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Pattern of Cardio-Renal Syndrome Amongst End Stage Renal Disease Patients on Maintenance Hemodialysis

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Abstract

Introduction: Cardio-renal syndrome includes a broad spectrum of diseases in which heart and kidney are both involved and is classified into five types. From the early stages of chronic kidney disease to end stage renal disease, cardiovascular involvement is present, but left ventricle hypertrophy is highly prevalent in end stage renal disease and is associated with unfavorable prognosis. This study aimed to determine factors associated with left ventricular hypertrophy in patients with end stage renal disease of type two, four and five cardio-renal syndromes.

Methods: This prospective study was conducted in two hemodialysis centers in Aden, Yemen from June 2016 to January 2017. Data collected included socio-demographic, clinical and biochemical variables. Data analysis included descriptive statistics and multivariable logistic regression modelling.

Results: One hundred and five end stage renal disease patients were included in the study with a mean age of 47.1±12.96 years. Men constituted 67.6%. Cardio-renal syndrome type 4 (kidney disease), type 2 (hypertensive nephron-sclerosis) and type 5 (diabetic nephropathy) were observed in 39%, 30% and 17.2% of patients respectively. Echocardiographic left ventricle hypertrophy was observed in 40% with the aforementioned types of cardio-renal syndrome. Older age, male sex, arterial hypertension, prior history of chronic Kat use, low albumin and calcium, high creatinine in blood and anemia were the predominant features of patients with left ventricular hypertrophy and type four, two and five cardio-renal syndromes. However; on multivariate analysis, left ventricular hypertrophy was found to be only significantly related to systolic hypertension.

Conclusion: Left ventricular hypertrophy was prevalent in cardio-renal syndrome type 2, 4 and 5 of patients with end stage renal disease on maintenance hemodialysis and although it was found to be prevalent among patients with older age, males, chronic Kat user, hypertensive, those with low albumin and calcium, high creatinine and anemia yet it was only significantly related to systolic hypertension.

Keywords: Cardio-Renal Syndrome, Left Ventricle Hypertrophy, Hemodialysis, Echocardiography, Hypertension.

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نمط متلازمة القلب والكلى عند مرضى الطور النهائي للاعتلال الكلوي الخاضعين للغسيل الدموي المستدام

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ملخص الدراسة

المقدمة: متلازمة القلب والكلى هو مصطلح يشمل طائفه واسعه من الأمراض التي يصاب بها القلب والكلى على حد سواء وهذه المتلازمة تصنف إلى خمسة أنواع. يسود تضخم البطين الأيسر بشكل كبير وسط مرضى الطور النهائي للاعتلال الكلوي حيث ينطوي بجلاء على تنبؤ غير مستحب. هدف الدراسة هو تحديد العوامل التي تتحكم بتضخم البطين الأيسر لمرضى الطور النهائي للاعتلال الكلوي من النوع الثاني والرابع والخامس حسب تصنيف متلازمة القلب والكلى.

المنهجية: أجريت هذه الدراسة المستقبلية على مرضى مصابون بالطور النهائي للاعتلال الكلوي في مركزين للغسيل الكلوي في عدن باليمن في الفترة من يونيو2016 حتى يناير 2017. تم جمع البيانات المتعلقه بالمتغيرات الاجتماعية-الديموغرافية والمتغيرات السريرية والمخبرية. تضمن تحليل البيانات الخصائص الوصفيه وكذلك نموذج الانحدار اللوجيستي متعدد المتغيرات.

النتائج: تضمنت الدراسة 105 من مرضى الطور النهائي للاعتلال الكلوي بمتوسط عمر بلغ47.1±12.96 شكل الذكور67.6 % منهم. لقد لوحظت متلازمة القلب والكلى من النوع الرابع (ما يسمى بأمراض الكلى الحقيقية) والنوع الثاني (أمراض الكلى الناتجة عن تصلبها بسبب ارتفاع ضغط الدم) والنوع الخامس (الناجمة عن مرض السكري) لوحظت في 39% و30% و 17.2% من المرضى على الثوالي. باستخدام الابكو القلبي فان تضخم البطين الايسر قد لوحظ على 40% من مرضى متلازمة القلب والكلى من الانواع السابقة الذكر. التقدم في العمر والجنس الذكري وارتفاع ضغط الدم الشرياني وتاريخ تعاطي القات المزمن وانخفاض نسبة الألبومين والكالسيوم وارتفاع نسبة الكرياتينين في الدم وفقر الدم كانت جميعها خصائص مترافقة لتضخم اليطين الايسر عند مرضى الطور النهائي للاعتلال الكلوي من النوع الرابع والثاني والخامس لمتلازمة القلب والكلى. لكنه عند إجراء التحليل الإحصائي متعدد المتغيرات تبين أن تضخم البطين الايسر كان ذات صله كبيره بارتفاع ضغط الدم الانقباضي دون غيره العوامل الأخرى.

الاستنتاج: أن تضخم البطين الايسر هو أكثر انتشارا في متلازمة القلب والكلى من النوع الثاني والرابع والخامس لمرضى الطور النهائي للاعتلال الكلوي الخاضعين للغسيل الكلوي الدموي وهو مرتبط بنسب متفاوتة بعوامل تقدم السن والجنس الذكري وارتفاع ضغط الدم الشرياني وتاريخ تعاطي القات المزمن ونسبة الألبومين والكالسيوم وارتفاع الكرياتينين بالدم وفقر الدم ولكنه ذات صله كبيره فقط بعامل ارتفاع الضغط الشرياني الانقباضي دون غيره من العوامل الاخرى.

الكلمات المفتاحية: متلازمة القلب والكلى، تضخم البطين الأيسر، الغسيل الكلوي، الايكو القلبي، ارتفاع الضغط الشرياني.

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Introduction

There are a number of important interaction between heart disease and kidney disease. This bidirectional relationship had been manifested as cardio-renal syndrome (CRS). This includes a broad spectrum of diseases in which heart and kidney are both involved and is classified into five types. Type one CRS reflects an abrupt worsening of cardiac function, leading to acute kidney injury. Type two CRS describes chronic abnormalities in cardiac function causing progressive and permanent chronic kidney disease. Type three CRS consists of an abrupt worsening of renal function causing acute cardiac disorder. Type four CRS describes a state of chronic kidney disease contribute to decrease in cardiac function, cardiac hypertrophy and or increase risk of adverse cardiovascular events. Type five CRS reflects a systemic condition, e.g diabetes mellitus (DM), sepsis causing both cardiac and renal dysfunction [1].

Left ventricular abnormalities including left ventricular hypertrophy (LVH) represent a key feature of systolic and diastolic left heart involvement in chronic kidney disease (CKD) patients as well as the main abnormality in uremic cardiomyopathy (type four CRS) [2]. Studies have showed that LVH is highly prevalent in end stage renal disease (ESRD) and is associated with unfavorable prognosis [3].

More than 2/3 of ESRD patients undergoing dialysis with LVH die of congestive heart failure or sudden death which is the reason why LVH is one of the main interventional therapeutic targets, together with coronary artery disease [4].

Pathophysiologic factors involved in LVH of CKD and ESRD patients have generally been divided into three categories first, those related to afterload, second, those related to preload and third**,** not related to after or preload [5]. Factors included in the first category are represented by an increase in systemic arterial resistance, elevated arterial blood pressure and reduced large-vessel compliance [6]. Among the preload-related factors, the role of intravascular volume expansion (salt and fluid loading) has to be underlined, as well as secondary anemia and the presence of arteriovenous fistulas [7]. These factors result in myocardial cell lengthening and eccentric or asymmetric left ventricular remodeling [8].

ESRD patients are also exposed to nontraditional risk factors (inflammation, malnutrition, oxidative stress) which increase in prevalence as kidney function declines. A higher level of homocysteine, lipoproteins, and lipoprotein remnants can be mentioned among these factors [9].

The evaluation of LVH is a heterogeneous process, and few standard imaging methods can estimate it accurately. However, Echocardiography is another simple, non-invasive, and accurate method to evaluate cardiac geometry and functions in dialysis patients, as well as in stratifying prognostic risk [10].

This study aimed to determine factors associated with left ventricular abnormalities, specifically LVH, in

type two, four and five CRS of patients with ESRD under maintenance hemodialysis.

Methods

Study design and setting

This is a prospective study targeted patient with ESRD on maintenance hemodialysis during June 2016 to January 2017 in two hemodialysis centers: Abood Hemodialysis Center and Taiba Hemodialysis Center in Aden- Yemen.

Participants enrollment:

Inclusion and exclusion criteria

The study included ESRD patients aged ≥ 18 years on maintenance hemodialysis during the study period. These patients received twice weekly 4 hours each of hemodialysis sessions with duration of hemodialysis of more than 3 months. Patients who did not met the criteria of inclusion or who refused to participate in the study, were excluded. Studied subjects were evaluated for a cause of ESRD and were divided into those with history of arterial hypertension (type two CRS), diabetes mellitus (type five CRS) or intrinsic renal disease (type four CRS). They were also evaluated for three echocardiographic abnormalities: LVH, left ventricular dilatation (LVD) and left ventricular systolic function.

Excluded subjects were 25 patients because of proven coronary artery disease (CAD), severe valve heart disease, pericardial effusion and regional wall motion abnormality on echocardiogram. (CAD) was defined as prior history of documented myocardial infarction, coronary artery bypass grafting surgery or coronary angioplasty and evidence of angina. Clinical and biochemical assessment of the patients included blood pressure (BP) recordings or antihypertensive therapy, erythropoietin therapy, hemoglobin, serum electrolytes, serum albumin, calcium, urea and creatinine level in blood.

Variables

Variables included demographic (age, sex, socioeconomic status, prior history of Kat chewing), clinical and para-clinical characteristics of patients as well as duration of hemodialysis. Measurement of weight and height and calculation of body mass index (BMI) were assessed. BP measurements were carried out by a trained nurse prior to hemodialysis. An average value of a three consecutive reading during three hemodialysis session were taken. Systolic and diastolic hypertension was defined as values of >140 or>90 mmHg respectively or arterial hypertension if both values are elevated [11]. Updated pre-dialysis para-clinical results of investigations including blood examination for hemoglobin, urea, creatinine, calcium, albumin, hepatitis B surface antigen (HBs Ag) and anti-hepatitis C virus (HCV) were collected from patients' clinical records.

Echocardiographic assessment

All patients were scheduled for two dimensional trans-thoracic and color Doppler echo-study. This investigation was performed within 24 hours of the patient's last hemodialysis session. The echo-examination was carried out at private cardiac center using General Electric VIVID S5 echocardiographic system. M-mode echo evaluation followed the recommendations of the American

Society of Echocardiography recommendation on M- mode evaluation [12], included: 1) measurement of LV internal dimension in end systole (LVIDs) and end diastole (LVIDd); 2) inter-ventricular septum (IVSd) and posterior wall thickness in diastole (LVPWd) and 3) measurement of left ventricular ejection fraction (EF) and fraction shortening (FS).

LVH was defined as left ventricular mass index of >131 gram/m^2 in male and >100 gram/m^2 in female [13] and was calculated using the formula: $0.00083 \times [(LVEDD + IVSd + PWd)^3 - (LVEDD)^3 + 0.6]$ and indexed to body surface area [13] were LVEDD (left ventricular end dimension in diastole), IVSd (interventricular septum dimension in diastole) and PWDd, posterior wall dimension in diastole and measurements in millimeters. Further evaluation of LVH into concentric or eccentric was done by assessing left ventricle (LV). Relative wall thickness (RWT) is calculated from the formula: 2 × posterior wall thickness in diastole/LV internal dimension in diastole. Normal [14] RWT is <0.45. Concentric or eccentric hypertrophy of LV is defined if RWT was >0.45 or <0.45 respectively in the presence of LVH [14].

Left ventricular volume (LVV) was calculated as 0.001047 (LV end diastolic diameter mm)^3 and indexed to body surface area (BSA). LVD was considered as left ventricular volume index of more than 90 ml/m^2 with or without LVH and with normal systolic function. Left ventricular systolic dysfunction was defined as FS <25 or EF<50% [12]. Color Doppler echo-study was undertaken for assessment of valvar blood flow. CAD was defined as angina and documented myocardial infarction by electrocardiography and/or previous history of coronary angioplasty or coronary artery bypass grafting surgery.

Patients groups

Clinically, patients were divided into three groups according to cause of ESRD, patients with chronic renal diseases (type four CRS), patients with hypertensive nephron-sclerosis (type two CRS), and patients with diabetic nephropathy (type five CRS). Using echocardiographic study, patients were assessed for three cardiac abnormalities: LVH, LVD and systolic function. For methodological purpose, two groups of patients were particularly recognized Group I patients with left ventricular hypertrophy and Group II patients with normal echocardiographic findings.

Statistical analysis

Descriptive statistics was undertaken to report patients' characteristics. Parametric analysis was conducted for normally distributed continuous variables, if Kolmogorov-Smirnova assumptions met, and presented as mean ±standard deviation (±SD). None parametric analysis was presented for none normally distributed variables and presented as median with range. Categorical variables were presented as numbers with percentages. Factors associated with LVH (concentric, eccentric), LVD and LV systolic dysfunction were explored in bivariate analysis using both parametric and none parametric (Unpaired T tests, the Mann Whitney Tests and Chi squared). Factors associated with outcome of interest, LVH (concentric, eccentric), LVD and LV systolic

dysfunction in bivariate analysis at $p \leq 0.05$ were considered to enter into Logistic regression modeling to detect the potential predictors for the outcomes of interest. Post hoc statistical sample power calculation [R^2=.154 and 0.094 (for LVH concentric and LVD, respectively), predictors =3, $p \leq 0.05$] was conducted and found the sample power was sufficient to run the logistic regression modeling (observed statistical power =0.96 and 0.79 for both LVH and LVD respectively). For all analyses, a two-sided $p<0.05$ was considered statistically significant. The IBM SPSS for windows version 21.00 was used for all the analyses.

An ethical approval was obtained from the Research and Ethics Committee in the Faculty of Medicine and Health Sciences, University of Aden. Patients were informed about the aims of the study and oral consent was obtained from all patients participating in this study.

Results

The study included 105 ESRD patients their socio-demographic, clinical, and biochemical Characteristics are shown in Table 1. The mean age of patients was 47.1±12.96 years; 67.6% of them were men. The highest percentage of patients has primary to secondary school (58.1%); unemployed (65.7%); married (78.1%), with prior history of chronic Kat use (51.4%), and tested positively for HCV (67.6%). Other characteristics are clearly presented in the table.

Table 1: Socio-Demographic, Clinical and Biochemical Characteristics of the Participants (n=105)

Variables	No.	%	Mean ±SD
Age (years)			47.1 ±12.96
Gender			
Male	71	67.6	
Female	34	32.4	
Education			
Illiterate	19	18.1	
Primary to secondary school	61	58.1	
University	25	23.8	
Unemployed	69	65.7	
Married	82	78.1	
Prior history of Khat chewing	54	51.4	
Having positive HCV	71	67.6	
Duration (months) of haemodialysis			
BP records (mmHg) Mean ±SD			
Systolic BP			150.6±14.72
Diastolic BP			91.8±18.24
Mean BP			105.8±9.16
Biochemical and serological findings Mean ±SD			
Serum hemoglobin			8.0±1.46
Serum Creatinine			9.3±2.58
Serum Albumin			3.6 ±1.41
Serum Calcium			8.6±1.06

Table 2 shows echocardiographic findings of patients by the type of CRS. Basic renal disease (CRS type 4) found in 33.3% of patients. This included, polycystic kidney diseases (10%), obstructive uropathy (8.6%), chronic pyelonephritis (7.6%), chronic glomerulonephritis (5.7%), and nephrotic syndrome in one patient (0.95%). Hypertensive nephron-sclerosis (CRS type 2) encountered in 30.5% and diabetic nephropathy (CRS type 5) in 18 patients (17.2%). Number of patients requiring antihypertensive therapy was 75 (71.4%) and 50 patients (47.6%) were receiving erythropoietin therapy. As shown in Table 2, echocardiographic abnormalities were detected in 82 patients (78.1%), while 23 (21.9%) had normal echocardiography. LVH was observed in 40%, LVH in 26.7% and systolic dysfunction in 11.4%.

Table 2: Patients with ESRD According to Type of CRS and Echocardiographic Findings (n=105)

Variable	**No.**	**%**
Type of CRS		
Hypertensive nephrosclerosis (type 2 CRS)	32	30.5
Diabetes mellitus (type 5)	5	4.8
Diabetes and hypertension (type 2 and 5 CRS)	13	12.4
Kidney diseases (type 4 CRS):	35	33.3
Polycystic kidney	11	10.0
Obstructive uropathy	9	8.6
Pyelonephritis	8	7.6
Glomerulonephitis	6	5.7
Nephrotic syndrome	1	1.0
Other causes	14	13.3
Unknown cause	6	5.7
Echocardiographic findings		**Mean ±SD**
Left ventricular volume index (LVVI)		92.7±39.36
Left ventricular mass index (LVMI)		152.2±46.43
Fraction shortening (FS)		32.3±6.48
Different echo-cardiographic findings	**No.**	**%**
Normal Echocardiographic findings	23	21.9
Left ventricle hypertrophy	42	40.0
Left ventricular dilatation	28	26.7
Left ventricle systolic dysfunction	12	11.4

CRS, cardio-renal syndrome, ESRD, end stage renal disease

Table 3 shows a comparision between ESRD patients with LVH and those with normal echo according to CRS classification. Mean age of patients with LVH was 43.6±10.33 years vs. 32.1 ±12.58 for patients with normal LV geometry. Previous chronic Kat use was found in 66.7% of patients with LVH and in only 21.7% of patients with normal echo-cardiographic. Of the forty-two ESRD patients with LVH, 25 (59.5%) had hypertensive nephrosclerosis and diabetes mellitus (CRS type 2 and 5) while 17(40.5%) had chronic renal diseases (CRS type 4). Most of ESRD patients with normal echocardiographic findings had

chronic renal diseases (19 out of 23 patients or 82.61%).
LVH was seen in 14 (43.7%) out of 32 hypertensive ESRD patients (CRS type 2) and only 2 (6.3%) had normal echocardiographic findings. Of the 18 diabetic patients, 11 (61.1%) had LVH and normal echocardiography was the finding in 7 of them (38.9%). Compared to patients with normal echocardiography, patients with LVH had higher percentages of older age, male sex, prior history of chronic Kat use, hypertension and diabetes (type 2 and 5 CRS).

Table 3: CRS Type 2, 4 and 5 in ESRD Patients with LVH Compared with ESRD Patients with Normal Echo-Findings

Variable	**LVH (n=42)**		**Normal Echo (n=23)**		***p***
	No.	**%**	**No.**	**%**	
Age (year)	43.6±10.33		32.1 ±12.58		0.001
Gender					
Male	34	81.0	13	56.5	0.020
Female	8	19.1	10	43.5	0.010
Prior history of Kat chewing	28	66.7	5	21.7	0.020
Patients by underlying type of CRS /n, %					
Hypertensive nephrosclerosis*	14	33.3	2	8.7	0.001
Diabetes mellitus**	2	4.8	-	0.0	0.010
Diabetes and hypertension	9	21.4	2	8.7	0.004
Kidney diseases* **					
Polycystic kidney disease	4	9.5	4	17.4	0.900
Chronic pyelonephritis	6	14.3	1	4.3	0.010
Chronic glomerulonephitis	2	4.8	3	13.0	0.080
Nephrotic syndrome	-		1	4.3	0.060
Obstructive uropathy	2	4.8	4	17.4	0.040
Others, post partam hemorrhage	1	2.4	1	4.3	0.380
Unknown kidney disease	2	4.8	5	21.7	0.280

CRS, cardio-renal syndrome, CRS type 2, type 4***: type 5***

In addition, LVH patients had higher BP records (systolic and diastolic), lower-hemoglobin and serum albumin and high serum creatinine levels Table 4.

On multivariate analysis, LVH was found to be only significantly related to systolic hypertension, while LV dilatation was only significantly associated with anemia (Table 5).

Table 4: Clinical, Biochemical and Echocardiographic Findings of ESRD Patients with LVH, Compared with Those of Normal Echocardiography

Variable	LVH (n=42)	Normal Echo (n=23)	*p*
Blood pressure/BP (mmHg)			
Systolic BP	153.8±17.14	121.6±14.72	<0.001
Diastolic BP	96.8±15.41	80.0 ±18.24	0.010
Biochemical findings(mg/dl)			
Hemoglobin	8.9±1.16	9.9±2.35	0.030
Serum Creatinine	10.0±2.53	8.1±2.56	0.030
Serum Albumin	3.3±0.61	3.5±0.48	0.040
Serum Calcium	8.3±0.80	8.7±2.65	0.040
Echocardiographic findings/Mean ±SD			
Fractional Shortening (%)	35.1±12.22	38.2+8.11	0.090
LV Mass Index (gm/m2)	175.8±42.02	105.3+16.83	0.001
LV Volume (ml/m2)	89.6±39.59	63.2+19.33	0.089
Interventricular septum in diastole	16.4±2.28	10.4±8.12	0.010
Posterior wall thickness in diastole	14.4±2.56	9.0±4.72	0.010

Table 5: Significant Predictors of Concentric LVH and LVD in ESRD Patients with Type Two, Four and Five CRS

Variables	AOR (95% CI)*	*p*
Concentric LVH		
Age	0.99 (0.96-1.03)	0.868
Gender		
Female	1	
Male	1.17 (0.47-2.90)	0.737
Systolic hypertension		
No (systolic BP<140mmhg)	1	
Yes (systolic BP ≥140mmhg)	4.60 (1.89-11.21)	**0.001**
Left ventricle dilation		
Age	1.00 (0.97-1.03)	0.979
Gender		
Female	1	
Male	2.21 (0.87-5.62)	0.095
Anemia		
No (HB ≥ 9)	1	
Yes (HB < 9)	2.43 (1.07-5.54)	**0.034**

***AOR (95% CI) = adjusted odd ratio and 95% confidence interval. LVH, left ventricular hypertrophy. LVD, left ventricular dilatation. CRS, cardio-renal syndrome.*

Discussion

Cardio-renal syndrome involves a spectrum of disorders affecting both heart and kidneys in which acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other organ. According to the present study, a significant number of patients (78.1%) were with different echocardiographic abnormalities. Concentric LVH was the prevalent abnormality and observed in 40% of ESRD patients. In other studies, LVH is reported in 50–70% of advanced

CKD patients, and in up to 70–90% of regular dialysis patients [3,15].

In the present study, LVH was found with a relatively lower frequency, compared to other studies [16-18] which may be due to prior exclusion of CAD patients, and lower age of patients included. Our study shows that almost 40 % of ESRD patients on maintenance hemodialysis manifested with LVH after exclusion of CAD, which is an important risk factor for development of LV dysfunction. According to Shivendra *et al*, LVH was found in 48% of ESRD patients on maintenance dialysis [16]. In sub-group of patients with hemoglobin <10 gm%, LVH was present in 71.4% versus 14.2% in patient group with hemoglobin ≥ 10 gm% (p=0.002) [16]. They also observed that hypertensive patients had higher prevalence of LVH (51.9%). Laddha *et al* found LVH in 74%, with a statistically significant difference in LVH in hypertensive group, when compared to normotensive one [17]. In a related context, Zoccali *et al* had reported incidence of LVH and systolic dysfunction of 77% and 22% respectively in ESRD population on hemodialysis [18].

In this study, hypertensive ESRD patients (CRS type two) expectedly had higher frequency of LVH; however diabetic ESRD (type 5 CRS), unexpectedly had lower frequency of LV disorders, including LVH and LV systolic dysfunction but LVH was significantly observed in diabetic patients who also have hypertension. Prior exclusion of CAD might be the reason for lower frequency of LV disorders in diabetic ESRD patients [17]. LVH [concentric (40%), eccentric (45.7%)] and LV dilatation (26.67%) may be associated with pressure and volume/flow overload in a form of hypertension, anemia, arteriovenous fistula and sodium and water retention [19]. It was reported that higher systolic and diastolic blood pressure and inter-dialysis weight gain is strongly related to higher LVMI. Volume control, a predictor of increasing systolic blood pressure, lead to regression of LVH [20].

Hypertension as risk factor for LV abnormalities was identified among our studied ESRD patients as a cause (type two CRS) and as a consequence of chronic kidney disease. However; in the present study, concentric LVH was significantly only associated with systolic hypertension. This is consistent with a study that found progressive LVH in hemodialysis patients associated with hypertension but not to other risk factors including anemia [21].

Anemia, a common accompanying feature of ESRD was significantly associated with LV abnormalities as observed in different studies [22,23]. According to this study, anemia was significantly correlated with LVD, but not with LVH. In previous studies, hypoalbuminemia, low calcium and high blood urea have been associated with LV abnormalities, including LVH [24,25]. The present study demonstrated an insignificant relation of these biochemical findings which was only significantly correlated with LVD and LV systolic dysfunction.

In addition to the classic predictors, the nontraditional factors, like malnutrition, inflammation, infections and oxidative stress may also contribute to adverse outcomes

of ESRD patients [26]. In a related context, our study showed that HCV and chronic Kat chewing were more prevalent in ESRD patients with LVH, compared to ESRD patients with normal echocardiographic findings. Indeed, we found that 65% of patients with LVH in this study were anti-hepatitis C virus sero-positive. HCV is known to produce different cardiovascular diseases including dilated and hypertrophic cardiomyopathy and systolic and diastolic dysfunction [27].

In the present study, a significant number of patients specifically hypertensive and diabetic (type two and five CRS) had a prior history of systemic Kat use. Cathinone, the most active Kat alkaloid, has been shown to induce hypertension, acute coronary syndrome cardiac arrhythmias and LVH [28]. Although renal toxicological studies particularly in human are scanty, nephrotoxic effects are reported following Kat administration to laboratory animals [29]. A recent experimental investigation showed that Kat use at high dose is demonstrated to induce mild to moderate direct renal damage. Moreover, it creates synergy when combined with nephrotoxic drugs such as gentamicin [30]. Hence, Kat use may be associated with type two or four CRS.

Conclusion

The present study shows high prevalence of LVH among CRS type two, four and five patients with ESRD on maintenance hemodialysis. LVH was more prevalent among Kat chewers ESRD patients and specifically those with anti HCV positive infections. Although, older age, male sex, chronic Kat use, hypertension, low albumin and calcium, high creatinine and anemia were found to be prevalent in ESRD patients of the aforementioned types of CRS with LVH and other left ventricular disorders, yet LVH was only significantly related to systolic hypertension.

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