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RENAL ANEMIA AND CARDIAC DYSFUNCTION IN DIABETIC VERSUS NON-DIABETIC PATIENTS

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Abstract

Cardiac failure (CHF), renal disease and anemia are interconnected in the Cardio-Renal Anemia syndrome. Diabetes mellitus remains the most common cause of end-stage renal disease (ESRD) in the developed world and when it is associated with these three conditions it worsens the outcomes of these patients. ***Aim:*** *to evaluate renal anemia and cardiac dysfunction in patients with chronic kidney disease with and without diabetes mellitus (DM).* ***Materials and methods*** *– we assessed 100 patients (40 women and 60 men), 41 patients with DM and 59 patients without DM. All patients had Chronic Kidney Disease (CKD) - estimated glomerular filtration rate (eGFR) under 60 ml/min/1,73 mp. We considered anemia when the value of haemoglobin (Hb) was under 11 g/dl.* ***Results*** *– Mean age of the studied patients was 60.38±11.79 years old in women and 59.28±13.89 years old in men. The prevalence of anemia was high in diabetic and non-diabetic patients, too. Anemia was more severe in patients with cardiac dysfunction than in those with normal cardiac function. The higher prevalence of cardiac dysfunction was in patients which had both anemia and DM. There were no significant differences about prevalence of diastolic or systolic cardiac dysfunction in non-diabetic versus diabetic patients.* ***Conclusions*** *– Anemia was an independent predictor for the development of cardiac dysfunction in patients with CKD and the prevalence of cardiac dysfunction was higher in patients who had both anemia and DM than in those without anemia and DM.*

key words: *diabetes mellitus, chronic kidney disease, cardiac dysfunction, heart failure, anemia.*

Background

Anemia appears from early stages of kidney disease [1]. Hemoglobin concentrations were significantly lower in patients with eRFG less than 70 ml/min/1.73 m^2 compared with those with higher levels of eGFR [2, 3]. Forty-four percent of elderly

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CKD patients have CHF compared to just 20 percent of their counterparts without CKD [4]. Cardiovascular disease (CVD) represents a major cause of morbidity and mortality in patients with CKD and it is also a well-established feature of these patients. Anemia is one of the important predictors of poor outcome in heart failure [5]. When it is severe, anemia is responsible for the development of cardiac failure even in patients without previous cardiac dysfunction. Baseline anemia was strongly associated with mortality. Median survival in patients without anemia was longer than in anemic patients [6]. Severe anemia at hospital admission for ischemic stroke is a more potent predictor of death in the following year than a history of heart disease or cancer [7]. Many studies have demonstrated a strong relationship between anemia and mortality in populations with heart failure [8, 9]. Both impaired renal function and increasing severity of cardiac failure independently predicted more serious prognosis in heart failure patients [10]. Low haemoglobin is very detrimental to the haemodynamic state of the patient with decreased cardiac output as it further diminishes the oxygen supply to the tissues. In the presence of anemia, when the need for greater cardiac output is combined with decreased systolic and/or diastolic performance, the clinical state of congestive heart failure (HF) may develop or become aggravated [5]. Anemia, CHF and CKD are interrelated, each causing the other to worsen and thus resulting in a 'vicious cycle' of disease progression which we have called the Cardio-Renal Anemia syndrome. DM is the leading cause of CKD and it is associated with excessive cardiovascular morbidity and mortality [11]. The impact of DM and congestive HF as risk multipliers is also important in CKD patients, particularly given that cardiovascular risk factors are relatively under-treated [4]. Anemia has a high prevalence in patients with DM and stage 3 CKD [12]. It is estimated that one in five patients with DM and stage 3 CKD has anemia, and its severity worsens in the advanced stages of CKD and in those with proteinuria [13, 14]. Prevalence of anemia in patients with DM was 2 to 3 times higher than in patients without DM with comparable renal impairment and iron stores in the general population. In patients with DM, anemia can also contribute to the severity of cardiovascular disease [15]. The presence or absence of DM seems to add another layer of complexity to the relationship between anemia, CKD and CVD. In patients with DM, CKD, and anemia, cardiovascular risk is most strongly predicted by age, history of HF, C-reactive protein, urinary protein/creatinine ratio, abnormal electrocardiogram, and elevation of two specific cardiac biomarkers, serum N-terminal pro B-type natriuretic peptide and troponin T [16].

Aim: to evaluate renal anemia and cardiac dysfunction in patients with CKD with and without DM – prevalence, risk factors and clinical implications.

Material and method: In a prospective analysis, we assessed 100 patients (40 women and 60 men) with CKD, whose eGFR was under 60 ml/min/1.73 mp.

The GFR was estimated using the creatinine clearance calculated by the 4-variable Modification of Diet in Renal Disease (MDRD) formula. Mean age in studied patients was 60.38±11.7 years old in women and 59.28±13.8 years old in men. We included

in the study 41 patients with type 2 DM and 59 patients without diabetes (Figure 1).

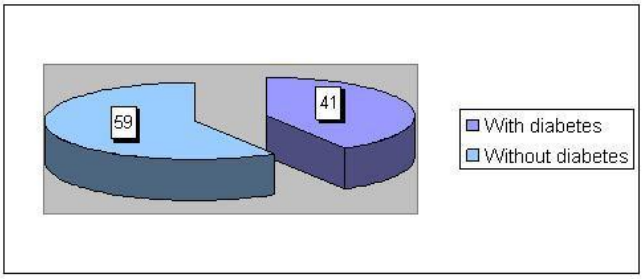

Figure 1. Distribution in the studied subjects

Table 1. Baseline characteristics of the studied population stratified by anemia, cardiac dysfunction and diabetes

	Without diabetes mellitus (n=59)				With diabetes mellitus (n=41)			
	Anemia		*Cardiac dysfunction*		*Anemia*		*Cardiac dysfunction*	
	Without anemia	With anemia	Normal cardiac function	Cardiac dysfunction	Without anemia	With anemia	Normal cardiac function	Cardiac dysfunction
Patients (n)	19	40	28	31	15	26	15	26
Demographics								
Age (years)[1]	60,95 ±9,16	57,98 ±15,86	57,18 ±15,02	60,52 ±13,13	60,07 ±14,41	61,31 ±9,78	56,13 ±13,05	63,58 ±9,81
Gender (n) (male/female)	13/6	21/19	14/14	20/11	14/1	12/14	10/5	16/10
High school graduate (%)	15,78	25	17,85	25,80	26,26	15,38	6,66	26,92
Medical history								
Smokes *(%)*	52,63	25	28,57	38,70	6,66	42,30	46,66	53,84
Drinks *(%)*	15,78	15	14,28	16,12	33,33	11,53	20	19,23
Diabetes (n)	-	-	-	-	15	26	15	26
HTA *(%)*	97,73	75	82,14	80,64	100	96,15	100	96,15
Physical characteristics								
BMI (kg/m^2)[1]	29,14 ±7,2	23,02 ±4,51	24,25 ±5,06	25,65 ±7,05	29,96 ±5,57	29,18 ±5,93	28,87 ±6,19	29,8 ±5,57
Diuresis[1]	1513,1 ±870,8	1217,5 ±932,2	1696,4 ±858,2	966,13 ±835,4	1520 ±1020,6	1253,8 ±772	1713,3 ±907	1142,3 ±788
Systolic BP[1,2]	150 ±10,2	165 ±15,5	146 ±15,6	175 ±22,5	175,20 ±25	155 ±23,2	168± 22,5	175± 15,4
CKD stage(n)								
Stage 3	6	-	4	2	6	-	4	2
Stage 4	4	4	2	6	4	4	2	6
Stage 5	-	5	1	4	-	5	1	4
Stage SPD	3	8	5	6	3	8	5	6
Stage SHD	2	9	3	8	2	9	3	8
Stage STx	1	1	2	-	-	-	-	-

[1]Continuous variable are mean±SD, [2]Systolic blood pressure (BP) was estimated in mmHg, HTA=arterial hypertension, BMI=body mass index.

There was no difference between mean age in patients with DM than in those without DM (60.85±11.53 versus 58.93±14.04 years, p=0.45).

History of hypertension, dyslipidemia, diabetes, ischemic cardiac disease, stroke and periferic arterial disease was assessed. For all patients were evaluated the following parameters: age, sex, environment, smoking, alcohol, body mass index, type of nephropathy and renal replacement therapy, diuresis, haemoglobin, serum creatinine and GFR, Kt/V used to quantify hemodialysis and peritoneal dialysis treatment adequacy, total cholesterol, triglycerides, ferritin and parathyroid hormone levels (PTH), C reactive protein level (CRP), serum albumin, serum phosphorus, proteinuria. We considered anemia when the

value of haemoglobin (Hb) was under 11g/dl. The number of hospitalization days was evaluated in the last 12 months prior to the inclusion in the study.

Table 2. Outcomes of the studied population stratified by anemia, cardiac dysfunction and diabetes

	Without diabetes mellitus (n=59)				With diabetes mellitus (n=41)			
	Anemia		*Cardiac dysfunction*		*Anemia*		*Cardiac dysfunction*	
	Without anemia	With anemia	Normal cardiac function	Cardiac dysfunction	Without anemia	With anemia	Normal cardiac function	Cardiac dysfunction
Cardiac status								
Systolic dysfunction (%)	21,05	35	-	30,50	13,33	34,61	-	26,84
Diastolic dysfunction (%)	31,57	35	-	33,84	33,33	38,46	-	36,58
IVS (mm)[1]	13,48 ±2,27	13,25 ±2,95	12,60 ±2,29	13,97 ±2,97	14,18 ±3,2	14,35 ±1,83	13,47 ±2,23	14,76 ±2,39
PW (mm)[1]	12,16 ±1,81	12,73 ±2,59	11,57 ±1,79	13,43 ±2,50	12,73 ±2,46	13,35 ±2,01	12,63 ±1,95	13,40 ±2,29
EF <40%[1]	50,47 ±6,04	49,50 ±6,77	52,07 ±3,6	47,77 ±7,83	49,67 ±6,11	47,59 ±8,40	52,29 ±4,44	46,8 ±8,21
NYHA II (%)	15,78	5	10,71	6,45	13,33	11,53	6,66	15,38
NYHA III (%)	21,05	32,5	0	54,83	20	61,53	13,33	65,38
NYHA IV (%)	0	2,5	0	3,22	6,66	3,84	0	7,69
Laboratory results								
Hb (g/dl)[1]	12,71 ±1,2	9,23 ±1,71	10,84 ±2,05	9,9 ±2,38	12,57 ±1,45	9,42 ±1,64	11,44 ±2,5	10,07 ±1,84
HCT (%)[1]	38,12 ±4,55	27,85 ±5,28	32,6 ±6,22	29,82 ±7,5	39,42 ±5,15	28,67 ±5,41	34,45 ±7,69	31,53 ±7,19
Col (mg/dl)[1]	192,37 ±40,37	175,03 ±45,71	174,5 ±40,9	186,4 ±47,4	175,73 ±37,05	201,77 ±60,79	199,13 ±49,83	188,27 ±57,33
TG (mg/dl)[1]	145,21 ± 66	128,62 ±65,83	131,14 ±55,9	136,7 ±74,6	137,13 ±91,98	182,73 ±130,6	160,6 ±96,72	169,19 ±131,6
Scr (mg/dl)[1]	3,3±2,5	6,3±3,1	4,6±3,3	5,9±3,1	4,28±3,09	9,4±16,46	5,17±3,36	8,88±16,5
GFR[1]	37,61 ±17,41	26,59 ±12,20	30,42 ±17,27	35,46 ±12,49	34,24 ±12,51	14,49 ±6,15	35,27 ±14,83	18,82 ±9,73
Kt/V PD[1]	2,46 ±0,44	3,51 ±1,08	2,49 ±0,12	3,05 ±1,01	1,91 ±0,54	2,68 ±0,97	2,55 ±1,03	2,41 ±0,91
Kt/V HD[1]	1,50	1,31 ±0,26	1,34 ±1,56	1,32 ±0,28	3,57 ±3,49	4,03 ±3,27	5,73 ±4,06	6,52 ±2,15
Clinical outcomes								
IHD (%)	31,57	20	21,42	25,80	60	57,69	46,66	65,38
Stroke (%)	15,78	5	7,14	9,67	0	7,69	0	3,84
Periferic vascular disease (%)	10,52	0	3,57	3,22	20	26,92	20	26,92
Hospitalization (days)	2,33 ±5,37	4,1 ±6,46	2,77 ±5,46	4,22 ±6,72	2,17 ±5,08	6,6 ±1,01	2,31 ±5,99	6,74 ±10,9
Mortality (%)	5,26	2,56	3,70	3,22	6,66	7,69	0	11,53

[1]Continuous variable are mean±SD, Hb=hemoglobin level, HCT=hematocrit level, NYHA=New York Heart Association, EF=left ventricular ejection fraction, IHD=ischemic heart disease, GFR=glomerular filtration rate (ml/min/1,73m^2, col=cholesterol, TG=triglycerides, Scr=serum creatinine, IVS=interventricular septum, PW=posterior wall of left ventricle.

Each patient had an echocardiography performed for evaluate cardiac function. Left ventricular hypertrophy (LVH) was evaluated using electrocardiography, interventricular septum (IVS) thickness and left ventricular posterior wall (PW) thickness. We evaluated systolic cardiac dysfunction using ejection fraction of left ventricle (LVEF) and diastolic dysfunction with A wave, E wave, E/A ratio and E wave deceleration time. Informations on symptoms of heart failure according to the New York Heart Association (NYHA) class were obtained. Cardiac dysfunction was assessed using echocardiography.

Data were analysed with Statistical Package for the Social Sciences (SPSS) 17.0. Pearson correlation coefficient were used to analyse associations between independent variables. To test the significance of the medians between groups Student test was used

and a P-value <0.05 was considered to be statistically significant.

Results and Discussions: Baseline characteristics and outcomes of the studied population stratified by anemia, cardiac dysfunction and diabetes were shown in Table 1 and Table 2.

Patients distribution according to CKD stages was: 16% patients with stage 3, 18% with stage 4, 8% with stage 5 (non-dialysed patients), 56% patients were dialysed (5D): 20% patients were treated by peritoneal dialysis (PD) and 36% were hemodialysis patients (HD); only 2% of the patients had received a kidney transplant (Tx). Distribution of patients according to the *type of nephropathy* was the following: 36% patients with interstitial nephropathy, 31% patients with diabetic nephropathy, 18% had glomerular nephropathy, 12% had autosomal dominant polycystic kidney disease (ADPKD) and 3% had hypertensive nephropathy (Figure 2).

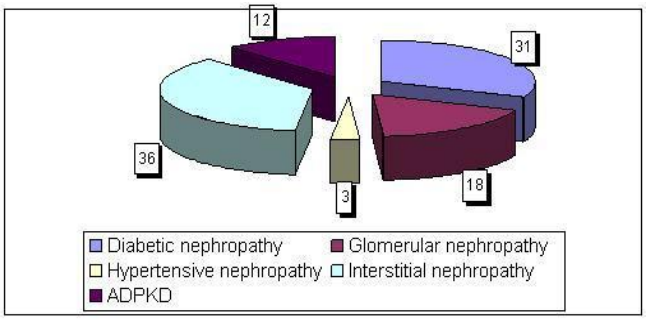

Figure 2. Type of nephropathy distribution

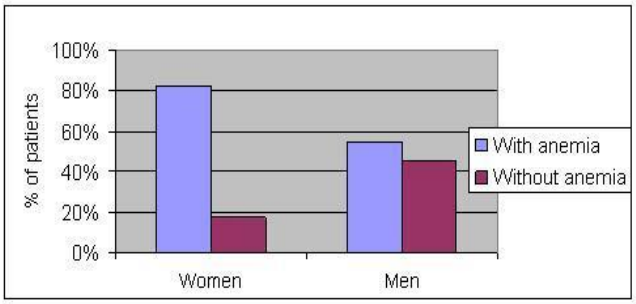

Figure 3. Anemia gender distribution

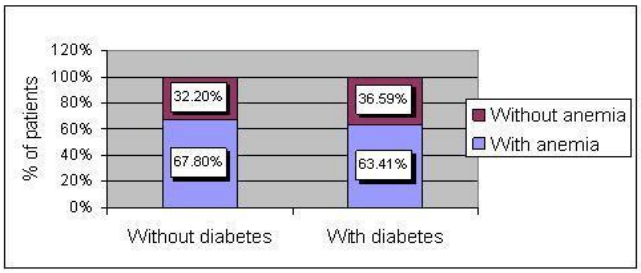

Figure 4. The prevalence of anemia in patients with DM versus subjects without DM

The mean Hb was higher in man than in women (10.78±4.09g/dl versus

10.08±5.98g/dl, p=0.12). The prevalence of anemia was greater in women than men (82.5% versus 55%, RR=1.5) (Figure 3).

Anemia had a high prevalence in patients with CKD independently of the presence of DM (63.41% and respectively 67.81%) (Figure 4).

Also, the mean Hb was 10.72 ± 2.37g/dl in diabetic patients and 10.36±2.26 g/dl in non-diabetic patients (p=0.44) (Figure 5).

S*moking* was not a risk factor for anemia in both non-diabetic and diabetic patients (RR=0.65 and respectively RR=0.69) but it was a risk factor for the development of cardiac dysfunction in non-diabetic and diabetic patients (RR=1.23, respectively RR=1.11).

Alcohol consumption was not associated with anemia or the development of cardiac dysfunction in non-diabetic and diabetic patients (RR=0.98 and RR=1.06, respectively RR=0.53 and RR=0.98).

The prevalence of anemia was greater in patients whose *source environment* was urban than in those with rural source environment (74.62% versus 48.48%, RR=1.53). This high prevalence of anemia in urban source environment was observed in DM and non-DM patients (78.94% and respectively 68.96%). *BMI* was higher in diabetic patients than non-diabetic patients 29.46 Kg/m^2 versus 24.98 Kg/m^2, p< 0.001) but was not correlated with anemia and cardiac dysfunction (Figure 6).

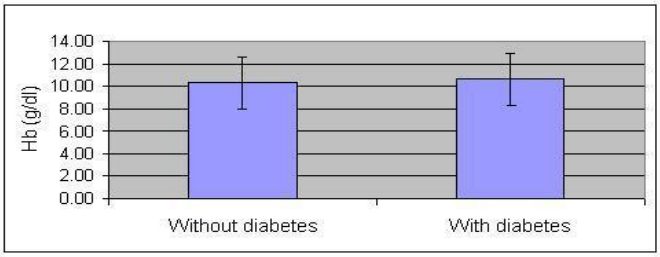

Figure 5. Mean Hb in diabetic versus non-diabetic patients

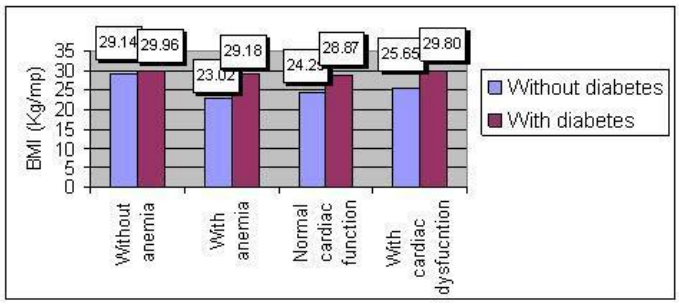

Figure 6. Body mass index, anemia and cardiac dysfunction distribution

In terms of Hb value according with the *stage of CKD*, the lower values of Hb were observed in patients with CKD stage 5 and 5D (9.73g/dl, respectively 9.27g/dl) and the higher value was in patients with stage 3 of CKD (12.65g/dl). In the early stage of CKD the mean Hb was higher in patients with DM than in those without DM (stage 3, 13.54±3.2g/dl versus 12.25±2.8g/dl, p=0.21) and in stage 5 of CKD, the mean Hb was higher in patients without DM than in those with DM (11.4±2.91g/dl versus 8.72±0.84g/dl, p=0.08). When the renal replacement therapy is initiated, mean Hb was greater in

hemodialysis diabetic patients than non-DM patients treated by hemodialysis (9.95±8.15g/dl versus 8.96±8.15g/dl, p=0.31) and the mean Hb was similar in patient treated by PD regardless of the presence of diabetes (10.36±7.75 g/dl in non-DM patients versus 10.47±2.11g/dl in DM patients, p=0.91).

Dialysis treatment adequacy: Mean Hb was lower in patients with Kt/V over 1.2 than in those with Kt/V under 1.2 (9.27g/dl versus 10.81g/dl, p=0.08). None of the patients with DM had Kt/V over 1.2.

The prevalence of *cardiac dysfunction* was higher in patients with DM than in those without DM (63.42% versus 52.55%, RR=1.20) (Figure 7); also it is higher in patients with anemia than in patients without anemia (63.64% versus 44.12%, RR=1.43) (Figure 8).

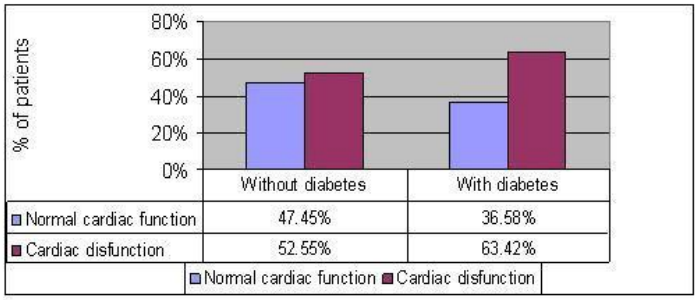

Figure 7. Prevalence of cardiac dysfunction in patients with diabetes, versus non diabetic patients

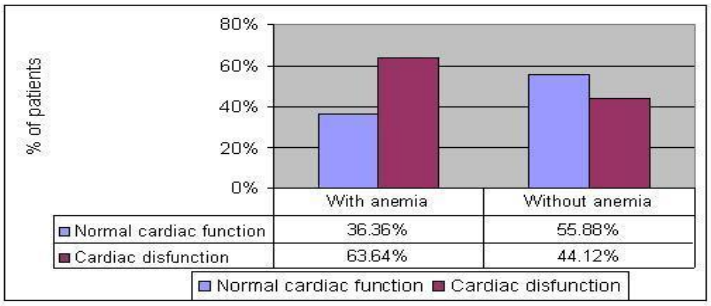

Figure 8. Prevalence of cardiac dysfunction in subjects with anemia, versus non anemic subjects

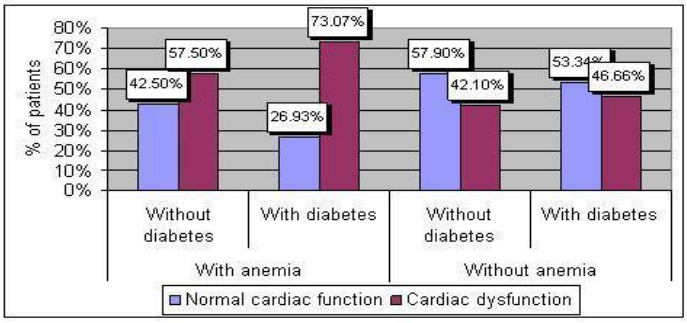

Figure 9. Prevalence of cardiac dysfunction in subject with anemia and diabetes.

The association of anemia with DM increases the risk of cardiac dysfunction in patients with CKD. The highest prevalence of cardiac dysfunction was observed in patients which had anemia and DM (73.07%) and the lowest prevalence of cardiac dysfunction was

noticed in patients which had neither anemia nor DM (42.10%) (Figure 9).

In terms of *type of cardiac dysfunction*, there were no significant differences between the prevalence of diastolic or systolic cardiac dysfunction in patients without DM versus patients with DM (33.89% versus 36.58%, respectively 30.50% versus 26.84%). Patients with systolic cardiac dysfunction had the lowest value of Hb independently of DM association (9.3g/dl) or its absence (9.72g%). In patients without DM, anemia was more severe in patients with systolic cardiac dysfunction than in those with normal cardiac function (9.72g/dl versus 10.84g/dl, p=0.12) and also than in patients with DM (9.3g/dl versus 11.44g/dl, p=0.01). Independently of the presence of DM the mean Hb was lower in patients with diastolic cardiac dysfunction than in those with normal cardiac function, but not statistically significant (10.08g/dl versus 10.84g/dl, p=0.24 in patients without DM and 11.02g/dl versus 11.44g/dl, p=0.63 in patients with DM). Anemia was an independent predictor for the development of systolic and diastolic cardiac dysfunction (RR=1.66 and respectively RR=1.10).

Between *left ventricular ejection fraction* (LVEF) and the value of Hb there was a linear correlation in all the studied patients, independently of the presence of DM. The lowest value of LVEF was found in DM patients with anemia (47.59%) and the highest value was found in non-DM patients without anemia (50.47%), p=0.18. Similar values of LVEF were observed in anemic non-diabetic patients and diabetic non-anemic patients (49.50% respectively 49.67%, p=0.20). The highest value of LVEF (55%) was noticed in patients with renal transplantation even in presence of anemia. The presence of anemia even in stage 3 of CKD was associated with a lower LVEF value (41.67% in anemic patients versus 49.15% in non-anemic patients).

In the early stage of CKD (GFR=30-60 ml/min1,73m^{2,}) the prevalence of LVH was lower than in advanced stages (31.25% in stage 3 versus 66.66% in stage 4, 75% in stage 5, 60% in stage 5 CAPD, 61.11% in stage 5HD and none of the two patients with renal transplantation had LVH). The prevalence of LVH was higher in patients with anemia versus in those without anemia (63.64% versus 44.12%) (Figure 10).

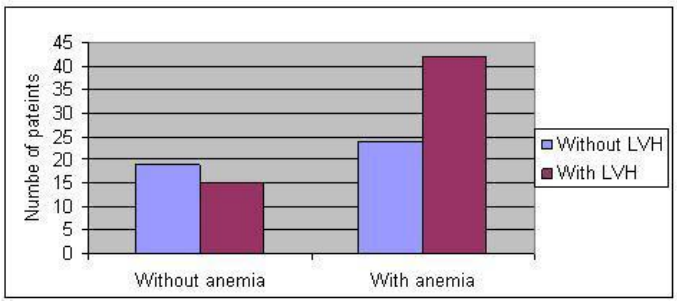

Figure 10. Pevalence of LVH in subjects with anemia, versus non anemic subjects

Mean Hb in patients with LVH was lower than in those without LVH (10.07g/dl versus 11.07g/dl, p=0.02). Anemia was an independent predictor for the development of LVH in patients without and with DM (RR=1.36, respectively RR=1.56). The mean value of Hb was lower in patients with LVH than in those without LVH in diabetic patients and non-diabetic patients (9.82g/dl versus 10.94g/dl, p=0.19, respectively 10.37g/dl

versus 11.31g/dl, p=0.05). Between Hb and SIV and respectively PPVS there was a linear correlation in non-diabetic and diabetic patients. Between SIV and PPVS in non-diabetic versus diabetic patients there were no statistically significant differences (p=0.66 for SIV and p=0.56 for PPVS).

Ischemic cardiac disease was more frequent in diabetic patients than in non-diabetic patients (65.38% in patients with DM and cardiac dysfunction versus 21.42% in patients without DM and cardiac dysfunction; 57.69% in patients with DM and anemia versus 31.57% in patients without DM and without anemia).

In terms of the *type of nephropathy* in patients with hypertensive nephropathy cardiac dysfunction had the highest prevalence (100%), followed by the diabetic renal disease where the prevalence of cardiac dysfunction was 70.97%. The lower prevalence of cardiac dysfunction was observed in patients with tubulo-interstitial nephropathy (36.12%).

NYHA class: In patients without signs of cardiac failure, DM had the lowest prevalence (29.41%) and in patients with cardiac failure class IV NYHA, DM had the highest prevalence (66.67%). DM was associated with an increased risk of cardiac failure (RR=1.6). We found an association between Hb values and symptoms of HF. The lowest values of Hb were found in diabetic patients with class IV NYHA (Hb=8.95g/dl) and the highest values (Hb=12.07g/dl) were observed in diabetic patients without signs of cardiac failure. The differences between Hb in diabetic versus non-diabetic patients for each NYHA class were not statistically significant. Only in patients without signs of cardiac failure mean Hb was statistically significant higher in diabetic versus non-diabetic patients (p=0.02) (Table 3).

Table 3. Mean Hb in subjects with DM versus non diabetic patients for NYHA classes

CF NYHA class	Without signs of CF	CF cls II	CF cls III	CF cls IV
Without diabetes	10.51	11.84	9.68	9
With diabetes	12.07	11.56	9.31	8.95
p	0.02	0.7	0.57	0.98

The highest prevalence of anemia was in non-diabetic patients with class IV NYHA (100%) and in diabetic patients with NYHA class III (84.21%). In stage 3 and 4 CKD, CF NYHA class II and III had a low prevalence (6.25% and 31.25%, respectively 22.22% and 27.27%) and none of the patients in these stages had CF NYHA class IV. In stage 5 of CKD, CF class III NYHA had a prevalence of 62.5%. In hemodialysed patients, CF class III NYHA had a prevalence of 41.66% and NYHA class IV 8.33%. None of the patients with renal transplantation had signs of CF.

Glycated Hb, anemia and cardiac function: The levels of glycated Hb were higher in patients with anemia and cardiac dysfunction than in those without anemia and normal cardiac function, but not statistically significant (7.62g/dl versus 7.01g/dl p=0.20 and respectively 7.80g/dl versus 6.55g/dl, p=0.12).

Patients with DM and anemia had a number of *hospitalization* days statistically significant higher compared to diabetic patients without anemia (22.8 days versus 8.53 days, p=0,04). The lowest number of hospitalization days (6.52 days) was in non-

diabetic non-anemic patients. Number of hospitalization days was low in stage 3 CKD, increased in stage 4 CKD for diabetic patients and in stage 5 CKD independently of the presence of DM. The patients treated with renal transplantation were not hospitalized in the following period.

Laboratory results: Phosforus serum levels were higher but not statistically significant in patients with normal cardiac function versus cardiac dysfunction, independently of the presence of DM (4.97mg/dl versus 4.74mg/dl in patients without diabetes, p=0.65, respectively 4.97mg/dl versus 4.62mg/dl, p=0.58). Between values of serum phosphorus and Hb there was a linear correlation in non-diabetic and diabetic patients (Pearson correlation coefficient 0.44, respectively 0.51). Feritin, PTH and CRP values were lower in patients without anemia and DM compared to those which had both anemia and diabetes. Also, albumin serum levels were higher in patients whithout anemia and DM than in those with both anemia and DM (Table 4).

Table 4. Inflamation, malnutrition and anemia

	Without anemia and diabetes	With anemia and diabetes	p
Ferritin	302.74±132.3	396.56±121.6	0.39
PTH	173.43±57.98	382.89±192.5	0.04
CRP	1.71±3.99	4.34±8.45	0.16
Albumin	3.86±0.73	3.49±0.28	0.1

Proteinuria and cardiac function in non-diabetic versus diabetic patients: in non-diabetic patients the highest value of proteinuria was observed in stage 5 CKD and it was higher in patients with cardiac dysfunction than in those with normal cardiac function (184.8mg/day versus 824.4mg/day, p=0.20). In diabetic patients, the highest value of proteinuria was observed in hemodialysed patients and it was also higher in patients with cardiac dysfunction than in those without (2538mg/day versus 911.5mg/day, p=0.14). Haemoglobin levels were lower in patients with macroalbuminuria compared to those with microalbuminuria (10.04±5.55g/dl versus11.62±2.88g/dl, p=0.001). Patients with persistent macroalbuminuria had a higher risk of anemia than those without albuminuria (RR=2.27).

Mortality rate in diabetic versus non-diabetic patients: The rate of mortality is higher in diabetic than in non diabetic patients. The highest mortality rate was found in diabetic patients with cardiac dysfunction (11.53%). In diabetic patients, the rate of mortality was higher in patients with anemia (7.69%) than in diabetic patients without anemia (6.66%).

The study's limitations included its relatively small number of subjects and that that the determination of the two specific cardiac biomarkers, serum N-terminal pro B-type natriuretic peptide and troponin T in our patients was not possible.

Conclusions

Anemia was an independent predictor for the development of cardiac dysfunction. Independently of the presence of DM, the mean Hb was lower in patients with systolic or diastolic cardiac dysfunction than in those with normal cardiac function. There were no

significant differences in the prevalence of diastolic or systolic cardiac dysfunction in non-diabetic versus diabetic patients. The prevalence of cardiac dysfunction was higher in patients which had both anemia and DM than in those without anemia and DM. Between LVEF and the value of Hb there was a linear correlation in all the studied patients, independently of the presence of DM. Diabetic and anemic patients had the highest rate of hospitalization, the most frequent and severe cardiac failure, the highest values of ferritin, parathormon and CRP, the lowest value of serum albumin. Proteinuria was higher in patients with cardiac dysfunction. Anemia was more severe in the patients with macroalbuminuria compared to those with microalbuminuria.

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