Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Original Article

Type 2 Cardiorenal Syndrome: Prevalence and Correlates in Nigerian Heart Failure Patients.

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Abstract

Background: Type 2 cardiorenal syndrome (Type 2 CRS) describes a relationship in which chronic congestive heart failure causes a progressive and permanent chronic kidney disease. Heart failure (HF) and chronic kidney disease (CKD) share similar cardiovascular risk factors and have a bi-directional relationship. A comprehensive approach including early screening of HF patients for CKD as well as management involving the nephrologist and cardiologist will most definitely reduce morbidity and mortality. The aim of this study was to determine the prevalence of and correlates for Type 2 CRS among HF patients in JUTH, Jos-Nigeria.

Methodology: A hospital-based cross-sectional descriptive study carried out in JUTH involving 120 patients with chronic HF recruited consecutively. History, physical examination and laboratory investigations including urinalysis using albustix were performed on all subjects. CKD was determined using estimated glomerular function rate (eGFR) and persistent albuminuria. The data were analyzed using Epi Info (CDC, Atlanta GA) and p-values <0.05 were considered statistically significant.

Results: The mean age of the participants was 52.00 ± 11.44 years, majority of whom were females consisting of 58.3%. The prevalence of CRS was 37.5%**.** Majoity (66.7%) of the patients had mild CRS, while 26.7% had moderate CRS, and only 6.7% had the severe CRS. The predictors of CRS were diabetes (OR=6.230; CI=2.094-19.093), New York heart Association (NYHA) grading I (OR=0.017; CI=0.002-0.142) and II (OR=0.089; CI=0.016-0.483), raised jugular venous pressure (JVP) (OR=7.099; CI=2.671-18.865), loud pulmonary component of the second heart sound (P2) (OR=3.769; CI=1.726-8.232), systolic dysfunction (EF<45%) (OR=3.316; CI=1.487-7.395), anaemia (OR=5.091; CI=1.657-15.640), albuminuria (OR:0.014, CI=0.004-0.052), rural/suburban dwelling (OR=2.875; CI=1.335-6.192) and increased cardiothoracic ratio (CTR) (OR=3.237; CI=1.019-10.278).

Conclusion: The frequency of Type 2 CRS among CHF patients in JUTH was high. The predictors of chronic CRS include diabetes mellitus, NYHA grade, raised JVP, loud P2, systolic dysfunction, anaemia, albuminuria, rural/suburban dwelling and increased CTR. These findings highlight the urgent need to incorporate screening for CKD among stable heart failure patients at regular intervals, and early referral to the nephrologist to prevent further deterioration to ESRD.

Keywords: Cardiorenal Syndrome; Heart Failure; Kidney Dysfunction; Type 2 CRS.

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How to cite: Uchendu DG, Okeahialam BN, Imoh LC, Esala AE, Zunman GM. Type 2 Cardiorenal Syndrome: Prevalence and Correlates in Nigerian Heart Failure Patients. Niger Med J 2025:66(2):607-620.https://doi.org/10.71480/nmj.v66i2.731.

Quick Response Code:

Introduction

CKD has become a major public health issue characterized by a steady rise in the incidence and prevalence in cases and a high financial burden on healthcare systems, emphasizing the need for effective interventions. [1] It affects between 8-16% of the population worldwide.[2] Greater than 26 million adults in the US (approximately 13% of the US population) are affected. According to a study in Congo, the prevalence of CKD among the study subjects was as high as 36%. [3, 4]

Heart failure (HF) is a complex pathophysiological syndrome that arises from a primary defect in the ability of the heart to fill and/or eject blood sufficiently. [5] According to the American Heart (Association/ American College of Cardiology (AHA/ACC) guidelines, HF is a major public health problem, with a prevalence of more than 5.8 million in the United States and more than 23 million worldwide.[6,7,8]

There are multiple interactions between heart diseases and kidney diseases. Cardiorenal syndromes (CRS) are disorders describing the bidirectional interactions between the heart and kidneys, whereby acute or chronic dysfunction in one organ may result in acute or chronic dysfunction of the other. This interaction is a complex and debilitating clinical condition. Type 2 CRS also known as chronic CRS describes chronic abnormalities in cardiac function (e.g. chronic congestive heart failure) causing progressive and permanent chronic kidney disease. [9]

The presence of type 2 CRS is a predictor of mortality and hospitalization among heart failure patients. It is established that cardiovascular disease (CVD) risk is increased by eight to ten folds in this population. [10] In spite of its high morbidity and mortality, the prevalence and predictors of type 2 CRS remain poorly understood. The implication of this interaction is that adequate management of CHF would prevent the progression of both CHF and CKD. [11]

There is a significant lack of data and research on the prevalence of type 2 CRS in Nigeria, and as a result, the factors that predict it are not yet fully understood. This research aims to investigate the epidemiology of type 2 CRS, exploring its prevalence and predictors in patients with HF. By elucidating the relationships between cardiac and renal dysfunction, this study seeks to inform strategies for early identification, prevention and the multidisciplinary management of type 2 CRS ultimately improving patients' outcomes and reducing healthcare burdens. This study therefore evaluated the prevalence and correlates of cardiorenal syndrome among Nigerians in a tertiary health center.

Materials and Methods

Study Area

The study was carried out at the Jos University Teaching Hospital (JUTH) which is in Jos, the cosmopolitan capital city of Plateau State in the North Central region of Nigeria. JUTH provides tertiary health care to Plateau State and 5 other neighbouring states such as Nasarawa, Bauchi, Taraba, Kaduna and Gombe States.

Study Design

This was a hospital based cross-sectional descriptive study.

Sample Size

The minimum sample size was determined using the Fisher's formula for estimating minimum sample size in health studies.[12] Using a prevalence of 47.3% [13] as obtained from a previous local study, the minimum sample size was determined to be 100, however 120 participants were recruited for the study.

Study Population

All patients diagnosed with congestive heart failure (according to Framingham criteria and confirmed by echocardiography) regardless of aetiology, admitted and discharged; undergoing follow up in the Cardiology Out-patient Department. All the subjects were adults aged 18-65 years.

Inclusion Criteria

This included adults CHF patients aged ≥18 years and ≤65 years on follow up at the Cardiology Clinic for at least 3 months post admission and discharge. The patient recruitment was without regard to the cause of HF.

Exclusion Criteria

This included patients < 18 years; with acute HF /or attending Cardiology Clinic for <3 months; patients with a history of CKD prior to attending the Cardiology Clinic; patients with febrile illness, UTI and patients who declined to participate in the study.

Sampling Technique

Patients with CHF from any cause, who met the inclusion criteria, and who were attending the Cardiology clinic of JUTH were consecutively recruited until the sample size was completed. A patient once enrolled was not further included in the study on subsequent attendance to the cardiology outpatient clinic.

Definition of terms

Type 2 CRS: For this study, type 2 CRS were CHF patients who developed CKD.

CKD was defined as: [13, 14, 15]

- Decreased glomerular filtration rate (GFR) of less than 60mls/minute/1.73m^2; measured twice, at least three months apart, obtained from serum creatinine concentration measurements using CKD-EPI.
- Persistent proteinuria, measured twice, at least three months apart.

Classification of Cardiorenal Syndrome [16]

- Mild: HF + eGFR 30-59ml/min/1.73m^2
- Moderate: HF + eGFR 15-29ml/min/1,73m^2
- Severe: HF + eGFR<15ml/min/1.73m^2 or dialysis

Heart failure severity by New York Heart Association (NYHA) functional classification was defined as follows: [17]

- Class I --- Dyspnoea during intense activity.
- Class II --- Dyspnoea during ordinary activity.
- Class III--- Dyspnoea during less than ordinary activity but comfortable at rest
- Class IV--- Dyspnoea at rest with inability to carry on any physical activity without discomfort.

Dyslipidaemia was defined as LDL ≥130mg/dl, TG >150mg/dl, or HDL <40mg/dl in men and < 50mg/dl in females.[18]

Diabetes mellitus was defined as history of diabetes, need for anti-diabetic agents, or a fasting blood glucose ≥7mmol/l or 126mg/dl. [18]

Study Procedure

Consenting patients who met the inclusion criteria were recruited during the cardiology clinics consecutively until the sample size was attained. Each participant was interviewed and examined by members of the research team using a proforma. Information obtained included demographic data, clinical history, general examination, including anthropometric measurement and cardiovascular system examination. Anthropometric measurements included weight in kilograms (without shoes) using a weighing scale and height in meters using a stadiometer. Body Mass Index (BMI) was calculated (the patient's weight divided by the square of the height) and recorded in kg/m^2. Blood pressure was measured using a standard mercury sphygmomanometer (adult cuff size) with the patient in the supine and sitting positions. Korotkoff sounds phases I and V were considered as systolic and diastolic blood pressures respectively and recorded in mmHg. This was done after a 5-minute rest using the right and left upper limbs. Two additional recordings were made using the limb with the higher value. The average was then calculated to give a representative value**.** An abdominal examination was performed and positive findings documented. Ascites was graded as mild, moderate or severe [19] and the presence and extent of hepatomegaly (in cm) was also documented. Heart failure diagnosis was based on Framingham criteria. [20] Severity of clinical symptoms was assessed by New York Heart Association (NYHA) functional classification. [17]

Blood samples were obtained for analysis of serum electrolytes, uric acid, urea, creatinine, triglycerides, total cholesterol and fasting blood glucose; and this was done at the Chemical Pathology laboratory of JUTH. Urine specimen was collected and used for semi-quantitative determination of albuminuria for all participants by albustix.

Patients with elevated serum creatinine level were followed up and repeated after 3 months (for proper definition of CKD). The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI. A twelve-lead electrocardiography (ECG) and echocardiography were done for each patient.

Ethical Consideration

Ethical clearance was obtained from the Institutional Health Research Ethical Committee of JUTH. The study design and objectives of the study were explained to the participants in the language they best understood and informed consent was obtained from all individuals on agreeing to participate in the study. Consenting participants were at liberty to withdraw from the study at any stage without consequence. All information was treated with utmost confidentiality.

Statistical Analysis

The Epi Info version 7.1.4.0. software (Centers for Disease Control and Prevention, Atlanta, Georgia, USA) was used for data analysis. Qualitative variables were presented using frequency tables and proportions as appropriate while quantitative variables were presented as means and standard deviations. Non-uniformly distributed quantitative variables were presented as median and interquartile range (IQR). The comparison of means for quantitative variables was tested using the students t-test, while the associations between the qualitative variables were treated using the chi- square test. The strength of associations were analyzed using correlation coefficients; and linear logistic regression analysis was used

to determine the form of relationship between independent and dependent variables. Level of significance was set at $p \leq 0.05$ and 95% confidence interval was used throughout.

Results

A total of 120 participants were recruited. All participants had complete data for analysis. The mean age of the study participants was 52.00 ± 11.44 years. Most participants were 40 years and above and 70 (58.3%) of the study subjects were females. See Table 1.

Table 1: Demographic characteristics of study participants

Demographic variables	Frequency	Percentage (%)
Age group		
<30	8	6.7
30-39	12	10.0
40-49	23	19.2
50-59	34	28.3
≥60	43	35.8
Gender		
Male	50	41.7
Female	70	58.3
Residence		
Rural	31	25.8
Surburban	27	22.5
Urban	62	51.7

The aetiology of HF observed in this study in order of frequency are as follows: Hypertensive heart disease 54 (45%); dilated cardiomyopathy 50 (41.7%); postpartum Cardiomyopathy 4 (3.5%); pericardial disease 3 (2.5%); ischaemic heart disease 2 (1.7%) and other unidentified causes 7 (5.8%).

Estimated GFR distribution among the study participants

The percentage distribution of GFR status among study participants is shown in Figure 1. Most of the participants (75%) had GFR greater than or equal to 60ml/min/1.73m^2, while only 1.66% had GFR less than 15 ml/min/1.73m^2.

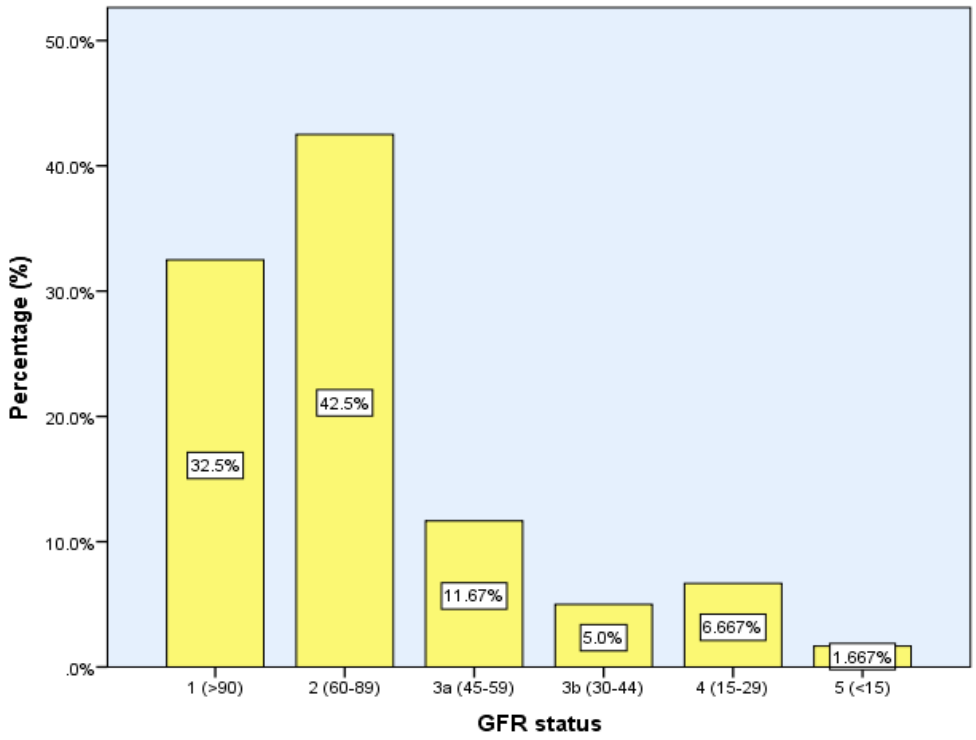

Figure 1: Bar chart showing percentage distribution of eGFR status of study participants

The prevalence of Type 2 CRS is summarized in the pie chart in Figure 2. Forty-five of the study participants had Type 2 CRS, accounting for 37.5%.

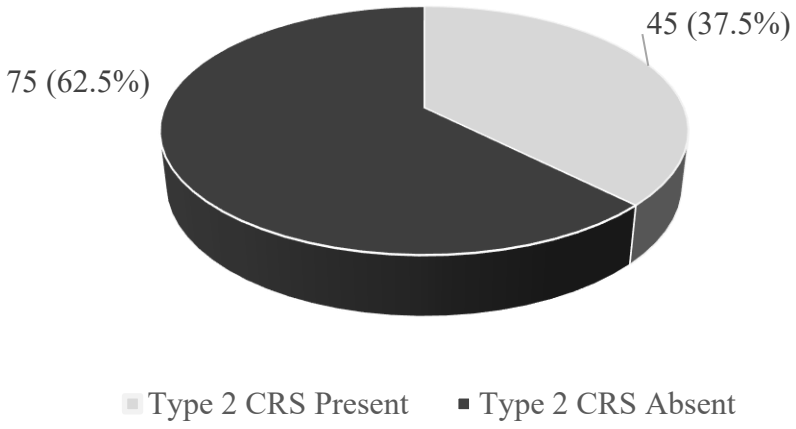

Figure 2: Prevalence Type 2 CRS among the study participants.

The distribution of type 2 CRS in the study population based on severity is shown in figure 3. Approximately 67% of the type 2 CRS patients had a mild form of CRS (HF + eGFR 30-59ml/min/1.73m^2), while an estimated 27% and 7% had moderate (HF + eGFR 15-29 ml/min/1.73m^2) and severe (HF + eGFR < 15 ml/min/1.73m^2) forms of CRS respectively.

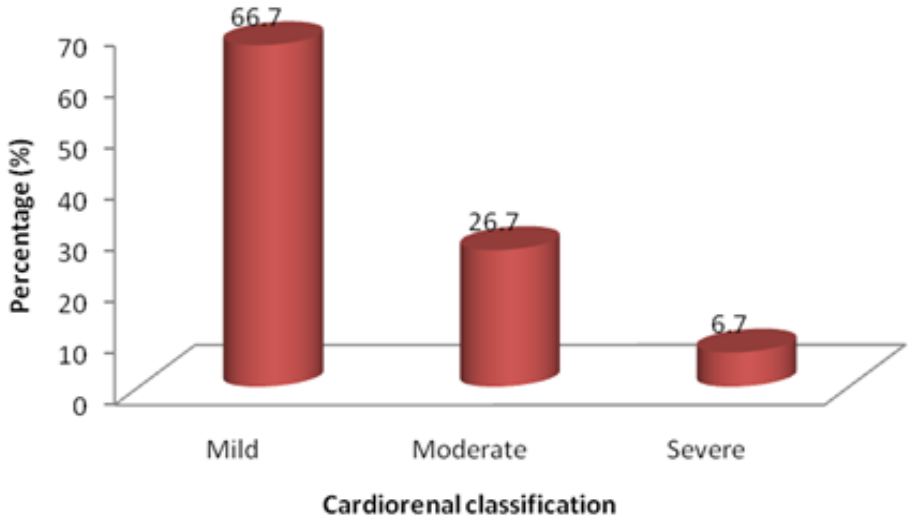

Figure 3: Distribution of Type 2 CRS based on severity.

The association between clinical variables (demography and history) and Type 2 CRS is summarized in Table 2. Age, sex, BMI, smoking, history of hypertension and myocardial infarction were not significantly associated with CRS. However, alcohol consumption and the history of diabetes were significantly associated with CRS. Patients who consumed alcohol were more likely to have Type 2 CRS than those who did not (57.9% vs 33.7%; p = 0.045). Also, patients who had diabetes were more likely to have CRS compared to those without a history of diabetes. (73.7% vs 30.7%; p=0.001). It was also observed that patients who were rural and suburban dwellers were more likely to have CRS compared to urban dwellers (50.0% vs 25.8%; p=0.006).

Table 2: Clinical correlates of Type 2 CRS

Variables	CRS present n=45	CRS absent n=75	χ^2	P
Age group				
<30	2(25.0)	6(75.0)	6.716	0.152
30-39	4(33.3)	8(66.7)		
40-49	4(17.4)	19(82.6)		
50-59	15(44.1)	19(55.9)		
≥60	20(46.5)	23(53.5)		
Gender				
Male	22(44.0)	28(56.0)	1.545	0.214
Female	23(32.9)	47(67.1)		
BMI				
Normal	27(42.9)	36(57.1)	4.936	0.086*
Overweight	14(41.2)	20(58.8)		
Obese	4(17.4)	19(82.6)		
Alcohol				
Yes	11(57.9)	8(42.1)	4.006	**0.045**
No	34(33.7)	67(66.3)		
Smoking				
Yes	1(33.3)	2(66.7)	-	1.000*
No	44(37.6)	73(62.4)		
HTN				
Yes	41(40.6)	60(59.4)	2.606	0.106
No	4(21.1)	15(78.9)		
DM				
Yes	14(73.7)	5(26.3)	12.611	**0.001**

No	31(30.7)	70(69.3)		
MI				
Yes	1(20.0)	4(80.0)	-	0.649*
No	44(38.3)	71(61.7)		
RESIDENCE				
Rural/Suburban	29 (50.0)	29 (50.0)	7.484	**0.006**
Urban	16 (25.8)	46 (74.2)		

Key: * Fisher's exact p-value, bold for p-value <0.05; BMI-Body Mass Index, HTN-hypertension, DM- diabetes, MI- myocardial infarction, NYHA- New York Heart Association, HHDX- hypertensive heart disease, DCM- Dilated cardiomyopathy, PPCM-peripartum Cardiomyopathy, IHD- Ischaemic heart disease.

The association between heart failure indices and Type 2 CRS is shown in Table 3. A higher proportion of patients with raised JVP were observed to have Type 2 CRS compared to those without a raised JVP (73.1 vs 27.7%, p=0.001). Similarly, patients who had a loud pulmonary component of the second heart sound (P2) were more likely to have Type 2 CRS compared to those who did not (53.6% vs 23.4%; p=0.001). Furthermore, patients with clinically detectable ascites irrespective of whether it was mild, moderate or severe were more likely to have Type 2 CRS compared to those with no clinically detectable ascites (66.7%, 63.0%, and 66.7% respectively vs 21.3%; p=0.001).We also found that patients with higher severity of heart failure symptoms (III and IV) according to the NYHA grading were more likely to have type 2 CRS compared to those with milder severity (I and II) (64.9% and 80.0% vs. 6.5% and 26.2 % respectively, P=0.001). On the contrary, a loud aortic component of the second heart sound (A2), as well as the aetiology of heart failure were not significantly associated with Type 2 CRS in this study.

Table 3: Association between Heart Failure Indices and Type 2 CRS

Variables	**CRS present n=45**	**CRS absent n=75**	χ^2	**P**
Raised JVP				
Yes	19(73.1)	7(26.9)	17.925	**0.001**
No	26(27.7)	68(72.3)		
Loud P2				
Yes	30(53.6)	26(46.4)	11.571	**0.001**
No	15(23.4)	49(76.6)		
Loud A2				
Yes	18(41.9)	25(58.1)	0.544	0.461
No	27(35.1)	50(64.9)		
Ascites				
Nil	16(21.3)	59(78.7)	22.366	**0.001***
Mild	10(66.7)	5(33.3)		
Moderate	17(63.0)	10(37.0)		
Severe	2(66.7)	1(33.3)		
NYHA				
I	2(6.5)	29(93.5)	34.571	**0.001**
II	11(26.2)	31(73.8)		
III	24(64.9)	13(35.1)		
IV	8(80.0)	2(20.0)		
Aetiology of Hf				
HHDX	15(27.8)	39(72.2)	9.436	0.051
DCM	24(48.0)	26(52.0)		
PPCM	2(50.0)	2(50.0)		
IHD	2(100.0)	0(0.0)		
OTHERS	2 (20.0)	8 (80.0)		

Key: * Fisher's exact p-value, bold for p-value <0.05, JVP- Jugular venous pulsation, P2- pulmonary component of the second heart sound, A2- aortic component of the second heart sound.

The association between laboratory variables and Type 2 CRS is depicted in Table 4. Participants with reduced ejection fraction (EF< 45) were more likely to have CRS compared to those without. (49.3% vs 22.6%; p=0.003). Majority of the subjects who had anaemia were found to have CRS compared to those without (70.6% vs 32.0%.; p=0.002). Also, subjects who had cardiomegaly (increased CTR) were more likely to have CRS compared to those without (41.8% vs 18.2%; p=0.038). Furthermore, subjects who had albuminuria irrespective of the degree were more likely to have CRS compared to those without albuminuria (66.7%, 78.9% vs 8.5%; p=0.001). On the contrary, there was no significant difference in the groups when hyperuricaemia was considered. This is similar to findings with AF and dyslipidaemia.

Table 4: Association between laboratory variables and Type 2 CRS

Variables	CRS Present	CRS absent	χ^2	P
AF				
Yes	3(33.3)	6(66.7)	-	1.000*
No	42(37.8)	69(62.2)		
***EF(*<45)**				
Yes	33(49.3)	34(50.7)	8.942	**0.003**
No	12(22.6)	41(77.4)		
Anaemia				
Yes	12(70.6)	5(29.4)	9.252	**0.002**
No	33(32.0)	70(68.0)		
Raised CTR				
Yes	41(41.8)	57(58.2)	4.298	**0.038***
No	4(18.2)	18(81.8)		
Albuminuria				
Nil	6(8.5)	65(91.5)	66.023	**0.001***
Trace	12(66.7)	6(33.3)		
≥One	15(78.9)	4(21.1)		
Dyslipidemia				
Yes	45(37.5)	75(62.5)	-	-
No	-	-		
Hyperuricaemia (>430umol/l)				
Yes	25(31.6)	54(68.4)	3.804	0.051
No	20(50.0)	20(50.0)		

Key: *Fisher's exact p-value; bold for p-value <0.05; AF- atrial fibrillation, CTR- cardio-thoracic ratio.

The predictors of Type 2 CRS following the logistic regression analysis of CRS with significantly associated variables is shown in table 5. The presence of diabetes in the study subjects was six times more likely to predict CRS (OR=6.323; CI=2.094-19.093). Also, NYHA was shown to predict CRS. It was observed that subjects with early grades of NYHA (I and II) were less likely to have CRS; but this was not the case with advanced grades of NYHA. Similarly, factors associated with congestion and decreased forward arterial flow, including raised JVP (OR=7.099; CI=2.671-18.865), Loud P2 (OR=3.769; CI=1.726-8.232) and reduced EF (<45) (OR=3.316; CI=1.487-7.395) were found to be predictors of CRS. Similarly, the presence of anaemia was found to be an independent predictor of CRS (OR=5.091; CI=1.675-15.640). Furthermore, our study showed that albuminuria was shown to be an independent predictor of type 2 CRS. The absence of albuminuria on dipstick made the subjects unlikely to have CRS (OR=0.001; CI=0.004-0.0052). Our study further revealed that subjects who were resident in the rural/ sub-urban areas were 2.8 times more likely to have CRS than those who were urban residents (OR=2.875; CI= 1.335-6.192). Furthermore, patients with cardiomegaly (raised CTR) were 3.2 times more likely to develop CRS than those without cardiomegaly (OR=3.237; CI=1.0110.278).

Table 5: Logistic regression of CRS with significantly associated variables

Variables	OR	95% C.I	P
Alcohol			
Yes	2.710	0.997-7.364	0.051
No	1.0		
DM			
Yes	6.323	2.094-19.093	**0.001**
No	1.0		
NYHA			
I	0.017	0.002-0.142	**0.001**
II	0.089	0.016-0.483	**0.005**
III	0.462	0.085-2.502	0.370
IV	1.0		
Raised JVP			
Yes	7.099	2.671-18.865	**0.001**
No	1.0		
Loud P2			
Yes	3.769	1.726-8.232	**0.001**
No	1.0		
Ascites			
Nil	0.136	0.012-1.592	0.122
Mild	1.000	0.072-13.868	1.000
Moderate	0.850	0.068-10.610	0.900
Severe	1.0		
EF(<45)			
Yes	3.316	1.487-7.395	**0.003**
No	1.0		
Anaemia			
Yes	5.091	1.657-15.640	**0.004**
No	1.0		
Albuminuria			
Nil	0.014	0.004-0.052	**0.001**
Trace	0.296	0.070-1.246	0.097
≥one	1.0		
Residence			
Rural/Sub-urban	2.875	1.335-6.192	**0.007**
Urban	1.0		
Raised CTR			
Yes	3.237	1.019-10.278	**0.046**
No	1.0		

Discussion

CRS has emerged as a major public health concern as the prevalence of both chronic heart failure and chronic kidney disease continue to rise, and this has very considerable implications for patients' outcomes. This is further compounded by the fact that its diagnosis and management pose significant challenges for healthcare providers. This study found a prevalence of 37.5% for type 2 CRS. This prevalence rate is similar to observations in the "Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity" (CHARM) study and various other large studies that showed a prevalence of 25-50%. [21, 22, 23, 24] A Nigerian study carried out in the Kano (Nigeria) which used only serum creatinine to define renal damage quoted a prevalence as low as 9.4%. [25] Another study done in Eastern Nigeria reported a prevalence of up to 76%. [26] However, in this study, only hypertensive heart failure patients were studied. Hypertension is an independent risk factor for CKD, and this may account for the higher prevalence.

This study found a higher frequency of mild CRS compared to moderate and severe CRS in order of decreasing frequency (66.7%, 26.7% and 6.7%) respectively. Supporting the findings of the present study, research done in Kano-Nigeria among elderly patients observed that a total of 48.1%, 38.9% and 3.1% of the subjects had mild, moderate and severe CRS respectively. [27] This implies that majority of HF patients usually present with mild renal diseases, a stage which offers a window of opportunity for early intervention to halt progression of CKD.

The interaction between the heart and kidneys in type 2 CRS is of great interest in heart transplant candidates. CKD has an adverse effect on heart transplant outcome. [28] It is reported that in potential heart transplant patients, advanced stages of kidney disease may deter many transplant physicians from carrying out the heart transplant. [28] The finding in our study where the majority of patients with type 2 CRS have mild disease suggests that most of the patients in our environment are at a stage where if carefully selected and offered heart transplants would generally have a relatively good prognosis. These groups of patients are also potential beneficiaries of simultaneous heart and kidney transplantation. Now, Heart-kidney transplants are quite uncommon when compared to single-organ transplants of the heart and kidney, as well as combined kidney-pancreas and combined kidney-liver transplants. [29] A major benefit in simultaneous heart-kidney transplant is the fact that recipients of such dual organs tend to have lower rates of heart and kidney rejection when compared to kidney-only or heart-only transplants, and this has been shown to have profound survival benefit in such patients. [29]

The predictors of type 2 CRS as observed in this study were diabetes mellitus, NYHA severity, raised jugular venous pressure, loud P2, reduced ejection fraction, anemia, albuminuria, rural/sub-urban dwelling and raised CTR (cardiomegaly). Diabetes and hypertension are known traditional cardiovascular risk factors whose presence amplifies the risk of CKD (type 2 CRS). [30,31] In this study, diabetes was found to be a major player in predicting type 2 CRS, but hypertension did not show any significant association. One review reported diabetes and poorly controlled hypertension as very strong risk factors for CRS in patients with CHF. [32] These authors suggest that an interplay exists between diabetes and hypertension, where either singly or in combination, these factors enhance renal injury from hypertension and heart failure associated with renal damage. [32] The contrast seen in our findings concerning the relationship of hypertension and CRS may be because most of our patients were receiving blood pressure control medications as at the time of this study, therefore having relatively well controlled blood pressure.

It was also obvious from this study that higher stages of NYHA (stages III and IV) were associated with development of CRS compared to patients with lower NYHA stages (I and II). This finding agrees with observations made by Salim A et al [33] where stage III and IV NYHA were found to be strongly associated with type 2 CRS. It is reported that with worsening severity of HF, renal perfusion is compromised, hence increasing the incidence and worsening already existing kidney dysfunction. [31, 34]

Damman et al [35] and Drazner et al [36] have shown that clinically detectable raised jugular venous pressure (JVP), loud pulmonary component of the second heart sound (P2) and ascites, which are clinical features of congestion are associated venous with worsening renal function in CRS. Studies have shown beyond reasonable doubt that in HF patients, there is an epidemiologic relationship between increasing CVP or venous congestion and reduced eGFR, independent of reduced renal blood flow. [34]

Decreased ejection fraction (EF<45) and cardiomegaly are related and were found to be independent predictors of CRS in our study. In another study, mean EF was significantly lower in the group with CRS than in the group without cardiorenal syndrome. [33] The finding of an enlarged heart with a consequent reduction in stroke volume and a reduced ejection fraction reflects the major pathogenetic mechanisms involved in CRS which are essentially under-perfusion from reduced cardiac output and venous congestion. [36] The resultant decreased forward flow causes reduced renal perfusion pressure and consequently leads to renal dysfunction. In addition, increased venous congestion with subsequent

activation of the neurohumoral pathway that affects renal blood flow and glomerular autoregulation leads to impairment in tubular function and glomerular filtration. [37]

Additionally, albuminuria was found to be an independent predictor of type 2 CRS. An increased urinary excretion of albumin is a well-known recognized early marker of kidney damage. Its measurement in urine has been used in monitoring patients with CKD. In a certain study, albuminuria was independently related to an increased risk for CVD among CHF patients, and these patients with albuminuria had worse renal function compared to normoalbuminuric individuals.[38] Several studies show that treatment with angiotensin receptor blockade does not affect albumin urinary excretion in CHF, contrary to observation in patients with diabetes, hypertension and kidney disease. [39] This might explain why even though most of the CHF patients are treated with a regimen which includes ACE inhibitors, a significant number of them still go on to develop CRS. This suggests that in this population, those who already have albuminuria may not benefit as much from its anti-proteinuric use and may go on to develop CKD (Type 2 CRS).

Interestingly, rural and suburban patients with HF are more likely to develop Type 2 CRS when compared to urban dwellers, as shown in our study. This finding agrees with results published by Gamble et al [40] which highlighted that even with universal health care system, differences exist in the outcomes based on the location of residence among patients with heart failure. This may be because adult HF patients living in urban locations are more likely to access medical care, therefore having lesser chances of untoward outcome, hospitalization or presentation to the emergency department in the first year after diagnosis.

The limitation of this study includes its single-centered cross-sectional design and therefore may not infer a temporal relationship. However, this study shows that the prevalence of CRS among chronic heart failure patients is high. Diabetes mellitus, NYHA grading of HF, increased JVP, Loud pulmonary component of the second heart sound (P2), reduced ejection fraction (EF<45%), anaemia, albuminuria, rural and suburban dwelling and increased cardiothoracic ratio were found to predict type 2 CRS in CHF patients. There is a need to incorporate screening for CKD among stable chronic HF patients at diagnosis and at regular intervals. Attention should be paid very closely to the population of chronic HF with factors predicting type 2 CRS and the presence of these predictors should prompt early referral to the Nephrologist.

References

1. Eknoyan G, Lamiere N, Barsoun R, Eckardt KU, Levin A, Levin N, Locatelli F, et al. The burden of kidney disease: improving global outcomes. *Kidney Int.* 2004; 66:1310-1314.
2. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, Saran R, Wang AY, Yang CW. Chronic kidney disease: global dimension and perspectives. The Lancet. 2013 Jul 20;382 (9888):260-72.
3. Sumaili K, Cohen EP, Zinga CV, Krzesinki J, Pakasa NM, Nazaire NM. High prevalence of undiagnosed chronic kidney disease among at risk population in Kinshasa Central Africa: The Democratic Republic of Congo. *BMC Nephrol.* 2009; 10. doi:10.1186/1471-2369-10-18.
4. Krzensinski JM, Sumaili KE, Cohen E. How to tackle the avalanche of chronic kidney disease in sub-Saharan Africa: the situation in the Democratic Republic of Congo as example. *Nephrol Dial transplant.* 2007; 22: 332-335.
5. Tanai E, Frantz S. Pathophysiology of heart failure. Compr Physiol. 2015 Dec 15; 6(1):187-214.
6. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al. ACC/ AHA 2005 Guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Cardiol.* 2005; 46 (6): e1-82.

7. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al. 2009 focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. *Circulation* 2009; **119** (14): e391-479.
8. Bui AL, Horwich TB, Fonarow GC. Epidemiology and risk profile of heart failure. Nature Reviews Cardiology. 2011 Jan; 8 (1):30-41.
9. Cruz DN, Schmidt-Ott KM, Vescovo G, House AA, Kellum JA, Ronco C, et al. Pathophysiology of cardiorenal syndrome type 2 in stable chronic heart failure: workgroup statements from the eleventh consensus conference of the Acute Dialysis Quality Initiative (ADQI). Contrib Nephrol. 2013; 182: 117-36. doi: 10.1159/000349968.
10. Salim A, Benouna ME, Habbal R, El Mourid M. Cardiorenal syndrome type 2: A strong prognostic factor of survival. International Journal of Cardiovascular Sciences. 2017 Sep; 30: 425-32.
11. Tuegel C, Bansal N. Heart failure in patients with kidney disease. Heart. 2017 Dec 1;103 (23):1848-53.
12. Araoye MO. Sample size determination. In: Araoye MO (ed) Research Methodology with statistics for Health and Social Sciences. Ilorin: *Nathadex publishers,* 2004; 115-120.
13. Arodiwe EB, Ijoma CK, Ulasi II, Onodugo OO. Renal function in Nigerian patients with heart failure. *Int J of Intern Med.* 2012;9(2
14. KDIGO CK. clinical practice guideline for the evaluation and management of chronic kidney disease (Chapter 1). Kidney Int Suppl. 2013; 3:19-62.
15. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009; (9):604–12. Epub 2009/05/06. pmid:19414839..
16. Kelly VL, Amy W, Eddie LG, Margaret MR. Acute decompensated heart failure and the cardiorenal syndrome. *Crit Care Med.* 2008; 36: S75-S78.
17. Wilson Tang WH and Mullens W. Cardio-renal syndrome in decompensated heart failure. *Heart* published online.2009; doi: 10.1136/ hrt.2009. 166256.Upated information and services at http://heart.bmj.com/cgi/content/abstract/hrt.2009.166256v1.
18. Aguilar M, Bhuket T, Torres S, Liu B, Wong RJ. Prevalence of the Metabolic Syndrome in the United States, 2003-2012. *JAMA.* 2015; 313 (19):1973–1974. doi:10.1001/jama.2015.4260
19. Samanta J, Rana A, Dhaka N, Agarwala R, Gupta P, Sinha SK, Gupta V, Yadav, T.D. and Kochhar, R., 2019. Ascites in acute pancreatitis: not a silent bystander. *Pancreatology*, *19*(5), pp.646-652.
20. McKee PA, Castelli WP, McNemara PM, Kannel WB. The natural history of congestive heart failure. The Framingham heart study. *N Engl J Med.* 1997; 285: 1441-1446.
21. Dries DL, Exner DV, Domanski MJ, Greenberg B, Stevenson LW. The prognostic implications of renal insufficiency in asymptomatic and symptomatic patients with left ventricular systolic dysfunction. *J Am Coll Cardiol*. 2000; **35**(3)681-689.
22. Heywood JT, Fonarow GC: High prevalence of renal dysfunction and its impact on outcome in 118,465 patients hospitalized with Acute decompensated heart failure: A report from the ADHERE database. *J Card Fail* 2007; 13: 422-430.
23. Campbell RC, Sui X, Filipatos G, Love TE, Wahle C, Sanders PW, Ahmed A. et al. Association of chronic kidney disease with outcomes in chronic heart failure: a propensity-matched study. *Nephrol Dial Transplant* 2009:24:186-193.
24. Hillege HI, Nitsch D, Pfeffer ME, Swedberg K, McMurray JJ, Yusuf S, et al. Renal function as a predictor of outcome in a broad spectrum of patients with heart failure. *Circulation* 2006;113: 671-678.
25. Muhammad N.S. Cardiorenal syndrome in patients with heart failure in Kano. Part II dissertation submitted to the National Postgraduate Medical College of Nigeria; 2013.

26. Osuji CU, Nwaneli CU, Onwubere BJ, Onwubuya EI, Ahaneku GI, et al. Renal function in patients with hypertension associated congestive cardiac failure seen in a tertiary hospital. *Int J Nephrol* 2012; 2012: 769103.
27. Cohen-Solal A, Kotecha D, J Van veld D, et al. Efficacy and safety of nebivolol in elderly heart failure patients with impaired renal function: insights from the SENIORS trial. *Eur J Heart Fail* 2009; 11:872-880.
28. Rafat C, Hertig A, Rondeau E. renal impairment an impediment to heart transplantation? *Iran J Kidney Dis.* 2015; 9(2):77-83.
29. Castilo-Lugo JA, Brinker KR. An overview of combined heart and kidney transplantation. *Curr Opin cardiol*. 1999; 14(2): 121-5.
30. Bagshaw SM, Cruz DN, Aspromonte N, Daliento L, Ronco F, Sheinfeld G, et al. Epidemiology of cardio-renal syndromes: workgroup statements from the 7th ADQI Consensus Conference," *Nephrol Dial Transplant*.2010; **25**(5): 1406–1416.
31. Kundhal K, Lok CE. Clinical epidemiology of cardiovascular disease in chronic kidney disease. *Nephron Clin Pract 2005;* 101**,** (2): c47–52.
32. Kishomoto T, Maekawa M, Abe Y, Yamamoto K. Intrarenal distribution of blood flow and renin release during renal venous pressure elevation. *Kidney Int*. 1973; 4(4):259-66.
33. Salim A, Benouna MEG, Habbal R, El Maroud M. Cardiorenal syndrome type 2: A strong prognostic factor. *Intl Journal of Cardiovasc. Sci* 2017; 30 (5); 425-432.
34. Braam B, Joles JA, Danishwar AH, Gaillard CA. Cardiorenal syndrome-current understanding and future perspective. *Nat Rev Nephrol* 10(1):48-55.
35. Damman K, Van Deursen VM, Navis G, Voors AA, van Veldhuisen DJ, Hillege HL. Increased central venous pressure is associated with impaired renal function and mortality in a broad spectrum of patients with cardiovascular disease. J Am Coll Cardiol 2009; 53: 582-588.
36. Drazner MH, Rame JE, Stevenson LW, Dries DL. Prognostic importance of elevated jugular venous pressure and a third heart sound in patients with heart failure. New England Journal of Medicine. 2001 Aug 23; 345 (8):574-81.
37. Viswanathan G, Gilbert S. The cardiorenal syndrome: making the connection. Int J Nephrol. 2010 Oct 4;2011:283137. doi: 10.4061/2011/283137.
38. Jackson CE, Solomon SD, Gerstein HC, Zetterstrand S, Olofsson B, Michelson EL, et al. CHARM investigators and committees. Albuminuria in chronic heart failure: prevalence and prognostic importance. *Lancet* 2009; 374:543-550.
39. Damman K, Hillege HL, van Veldhuisen DJ. Albuminuria in heart failure: a CHARMing new risk factor? *Lancet*. 2009; 374:506-508.
40. Gamble JM, Eurich DT, Ezekowitz JA, Kaul P, Quan H, Mc Alister FA. Patterns of care and outcomes differ for urban versus rural patients with newly diagnosed heart failure, even in a universal healthcare system. Circ Heart Fail. 2011; 4(3):317-23.