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Changes in Kidney Function (GFR), Albuminuria, Electrolytes, and Heart Affection in Diabetic Chronic Kidney Disease Patients

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Abstract

Background: Albuminuria is a prognostic marker for cardiovascular or renal risk. Cardiovascular risk as coronary artery disease, heart failure and even cardiac death was elevated in patients with chronic kidney disease (CKD). With progressive loss of kidney function, albuminuria and derangements in electrolytes contribute to poor patient outcomes. Adequate assessment of kidney function in different stages of renal failure and treatment will minimize complications and can be lifesaving.

Although electrolyte derangements and albuminuria are significant causes of morbidity and mortality in CKD and end-stage renal disease patients, they can be effectivelymanaged when diagnosed early with a preventive measures and pharmacological therapy.

Aim of Study: To detect what are the most common changes related to heart affection in diabetic chronic kidney disease patients.

In this study we will assess Kidney function (GFR), serum electrolytes, lipid profile and albuminuria and to detect which of these changesis more related to heart affection in Chronic Kidney Disease (CKD).

Material and Methods: This a cross-sectional study was conducted for 10 months from November 2020 to August 2021 in Nephrology and Cardiology Departments in Italian hospital. Patients were divided into in three groups each group contains 20 patients, normal control group, macroalbuminuric and normoalbuminuric groups, last two groups are diabetic and have CKD, The level of serum creatinine and electrolytes were measured using COBAS 6000 analyzer. Then, glomerular filtration rate (GFR) was calculated using MDRD equation. Also we detect fasting blood glucose, HA1C, sodium, potassium, phosphorus (ph), calcium (ca), lipid profile, albuminand Albumin/creatinine in urine (ACR) and ECG and Echocardiography.

Results: In this study there were significance difference in albumin/creatinine ratio (ACR) (p 0.000) and S albumin in both groups (p 0.001) and heart affection strongly correlated with ACR and more in macroalbuminuric group (r=–0.67). Also other factors significant parameters in heart affection, like duration of the CKD (p 0.004), ca (p 0.003) ph (p 0.007). Data analysis were done using SPSS version 20.

Conclusion: Cardiovascular disease (CVD) more significant in macroalbuminuric group so albuminuria is a potent risk factor than other risk factors in occurrence of cardiovascular complications.

Thera are many risk factors in diabetic, CKD patients which lead to CVD and complcationsIn this study we found the duration of the disease, reduced GFR, Ca and Ph changes lead to CVD and complications.

Key Words: *Chronic kidney disease (CKD) – Cardiovascular disease (CVD) – Albuminuria.*

Introduction

CHRONIC kidney disease CKD is defined structurallyas kidney damage for ›_3 months which is confirmed by kidney biopsy or any markers of kidney damage such as proteinuria, with or without a decrease in glomerular filtration rate (GFR), or defined functionally as GFR <60mL·min^{-1} per 1.73m^2 for ›_3 months, with or without kidney damage **[1,2]**.

Abbreviations:

CKD	: Chronic kidney disease.
CVD	: Cardiovascular disease.
BMI	: Body mass index.
GFR	: Glomerular filtration rate.
ACR	: Albumin/creatinine ratio.
TG	: Triglyceride.
LDL	: Low density lipoprotein.
HDL	: High density lipoprotein.
IHD	: Ischemic heart disease.
AF	: Atrial fibrillation.
SWAMA	: Segmental wall motion abnormalities.
LVH	: Left ventricular hypertrophy.
ESRD	: End stage renal disease.
MR	: Mitral regurge.
AS	: Aortic stenosis.
RWMA	: Regional wall motion abnormalities.
LAD	: Left atrial dilatation.

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There is a good relation between albuminuria and cardiorenal risk in the renal patients and even nonrenal **[3,4]**.

Also albuminuria is a prognostic marker for cardiovascular or renal risk, or both **[5]**.

Higher levels of albuminuria increase risk for mortality independent of eGFR according to Kidney Disease Improving Global Outcomes (KDIGO) guidlines **[6]**.

There are many factors that increases the incidence and prevalence of CKD like aging, type II diabetes, dyslipidemia, smoking and hypertension and low detection and management in early stages **[7]**.

The development of CVD in CKD is due to many factors as kidney injury leads to release of hormones, enzymes, cytokines and CKD-associated mediators which lead to changes in the vasculature **[8]** also hemodynamic changes lead to cardiac damage **[9]**.

An albumin/creatinine ratio test measures both albumin and creatinine in a one-time sample, also known as a spot urine sample. Creatinine is a chemical byproduct of normal muscle activity, and it is normally removed from the body in urine. Total daily creatinine production is relatively consistent, so an albumin/creatinine ratio test is a way to estimate your total daily urine albumin level without having to do a full 24-hour urine sample **[26,27]**.

Microalbuminuria is an early sign of diabetic kidney disease, which is defined as urinary albumin excretion between 30mg and 300mg/24 hours, strongly associated with CVD **[10]**.

If urinary albumin excretion more than 300mg/24h is called macroalbuminuria.

People with microalbuminuria, with or without diabetes, have a higher incidence of cardiovascular disease **[11]**.

Many studies reported association between albuminuria and increased intima-media thickness of the carotid artery in hypertensive subjects, concentric LVH and electrocardiographic evidence of myocardial ischemia **[12]**.

The pathophysiological processes that underlie the association between albuminuria and CVD still uncertain, may microalbuminuria causes atherothrombosis or microalbuminuria demonstrate end-organ damage and an inflammatory status where endothelial dysfunction and abnormalities in the coagulation cascade system which plays a direct role in the progression of the vascular disease **[13]**.

Trials that aims to reduce the progression of proteinuria through the blockade of the Renin-Angiotensin-Aldosterone System (RAAS) have been successful, However, once nephropathy has been established, the effect of RAAS blockade is not observed **[14]**.

Patients with CKD also have a high prevalence of cardiomyopathy, Hypertension and arteriosclerosis which lead to left ventricular hypertrophy (LVH). These structural abnormalities may lead to diastolic and systolic dysfunction which detectable by echocardiography, heart failure and ischemic heart disease **[17]**.

The most common electrolyte disorders associated with the renal failure are potassium, sodium, magnesium, phosphorus and calcium that lead to serious complications like a bone demineralization, muscle wasting, vascular calcification and even can result a death **[18]**.

Also, Guerin et al., reported that abnormal calcium and phosphorus metabolism is associated with vascular calcification and stiffness of blood vessels **[19]**.

CKD lead to electrolyte imbalance due to kidney damage, the pathophysiology by which Calcium affect cardiac structure and function are: (1) Direct effects to alter cell signaling, (2) Deposition of calcium and phosphate in the myocardium and small cardiac arterioles, (3) Cardiomyocyte hypertrophy, and (4) Increased aorta calcification resulting in chronic increased afterload leading to hypertrophy and arterial calcification **[46]**.

MDRD equations: Original MDRD equation, GFR is estimated as: GFR (ml per minute per $1.73m^2$)=186 x (Scr in mg/dL)-1.154 x (age in year) – 0.203 x (0.742, if female) x (1.210, if black). Where, Scr is non standardized serum creatinine **[15]**.

Reexpressed MDRD equation, GFR is estimated as: GFR (ml per minute per $1.73m^2$)=175 x (Scr in mg/dL) – 1.154 x (age in year) – 0.203 x (0.742, if female) x (1.210, if black). Where, Scr is standardized serum creatinine **[16]**.

MDRD is still the most commonly used method to calculate eGFR according to the 2018 CAP chemistry survey.

Stages of CKD as described by National Kidney Foundation are: Stage 1 Kidney damage with normal or increased GFR ›_90, stage 2 Kidney damage with mildly decreased GFR 60-89, stage 3 Moderately decreased GFR 30-59, stage 4 Severely decreased GFR 15-29 and stage 5Kidney failure ≤15 or dialysis **[20]**.

GFR less than 60mL·min^{1} per 1.73m^{2} is considered as the cutoff value for definition of CKD because it represents a reduction by more than half of the normal value of 125mL·min^{1} per 1.73m^{2} in young men and women, also associated with the onset of laboratory abnormalities of renal failure and increase the risk of CVD **[20]**.

Material and Methods

This A cross-sectional study was conducted for 10 months from November 2020 to August 2021 in Nephrology and Cardiology Departments in Italian Hospital.

The study participants were signed written informed consent before the start of data collection.

Study groups:

Patients aged from 40 years to 81 years, males and females.

Patients were divided intoin three groups each group contains 20 patients, normal group, macroalbuminuric and normoalbuminuric groups, last two groups are diabetic (type II DM) and have CKD.

Normoalbuminuric group (urinary albumin less than 30mg/24 hours) and other macroalbuminuric (urinary albumin excretion more than 300mg/24 hours).

Complete history was takenbased on Kidney Disease Improving Global Outcomes (KDIGO) guidelines which included sex, age, behavioral data if smoker or not and clinical history of hypertension and CVDs.

Normal group contains 20 healthy individuals not diabetic nor hypertensive or have CKD.

Inclusion criteria:

Both macroalbuminuric and normoalbuminuric groups have type II diabetes and CKD.

Exclusion criteria:

Patients who have ACR more than 30mg/24h were excluded from Normoalbuminuric group.

Measured parameters:

Anthropometric variables:

Weight by Kg, height by Meter and calculate body mass index (BMI):

BMI = Weight (kg)/height(m^{2}) **[21]**

Blood pressure ›_140/90mmHg was defined as high or hypertension.

Blood sample collection and biochemical analysis:

Fasting blood sugar test. A blood sample was taken after an overnight fast. A fasting blood sugar level less than 100mg/dL is normal. A fasting blood sugar level from 100 to 125mg/dL is considered prediabetes. If it's 126mg/dL or higher on two separate tests is diabetes. Used glucometer kits (Dario blood glucose monitoring kit).

Glycated hemoglobin (HA1C) test. This blood test, which doesn't require fasting, indicates the average blood sugar level for the past two to three months. It measures the percentage of blood sugar attached to hemoglobin, the oxygen-carrying protein in red blood cells. The higher the blood sugar levels, the more hemoglobin with sugar attached. An A1C level of 6.5% or higher on two separate tests indicates that you have diabetes. An HA1C between 5.7 and 6.4% indicates prediabetes. Below 5.7 is considered normal **[24]**. Used Human Hemoglobin A1c (HbA1c) Assay Kit crystal chem.

Serum albumin: The normal range is 3.4 to 5.4g/dL **[25]**.

An albumin/creatinine ratio test measures both albumin and creatinine in a one-time sample, also known as a spot urine sample. Microalbuminuria 30mg-300mg/24 hours andmacroalbuminuria more than 300mg/24h **[10,11]**.

Serum albumin measured by using TRUE chemie Albumin test kit.

Serumcreatinine was performed by an isotope dilution mass spectrometry (IDMS)-traceable enzymatic methods using Roche Modular Diagnostic, GmbH with intra- and inter-assay coefficients of variation of 0.9 and 2.9%, normal value 0.6 to 1.2mg/dL for adult males and 0.5 to 1.1mg/dL for adult females. Used creatinine assay kit **[28]**.

Then eGFR was calculated by Reexpressed MDRD equation, GFR is estimated as: GFR (ml per minute per 1.73m^{2})=175 x (Scr in mg/dL)-1.154 x (age in year) – 0.203 x (0.742, if female) x (1.210, if black). Where, Scr is standardized serum creatinine **[16]**.

The level of serum electrolytes:

(Electrolyte panel) were determined by the ion selective electrode principle of COBAS 6000 (c501) analyzer. The expected normal value of serum sodium 135-145mmol/L, potassium 3.5-5.0mmol/L, serum ca 8.5-10.6mg/dl and serum phosphorus 2.5-5.1mg/dl **[22]**.

Lipid profile: Patient must fast 9-12h before blood sample. Used lipid profile collection kit (Mail-In).

The optimal level for each part of the standard lipid test are:

- Total cholesterol: Below 200mg/dL.
- HDL (good) cholesterol: Above 60mg/dL.
- LDL (bad) cholesterol: Below 100mg/dL (For people with diabetes: Below 70mg/dL).
- Triglycerides (TG): Below 150mg/dL **[23]**.

ECG and Echocardiography were done for both groups.

Results

Table (1): Comparison of sociodemographic characters of the studied groups.

Characteristic	Control (n=20) No. (%)	Normo Albumin (n=20) No. (%)	Macro Albumin (n=20) No. (%)	*p*-value ¥
Gender:				
Male	12 (60.0)	11 (55.0)	14 (70.0)	0.327
Female	8 (40.0)	9 (45.0)	6 (30.0)	
Smoking:				
Nonsmoker	13 (65.0)	9 (45.0)	10 (50.0)	0.752
Smoker	7 (35.0)	11 (55.0)	10 (50.0)	
		Mean (SD)	Mean (SD)	*p*-value #
Duration (ys)		5.80 (2.97)	10.10 (5.58)	0.004*
Age (ys)	54.3 (3.4)	58.60 (9.31)	56.15 (10.19)	0.432
Height (m)	1.62 (0.17)	1.72 (0.07)	1.68 (0.11)	0.158
Weight (kg)	86.4 (7.56)	96.73 (16.68)	88.69 (10.05)	0.072
BMI (Kg/m^2)	27.9 (3.6)	32.64 (5.38)	29.34 (5.14)	0.055

* The test was statistically significant at 95% level of confidence.
¥ Chi square test.
Student *t*-test.

There was a significant difference between normoalbuminuric and macroalbuminuric groups in duration of the disease only as *p*-value 0.004.

But no significant difference between all groups regarding habits (smoking), age, height, weight and BMI.

Table (2): Comparison of the groups under the study regarding biochemical parameters.

Chara-cteristic	Control (n=20) Mean (SD)	Normo Albumin (n=20) Mean (SD)	Macro Albumin (n=20) Mean(SD)	*p*-value¥
FBS (mg/dL)	112 (11.4)	160.33 (73.01) **a**	162.45 (57.19) **a**	0.919
HA1C (%)	4.2 (1.3)	7.73 (1.59) **a**	8.86 (1.94) **a**	0.052
SBP	110 (25)	136.25 (22.76) **a**	133.50 (22.77) **a**	0.705
DBP	70 (22)	86.25 (13.56) **a**	81.25 (10.50) **a**	0.200
S.GFR	88 (7.4)	51.34 (3.91) **a**	27.12 (5.43) **a,b**	0.000*
ACR (mg/24h)	9.8 (3.3)	14.47 (6.98)	462.70 (219.89) **a,b**	0.000*
S. Creat	0.8 (0.48)	1.29 (0.17)	2.16 (1.04) **a**	0.273

- Results were expressed as mean ± SD and analyzed using one-way ANOVA followed by Bonferroni's post-hoc test at $p<0.05$ **a** and **b** Represents a statistically significant difference when compared to Control and normoalbuminuric respectively.

There was a significant difference in normoalbuminuric group in FBS, HA1c, BP and GFR when compared to normal group and no significant difference between both groups in ACR and S. Creatinine.

There was a significant difference in macrooalbuminuric group in FBS, HA1c, BP, GFR ACR and S. Creatinine when compared to normal group.

There was a significant difference in macrooalbuminuric group in GFR and ACR when compared to normoalbuminuric group.

Table (3): Comparison of the groups under the study regarding biochemical parameters.

Characteristic	Control (n=20) No. (%)	Normo Albumin (n=20) No. (%)	Macro Albumin (n=20) No. (%)	*p*-value¥
Normal	13 (65.0)	14 (70.0)	5 (25.0)	
Total Cholesterol mg/dL:				
Abnormal	7 (35.0)	6 (30.0)	15 (75.0) **a,b**	0.004*
TG (mg/dL):				
Low	6 (30.0)	4 (20.0)	11 (65.0)	0.204
High	14 (70.0)	16 (80.0)	2 (10.0)	
LDL (mg/dL):				
Low	3 (15.0)	4 (20.0)	18 (90.0)	0.376
High	17 (85.0)	16 (80.0)	2 (10.0)	
HDL (mg/dL):				
Low	5 (50.0)	4 (20.0)	2 (10.0)	0.661
High	5 (50)	16 (80.0)	18 (90.0)	

* The test was statistically significant at 95% level of confidence.
¥ Chi square test.
- $p<0.05$ **a** and **b** Represents a statistically significant difference when compared to Control and normoalbuminuric respectively.

There was a significant difference between macroalbuminuric group in total cholesterol only as *p*-value 0.004 when compared to Control and normoalbuminuric.

But no significant difference between all groups regarding TG, LDL and HDL.

Table (4): Comparison of the groups under the study regarding biochemical parameters.

Characteristic	Control (n=20) No. (%)	Normo Albumin (n=20) No. (%)	Macro Albumin (n=20) No. (%)	*p*-value¥
Na (mmol/L):				
Normal	20 (100.0)	16 (80.0)	13 (65.0)	0.480
Abnormal	0 (0.0)	4 (20.0)	7 (35.0)	
K (mmol/L):				
Normal	20 (100.0)	17 (85.0)	14 (70.0)	0.256
Abnormal	0 (0.0)	3 (15.0)	6 (30.0)	
Ca (mg/dl):				
Normal	17 (85.0)	19 (95.0)	12 (60.0)	0.020*
Abnormal	3 (15.0)	1 (5.0)	8 (40.0) **a,b**	
Ph (mg/dl):				
Normal	20 (100.0)	20 (100.0)	12 (60.0)	0.003*
Abnormal	0(0.0)	0(0.0)	8 (40.0) **a,b**	
S. Albumin (g/dl):				
Normal	20 (100.0)	17 (85.0)	4 (20.0)	0.000*
Abnormal	0 (0.0)	3 (15.0)	16 (80.0) **a,b**	

* The test was statistically significant at 95% level of confidence.
¥ Chi square test.
- $p<0.05$ **a** and **b** Represents a statistically significant difference when compared to Control and normoalbuminuric respectively.

Table (5): Comparison of the groups under the study regarding biochemical parameters.

Characteristic	Control (n=20) Mean (SD)	Normo Albumin (n=20) Mean (SD)	Macro Albumin (n=20) Mean (SD)	*p*-value¥
Ca	10.4 (0.6)	9.03 (0.33)	8.64 (0.59) **a,b**	0.015*
Ph	3.4 (1.1)	4.16 (0.57)	4.80 (0.86) **a,b**	0.008*
S. Albumin	3.66 (0.9)	4.08 (0.36)	3.07 (0.33) **a,b**	0.000*
EF (ejection fraction)	74 (7.3)	61.00 (6.49)	45.40 (9.53) **a,b**	0.000*

- Results were expressed as mean ± SD and analyzed using one-way ANOVA followed by Bonferroni's post-hoc test at $p<0.05$ **a** and **b** Represents a statistically significant difference when compared to Control and normoalbuminuric respectively.

In Tables (4,5) there was a significant difference between macroalbuminuric when compared to Control and normoalbuminuric respectively in ca, ph,s albumin and EF.

But no significant difference between all groups regarding Na and K.

Table (6): Comparison of the groups under the study regarding cardiac effects.

Characteristic	Control (n=20) No. (%)	Normo Albumin (n=20) No. (%)	Macro Albumin (n=20) No. (%)	*p*-value¥
ECG:				
Normal	19 (95)	15 (75.0)	3 (15.0) **a,b**	0.000*
IHD,ST segment elevation, inverted T wave		0 (0.0)	9 (45.0)	
AF,ST segment depression		2 (10.0)	5 (25.0)	
Bradycardia or AF	1 (5)	3 (15.0)	3 (15.0)	
Echo:				
Normal	20 (100)	17 (85.0)	2 (10.0) **a,b**	0.000*
SWAMA		0 (0.0)	7 (35.0)	
LVH		3 (15.0)	3 (15.0)	
Mild aortic regurge, MR		0 (0.0)	2 (10.0)	
Mild AS, RWMA		0 (0.0)	3 (15.0)	
LAD		0 (0.0)	3 (15.0)	
EF:				
Normal	20 (100.0)	20 (100.0)	6 (30.0)	0.000*
Abnormal	0 (0.0)	0 (0.0)	14 (70.0) **a,b**	

* The test was statistically significant at 95% level of confidence.
¥ Chi square test.
$p<0.05$ **a** and **b** Represents a statistically significant difference when compared to Control and normoalbuminuric respectively.

There was a significant difference between macroalbuminuric when compared to Control and normoalbuminuric respectively in ECG and Echo abnormalities.

And there was a significant difference between macroalbuminuric when compared to Control and normoalbuminuric respectively in EF.

Table (7): Comparison of heart affection with different parameters under the study.

Characteristic		Normal Heart (n=17) No. (%)	Abnormal Heart (n=23) No. (%)	*p*-value¥
FBS	Normal	8 (47.1)	5 (21.7)	0.091
	Abnormal	9 (52.9)	18 (78.3)	
HA1C	Normal	0 (0.0)	0 (0.0)	
	Pre-diabetic	17 (100.0)	23 (100.0)	
Pressure	Normal	12 (70.6)	11 (47.8)	0.150
	High	5 (29.4)	12 (52.2)	
S. create	Normal	7 (41.2)	1 (4.3)	0.004*
	Abnormal	10 (58.8)	22 (95.7)	
S.GFR	Moderate affection	17 (100)	8 (34.8)	0.000*
	Severe affection	0 (0.0)	15 (65.2)	
ACR	Normal	15 (88.2)	5 (21.7)	0.000*
	Macroalbuminea	2 (11.2)	18 (78.3)	
Total Cholesterol	Normal	9 (47.1)	10 (43.5)	0.554
	Abnormal	8 (52.9)	13 (56.5)	
TG	Normal	9 (47.1)	13 (56.5)	0.882
	Abnormal	8 (52.9)	10 (43.5)	
LDL(<70)	Low	1 (5.9)	5 (21.7)	0.165
	High	16 (94.1)	18 (78.3)	
HDL	High	4 (23.5)	2 (8.7)	0.194
	Low	13 (76.5)	21 (91.3)	
Na	Normal	15 (88.2)	14 (60.9)	0.055
	Abnormal	2 (11.2)	9 (39.1)	
K	Normal	17 (85.0)	14 (70.0)	0.256
	Abnormal	3 (15.0)	6 (30.0)	
Ca	Normal	17 (100.0)	14 (60.9)	0.003*
	Abnormal	0 (0.0)	9 (39.1)	
Ph	Normal	17 (100.0)	15 (65.2)	0.007*
	Abnormal	0 (0.0)	8 (34.8)	
S. Albumin	Normal	4 (23.5)	7 (30.4)	0.001*
	Abnormal	13 (76.5)	16 (69.6)	

* The test was statistically significant at 95% level of confidence.
¥ Chi square test.

S creatinine, GFR, s albumin, Ca and Ph are most common parameters that lead to heart affection in this study.

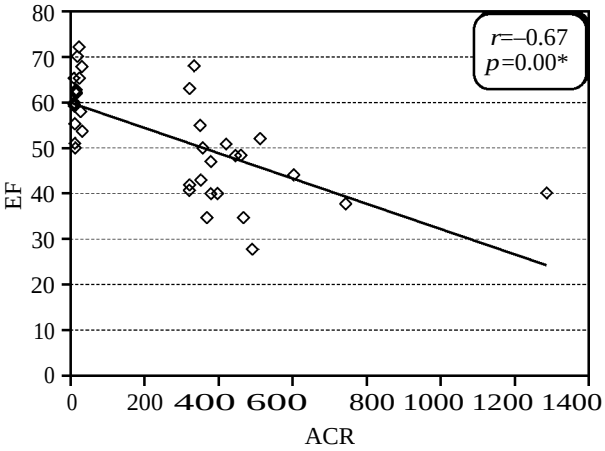

Fig. (1): Correlation between ACR and EF within study sample.

In Fig. (1) we found that there was strong negative correlation (r=–0.67) between ACR and EF as in macroalbuminuric group. (The strength of a correlation relationship is quantified by its correlation coefficient, the strongest possible being "perfectly" correlated. ... In general, –1.0 to –0.70 suggests a strong negative correlation, –0.50 a moderate negative relationship, and –0.30 a weak correlation).

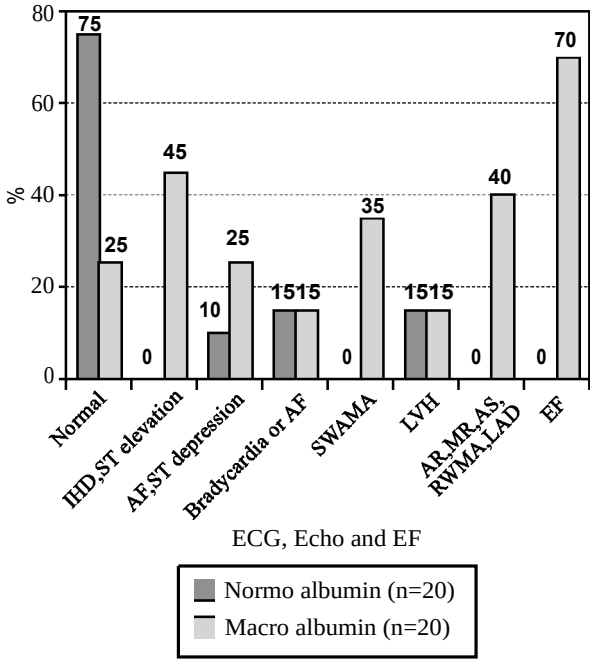

Fig. (2): Comparison of ECG, Echo and EF according to albumin. As albumin (S. albumin or ACR) increase ECG and Echo changes increases. 70% of macroalbuminuric group have abnormal EF which is normal in normoalbuminuric group.

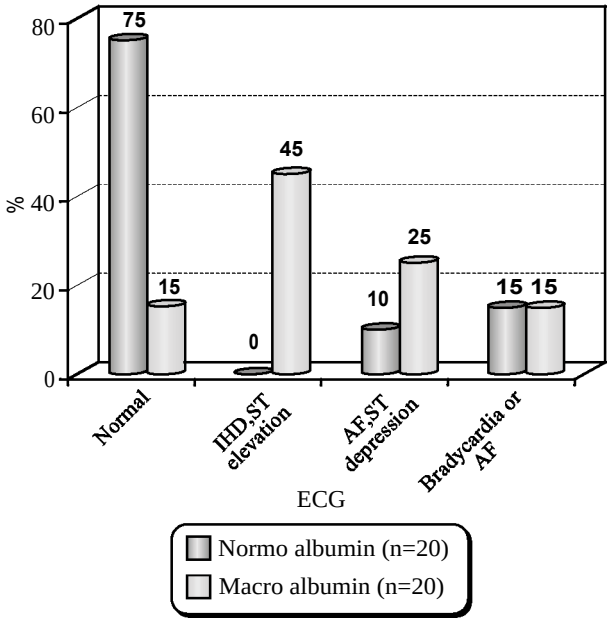

Fig. (3): Comparison of ECG according to albumin.

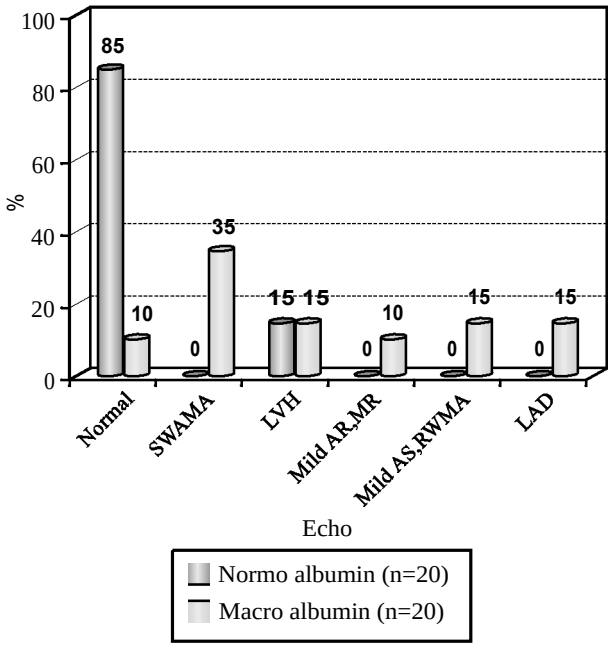

Fig. (4): Comparison of Echo according to albumin.

Discussion

CKD accelerate aging of the cardiovascular system and CKD causes a systemic, chronic proinflammatory state that contribute to vascular and myocardial remodeling processes resulting in atherosclerotic lesions, vascular calcification, myocardial fibrosis and calcification of cardiac valves.

In this study we compared two groups both diabetic and has CKD (GFR <60) with normal healthy patients.

One group normoalbuminuric (no kidney damage) and other group macroalbuminuric (kidney damage).

In our study both groups were diabetic because hyperglycemia is strongly associated with the development of both CKD and CVD **[29]** because Diabetes Meletus lead to microvascular and macrovascular changes.

Glycemic control in type 2 diabetes mainly contributes to a reduction in microvascular events such as nephropathy, although various studies failed to show a significant effect on macrovascular changes and cardiovascular complications.

Hill NR et al., found that the incidence and prevalence of CKD is associated with different socio-demographic, behavioral and co-morbid conditions **[30]**.

In this study Table (1) show Comparison of sociodemographic characters between two groups as gender, smoking, age, Hight, weight, BMI and duration of disease all these factors contributed in kidney disease but only the duration of diseaseMean (SD) was 5.8 (2.97) in normoalbuminuric group versus 10.1 (5.58) in macroalbuminuric group was statistically significant as p-value 0.004 in heart affection which occur in CKD, so most of CVD complications in CKD stage II and III and end stages. This due to with progressive kidney disease, kidney damage increase and proinflammatory state that contribute to vascular and myocardial remodeling processes increase.

These results agreed with data from the ARIC (Atherosclerosis Risk In Communities) and CHS (Cardiovascular Health Study) trials which found that the elevated cardiovascular risk in CKD cannot solely be explained by the presence of traditional risk factors **[31]**.

Hypertension is one of risk factors of Vascular disease in CKD. The SPRINT trial (Systolic Blood Pressure Intervention Trial) found that treatment of hypertension is beneficial in CKD.

As we found inthis study, hypertension was not significant between all groups Table (2) and also not significant parameterto cause heart affection Table (7) which agreed with Roehm B and Weiner DEwho found that the optimal target blood pressure in patients with CKD has not yet been established **[32]**.

Recent clinical evidence suggests that vascular effects of HDL can be heterogeneous in different conditions. And others suggest that progressive kidney dysfunction and in CKD, factors such as uremic toxins, increased oxidative stress, and the proinflammatory microenvironment, these factors contribute to changes the composition and quality of blood lipid **[33]**.

Our study Table (3) revealed that there was a significant difference between macroalbuminuric group in total cholesterol only as p-value 0.004 when compared to Control and normoalbuminuric.

But no significant difference between all groups regarding TG,LDL and HDL.

And revealed that lipid profile (dyslipidemia) not significant parameter in heart affection Table (7).

Reduction in GFR is still controverse between studies, in our study we found that abnormal serum creatinine level and reduction in GFR Table (2) were significant between all groups and significant parameters in heart affection as p-value were 0.004 and 0.000 respectively Table (7).

This agreed by studies that found reduced GFR is a strong risk factor for acute kidney failure and through this mechanism may lead to an increase in CVD events and all-cause mortality **[34]**, as decrease in GFR means that the kidney disease in progressive state so more uremic toxins and more inflammatory state and more vascular affection, decreased GFR itself may be a risk factor for progression of ventricular remodeling and cardiac dysfunction.

And by studies that found reduced GFR may be a marker of undiagnosed vascular disease or alternatively a marker for the severity of diagnosed vascular disease, especially in high- or highest-risk populations **[35]**.

But in high-risk populations, most but not all studies have suggested that decreased GFR is an independent risk factor for outcomes. This is true in the elderly, in whom even mild reductions of kidney function are associated with worse outcomes **[36]**.

Even though there are limited number of studies on the relationship between the electrolyte derangement and kidney function test, CKD is one of the major cause of the electrolyte derangements **[37]**. Electrolyte disorders in CKD indicate tubular damage and become common when CKD transforms into ESRF **[38]**.

In our study we found in Tables (4,5) there was a significant difference between macroalbuminuric

when compared to Control and normoalbuminuric respectively in calevel (hypocalcemia).

Our finding is also supported by another review **[39]** that showed hypercalcemia is less common than hypocalcemia in the general population.

Also we found abnormal Ph level (hyperphosphatemia) was significant in macroalbuminuric when compared to Control and normoalbuminuric respectively.

But no significant difference between all groups regarding Na and K.

Hypocalcemia and hyperphosphatemia are significant parameter in heart affection Table (7) which is supported by **[37]** that showed hypocalcemia and hyperphosphatemia were in stage II kidney disease.

In CKD there is decreaseintestinal calcium absorption due to decreased 1,25-vitamin D lead to hypocalcemia and hyperphosphatemia which stimulate PTH release that stimulate release of ca from bone and PTH is a major risk factor for heart failure and myocardial infarction **[53]**.

As CKD progresses, the urine calcium excretion drops dramatically; in theory this may be an appropriate compensation to maintain balance in the setting of decreased intestinal calcium absorption.

Thus, CKD may induce cardiac abnormalities through (1) Direct effects to alter cell signaling due to increased [Ca2+]i from altered function and expression of calcium transport exchangers and channels, (2) Extra-skeletal deposition of calcium and phosphate in the myocardium and small cardiac arterioles, (3) Inducing cardiomyocyte hypertrophy through calcium and hormone, and (4) Increased aorta calcification resulting in chronic increased after load leading to cardiac hypertrophy **[54]**.

Altered [Ca2+]i homeostasis has been found in atherosclerosis and arteriosclerosis.

Calcium regulates cardiomyocyte contraction, growth and remodeling. Abormalities in calcium dependent cardiac ion channel remodeling lead to hypertrophic cardiomyopathy and predisposes to arrhythmia **[55]**.

Studies revealed that management of electrolyte imbalances is potential targets for managing coronary artery calcification **[47]**.

There is a strong association between microalbuminuria and CVD in cross-sectional analysis. For example, microalbuminuria is associated with surrogates of CVD, such as increased intima-media thickness of the carotid artery in hypertensive subjects, **[40]** more frequent concentric LVH in hypertensive men, **[41]** abnormal left ventricular geometry and mass in subjects with hypertension and LVH, **[42,43]** and electrocardiographic evidence of myocardial ischemia **[44]**. Subjects with microalbuminuria also have a higher prevalence of clinical CVD than those without microalbuminuria.

These results supported by our study as there was a significant difference in macrooalbuminuric group in ACR when compared to normal group.

There was a significant difference in macrooalbuminuric group in ACR when compared to normoalbuminuric group (Tables 4,5) and significant parameter in heart affection Table (7).

And there were a significant difference between macroalbuminuric when compared to Control and normoalbuminuric respectively in s albumin (Tables 4,5) and significant parameter in heart affection Table (7).

Microalbuminuria may reflect generalized endothelial dysfunction and increased vascular permeability or abnormalities in the coagulation and fibrinolytic systems **[49,50]** and microalbuminuria may be associated with inflammatory markers, may denote the greater severity of end organ damage. Therefore, the subject with microalbuminuria likely has more advanced disease **[51]**.

When we compare both groups we found that ECG changes more significant in macroalbuminuric group including IHD, ST segment elevation, inverted T wave, AF, ST segment depression, Bradycardia or AF (Table 7 and Figs. 2,3).

Also, When we compare both groups we found that ECHO changes more significant in macroalbuminuric group including SWAMA, mild aortic regurge, MR, mild AS. RWMA and LAD (Table 7 and Figs. 2,4).

In Fig. (1) we found that there was strong negative correlation (r=–0.67) between ACR and EF as in macroalbuminuric group there was more heart affection so EF of the heart decrease significantly less than normoalbuminuric group (Table 7) (The strength of a correlation relationship is quantified by its correlation coefficient, the strongest possible being "perfectly" correlated. ... In general, –1.0 to –0.70 suggests a strong negative correlation, –0.50 a moderate negative relationship, and –0.30 a weak correlation).

Our results found that CVD and complications significantly more in macroalbuminuric group.

Which is supported by many studies which found that increased albuminuria or proteinuria is a potent risk factor for CVD in both diabetic and nondiabetic patients with CKD **[45]**.

Three main mechanisms are considered to contribute to LVH in CKD: (1) After load- and (2) Preload-related factors as well as (3) Nonafterload, nonpreload-related factors.

Include abnormal arterial stiffness, increased systemic arterial resistance, and systolic hypertension, leading to an initial concentric LVH, Continuous left ventricular overload subsequently leads to maladaptive changes and cardiomyocyte death, which in turn result in an eccentric hypertrophy and subsequent left ventricular dilatation, systolic dysfunction, and reduced ejection fraction (EF) **[49]**.

Atherosclerotic lesions in kidney failure are frequently calcified, as opposed to fibroatheromatous, and have increased media thickness compared with lesions in the general population **[49]**.

Conclusion:

– CVD more significant in macroalbuminuric group so albuminuria is a potent risk factor than other risk factors in occurrence of cardiovascular complications.
– Thera are many risk factors in diabetic, CKD patients which lead to CVD and complcations.

In this study we found the duration of the disease, reduced GFR, Ca and Ph changes lead to CVD and complications.

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التغيرات فى وظائف الكلى والالكتروليت والزلال وعلاقتها بمخاطر القلب فى مرضى السكر والكلى المزمن

وجود الزلال فى البول لدى مرضى الكلى المزمن يعتبر علامة تنبؤية لمخاطر القلب والأوعية الدموية.

فى المرضى الذين يعانون من مرض الكلى المزمن مع الفقدان التدريجى لوظائف الكلى، والاضطرابات فى الالكتروليتات كما يساهم وجود الزلال فى البول فى نتائج سيئة للمرض.

التقييم الكافى لوظايف الكلى فى مراحل مختلفة من الفشل الكلوى والعلاج سيقلل من المضاعفات ويمكن أن يكون منقذ للحياة.

الهدف: سنقوم بتقييم وظائف الكلى والالكتروليتات والزلال فى البول والدم وإكتشاف أى من هذه التغيرات أكثر ارتباطاً بمضاعفات ومرض القلب عند مرضى الكلى المزمن.

أجريت هذه الدراسة لمدة عشرة أشهر من نوفمبر ٢٠٢٠ حتى أغسطس ٢٠٢١ فى قسمى الكلى والقلب فى المستشفى الايطالى وتم تقسيم المرضى إلى مجموعتين كل منها ٢٠ مريض سكر وكلى مزمن احداهما لديه دلال عالى والآخر نسبة الزلال فى البول طبيعى.

وتم قياس الكرياتينين والالكتروليت وحساب وظايف الكلى وعمل رسم قلب وسونار على القلب لمرضى المجموعتين.

النتيجة: فى هذه الدراسة كان هناك فرق فى الالبيومين ومضاعفات القلب والأوعية الدموية مرتبطة جداً بوجود الزلال فى البول والدم. وجدنا أيضاً مدة الإصابة بمرض الكلى واضرابات الكالسيوم والفسفور تؤدى إلى مضاعفات القلب والأوعية الدموية.