specific for the diabetic environment.

Renal vascular lesions in diabetes are due to diabetic micro and macroangiopathy. Diabetic renal macroangiopathy is characterized by the presence of renal artery or abdominal aorta atheromatosis. Atherosclerotic lesions occurring in the aorta and renal arteries can lead to the generation of atheromatous emboli into the renal arteries and arterioles than that will cause renal infarction and ischemic atrophy of kidney glomeruli and tubules.

Diabetic microangiopathy induces changes in the renal arterioles and glomerular capillaries. Diabetic renal microangiopathy is characterized by thickening of the glomerular basement membrane (non-enzymatic glycosylation of proteins) and hyaline arteriosclerosis with subendothelial PAS-

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positive hyaline deposits. Glomerular ischemic lesions can appear secondary. Arteriolar hyalinosis lesions also occur in nondiabetic hypertensive patients and normotensive elderly persons. Advanced glomerular arteriolar hyalinosis is usually associated with large vessel atherosclerosis.

The combination of nodular lesions with afferent and efferent arteriolar hyalinosis is considered specific for the diabetic kidney disease, but may occur in rare circumstances also in nondiabetic subjects. These vascular lesions could contribute to the development of global ischemic glomerulosclerosis, since the severity of hyalinosis correlate significantly with the number of sclerosed glomeruli [1]. In patients with diabetic kidney disease, neovascular lesions similar to those of diabetic retinopathy can also occur [2].

Micro and macroangiopathy renal lesions frequently overlap with nephroangiosclerosis secondary to hypertension, and calcification of the intima and media of renal arterioles secondary to lipid disorders, both pathological conditions frequently encountered in diabetes, particularly in T2DM. Nephroangiosclerosis is a cause of end stage renal disease and classically is considered a consequence of hypertension, but may occur also in elderly patients and patients with diabetes. In terms of histopathology, nephroangiosclerosis is characterized by preglomerular arteriolar hyalinosis, with predominantly eosinophilic subendothelial deposits, intimal thickening, followed by hypertrophy and fibrosis [3]. Arteriosclerosis and arteriolosclerosis lesions are accompanied by focal and segmental glomerulosclerosis, progressing to glomerular obstruction, interstitial fibrosis and appearance of inflammatory infiltrates [4].

Renal infarction is a condition relatively rarely diagnosed, but in patients with diabetes can occur with greater frequency due to associated pathological conditions. Renal infarction occurs due to renal artery occlusion, causing necrosis of kidney adjacent anatomical area. It is characterized by the appearance of a triangular area of ischemic necrosis, which is replaced by fibrous tissue. Diagnosis is often retrospective, at necropsy, because clinical signs are often nonspecific, especially for small renal infarction secondary to progressive atherosclerotic occlusion of small renal arteries [5]. Obesity [6] and dyslipidemia may be additional risk factors for the emergence or worsening of renal disease progression in diabetic patients. Independent risk factors for development of diabetic nephropathy also include, according to some studies [7] male gender and smoking status.

This study aimed to examine renal vascular lesions occurring in diabetic patients and to assess whether correlations exist between these histopathologic findings and clinical and laboratory data. An aspect particularly aimed in T2DM patients was the association with obesity and dyslipidemia.

Material and method

We performed a retrospective histological study on a sample of 127 patients with diabetes, who died in Constanta County Emergency Hospital between 2006 and 2010. Necropsies were performed in the Department of Pathology. Histopathological data were correlated with the clinical and laboratory data collected from the clinical medical records of these patients, for a 5 years period prior to death. We collected data regarding gender, age, diabetes type and duration, antidiabetic therapy, comorbidities and causes of death,

fasting glucose, total cholesterol and triglycerides. We analyzed the correlation between the presence of nephroangiosclerosis and age, gender, rural-urban area, type of diabetes, diabetes duration, mean blood pressure, blood glucose and blood lipids.

Regarding statistical analysis, collection, analysis and interpretation of results we used a card type, containing the investigated parameters. For comparison we used Student and CHI² tests. To confirm the null hypothesis we set a $p > 0.05$. For $p < 0.05$ (or $p < 0.01$) the null hypothesis is disproven.

Results

The study group included 69 (54.33%) women and 58 (45.67%) men. A number of 83 patients (65.35%) were aged over 65 years. Age distribution is given in Table 1.

Table 1. Study group distribution according to age.

Age	No patients	Percent
30 - 39	3	2.36%
40 - 49	7	5.51%
50 - 59	18	14.17%
60 - 69	37	29.13%
70 - 79	53	41.73%
80 - 89	9	7.09%

From the study group, 108 patients (85.04%) had T2DM, 16 (12.6%) type 1 diabetes (T1DM) and 3 (2.36%) other types of diabetes mellitus. Diabetes duration was under 5 years in 29 patients (22.84%), between 5 and 10 years in 26 patient (20.47%), 10 to 20 years in 53 patients (41.73%) and over 20 years in 19 patients (14.96%).

The most common comorbidities were: dyslipidemia (113 patients, 88.98%), arterial hypertension (105 patients, 82.68%) and ischemic heart disease (78 patients, 61.4%). A total of 103 patients (91.1%) were overweight or obese. Of these, 69 patients had BMI over 30. Regarding the causes of death, the distribution was as follow: cardiovascular causes (61.42%), infectious causes (17.32%), renal failure (7.87%), acute diabetes complications (3.15%), neoplasms (2.36%), and other causes (7.87%).

In terms of pathology, the most common were renal vascular lesions, isolated or associated with lesions specific for diabetic nephropathy or other renal diseases. 100 patients (78.7%) had nephroangiosclerosis. Out of the 100 patients with nephroangiosclerosis, 86 (86%) had a medical history of hypertension. A number of 67 patients (67%) died due to a cardiovascular disease and 7 (7%) due to end stage renal disease. Following statistical analysis, positive correlations were established between nephroangiosclerosis lesions and diabetes duration greater than 5 years ($p = 0.0834$) as shown in Table 2 and Figure 1.

Table 2. Correlation between diabetes duration and nephroangiosclerosis.

Duration of diabetes mellitus (Years)	With nephroangiosclerosis	Without nephroangiosclerosis
Mean	11.89	9.70
Median	12	8
Standard Deviation	6.96	8.26
Kurtosis	0.40	-1.56
Skewness	0.59	0.28
	p	0.0834

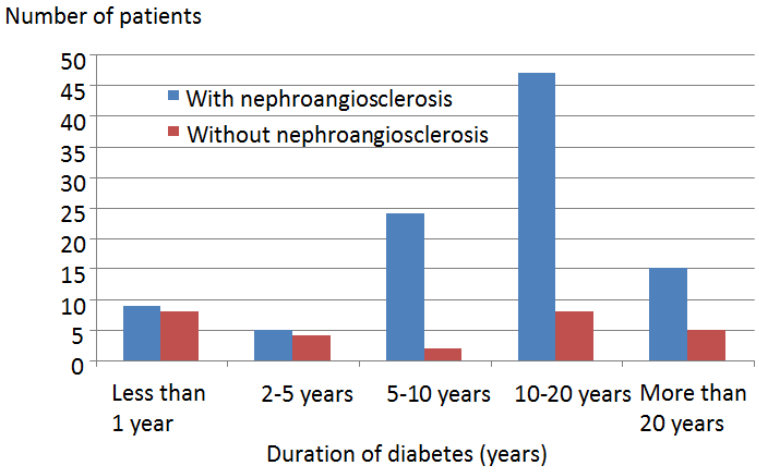

Figure 1. Duration of diabetes in patients with and without nephroangiosclerosis.

Table 3. Correlation between age of patients with diabetes and nephroangiosclerosis.

Age (Years)	With nephroangiosclerosis	Without nephroangiosclerosis
Mean	69.18	57.59
Median	71	59
Standard Deviation	8.69	13.16
Kurtosis	0.59	-1.02
Skewness	-0.64	-0.09
	p	0.0000001

Table 4. Correlation between mean blood glucose and nephroangiosclerosis lesions.

Glycemia (mg/dl)	With nephroangiosclerosis	Without nephroangiosclerosis
Mean	181.32	209.56
Median	169	214
Standard Deviation	48.36	61.28
Kurtosis	0.00	-1.16
Skewness	0.78	-0.17
	p	0.006205

There was a significant correlation between nephroangiosclerosis lesions and age of diabetic patients ($p < 0.01$) as shown in Table 3.

We tried to correlate the presence of nephroangiosclerosis lesions with the metabolic status of patients with diabetes mellitus. Since a significant percentage of patients had no glycated hemoglobin recorded on their clinical medical records, we tried to identify the most constant recorded parameter and this parameter was fasting plasma glucose. We considered the mean fasting glucose recorded in patient files for a period of 5 years before death. The presence of nephroangiosclerosis was correlated with mean fasting blood glucose levels, significantly increasing with the mean fasting glucose values above 160 mg / dl ($p = 0.006205$) as shown in Table 4 and Figure 2.

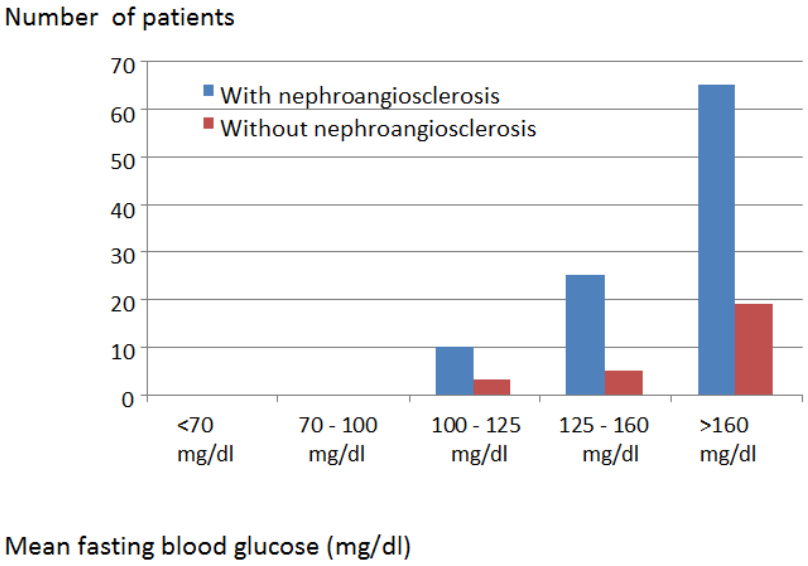

Figure 2. Mean fasting blood glucose in patients with and without nephroangiosclerosis.

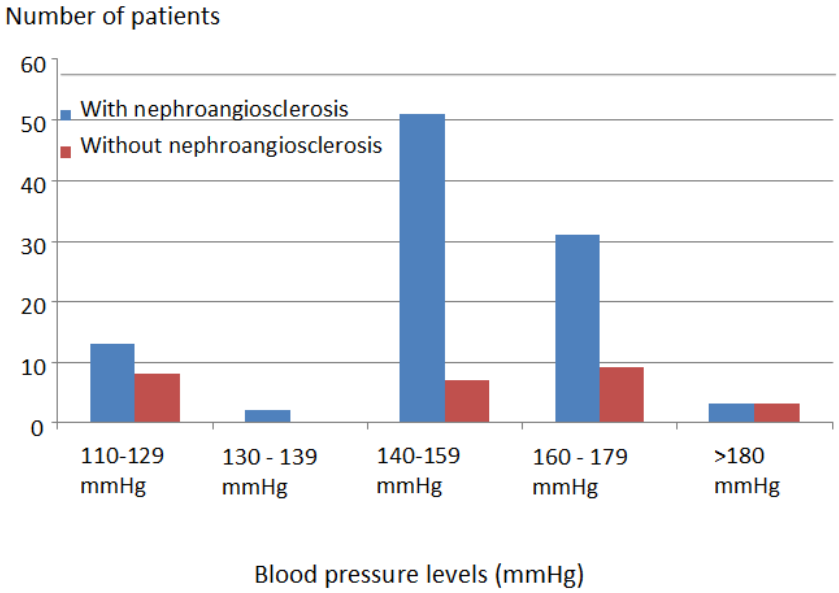

Figure 3. Blood pressure levels in patients with and without nephroangiosclerosis.

Most patients in the study group had arterial hypertension. Nephroangiosclerosis lesions correlated with elevated blood pressure, the highest prevalence being recorded in patients with systolic blood pressure between 140 and 159 mmHg (Figure 3).

Nephroangiosclerosis lesions were more commonly found in patients with triglyceride levels greater than 160 mg/dl, but data were not statistically significant. The appeareance of nephroangiosclerosis was not correlated with gender or rural or urban area of origin of the patients. Also, no statistically significant correlations were found with body mass index value or with the total cholesterol.

In the study group, renal infarction was identified in 9 patients out of 127, representing a rate of 7.1%. No correlations were established between the presence of renal

infarction and gender, urban or rural area, type or duration of diabetes, mean blood pressure, serum cholesterol, triglycerides and glucose. There was a trend for correlation between the presence of renal infarction and patients age (p=0.041341339) as shown in Table 5, but data are did not reach statistical significance due to the small number of patients with renal infarction.

Table 5. Correlation between patient age and renal infarction.

Age (Years)	With renal infarction	Without renal infarction
Mean	60.67	67.18
Median	63	69.5
Standard Deviation	12.20	10.66
Kurtosis	-0.08	0.57
Skewness	-0.86	-0.84
	p	0.041341339

Discussions

In the study group, some correlations were established between clinical and laboratory data and pathological lesions. Thus, there was a significant correlation between nephroangiosclerosis lesions and the age of diabetic patients ($p < 0.01$). Our results are consistent with the literature data [8-10], showing a high prevalence of nephroangiosclerosis lesions in elderly patients. It is difficult to say whether these lesions are due to age or to associated pathology [11]. Following statistical analysis, positive correlations were established between the presence of nephroangiosclerosis lesions and duration of diabetes ($p = 0.0834$).

The nephroangiosclerosis lesions are considered to be secondary to hypertension and we tried to assess whether this correlation also applies to patients in our study group. Most patients in the study group were hypertensive. The nephroangiosclerosis lesions correlated with elevated blood pressure values, the highest prevalence being recorded in patients with systolic values between 140 and 159 mmHg.

The presence of nephroangiosclerosis also correlated with mean fasting blood glucose levels (an indicator of the metabolic control), significantly increasing in frequency with average fasting glucose values above 160 mg/dl (p=0.006205).

Also, there was a correlation between the presence of hypertriglyceridemia and the lesions of nephroangiosclerosis, which are more common in patients with triglyceride levels greater than 160 mg/dl, but data did not reach statistical significance. Nephroangiosclerosis did not correlate with gender, rural or urban area of origin of patients, body mass index or total cholesterol value.

Correlations established between the nephroangiosclerosis lesions and patient age, duration of diabetes, systolic blood pressure and mean fasting glucose shows that the etiology is probably multifactorial, for this pleading also data from the literature [12,13]. Regardless of etiology, evolution is to end stage renal disease, the association of several risk factors precipitating this development [14,15].

We also established a correlation between patient age and presence of renal infarction ($p = 0.041341339$) and a trend for association with hypertension but no effect of gender, urban or rural area, type of diabetes, diabetes duration, mean serum cholesterol, triglycerides and mean fasting glucose could be found. In most cases, renal infarction was not diagnosed before death, renal infarctions having frequently nonspecific symptoms [5]. Association with older age, diabetes, hypertension and various cardiovascular disorders (especially permanent atrial

fibrillation and valvular heart disease) [16], as well as obesity and dyslipidemia [17] increase the risk of kidney and heart vessel atheromatosis, but our small number of cases did not allow to confirm these data.

Conclusions

Most patients in our study group had cardiovascular risk factors (advanced age, dyslipidemia, hypertension), correlated with a high prevalence of renal vascular lesions, isolated or confounding with other types of kidney damage. Nephroangiosclerosis correlated with patient age, duration of diabetes, mean fasting glucose higher than 160 mg/dl and systolic blood pressure higher of 140 mmHg. Appearance of renal infarction correlated with age and systolic blood pressure, but due to the small number of cases data were not statistically significant.

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