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Incidence and types of cardiorenal syndrome in Aswan University Hospital

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Abstract---Background: Heart and renal disease are common, increasingly encountered and often co-exist. Half of patients with chronic heart failure develop cardiorenal syndrome (CRS), which have a poor prognosis. Objectives: to identify the prevalence of different types & risk factors associated with cardiorenal syndrome in patients presented in Aswan university hospitals. Methods: We included CRS patients with age ≥ 20 years old, not pregnant or lactating. We performed echocardiography and pelvic abdominal ultrasound to the included participants. Results: We included 100 participants, with average age 58.73 ± 14.81 , half of them were male. The most common chronic diseases were hypertension (74.0%), and diabetes mellitus (63.0%). The prevalence of CRS type I, II, III, IV and V was 10%, 33.0%, 25.0%, 19.0%, and 13.0%, respectively. There was statistically significant relation between type of CRS and CKD ($P=0.011^*$). Conclusion: CRS type II had the highest prevalence of the CRS subtypes. Moreover, CKD and was a risk factor for CRS.

Keywords---CRS, heart failure, chronic kidney failure.

Introduction

Heart and renal disease are common, increasingly encountered and often co-exist. Half of patients with chronic heart failure develop cardiorenal syndrome (CRS),

which have a poor prognosis. CRS is defined as any acute or chronic problem in the heart or kidneys that could result in an acute or chronic problem of the other (1). CRS divided into 2 major groups, cardiorenal and renocardiac syndromes, based on the primum movements of the disease process. Moreover, CRS further grouped into 5 subtypes type 1, 2, 3, 4 and 5 based on disease acuity and sequential organ. (2,3) Type 1 and 2 CRS occurs in case of acute decompensation of cardiac function leading to a decrease in glomerular filtration rate (GFR). Many factors involved in the pathogenesis of types 1 and 2 CRS, such as elevated intraabdominal pressures, activation of the renin-angiotensin-aldosterone system (RAAS), activation of the sympathetic nervous system and increased inflammatory damage to the kidney related to heart failure. Types 3 and 4 CRS more likely result from volume overload from renal dysfunction, also cardiac deterioration may occur in the setting of metabolic disturbances and neurohormonal changes that accompany renal disease. However, type 5 CRS occur in the setting of sepsis, systemic lupus erythematosus (SLE), diabetes mellitus (DM), decompensated cirrhosis, or amyloidosis. (4–6)

The overall prognosis of CRS is poor, a multivariable mortality model is used to predict in-hospital mortality and readmission rate. The model include systolic blood pressure (BP), serum creatinine, and Pelvi abdominal us and echocardiography. (7) The prevalence and clinical impact of renal dysfunction in hypertrophic cardiomyopathy and the incidence of each type of CRS is not clearly identified. (8) Knowledge of the epidemiology of CRS subtypes is increasingly important for understanding the overall burden of disease for each CRS subtype, along with associated morbidity, mortality and health resource utilization, therefore, we aim to estimate the prevalence of different types, and clinical evaluation of cardiorenal syndrome patients presented in Aswan university hospitals.

Patients and Methods

This study was conducted in Internal Medicine& Cardiology departments at Aswan university hospital, and approved by institutional review board (IRB), Faculty of Medicine, Aswan University. We included patients with CKD aged ≥ 20 years old. Those < 18 years old. Moreover, pregnant, and lactating women were also excluded from the study. The demographic data such as age, gender comorbid data and primary diagnosis were recorded. Moreover, echocardiography parameters (left ventricular ejection fraction and left ventricular diastolic dysfunction) and pelvic abdominal ultrasound were measured and recorded. Patients were classified according to the five types of CRS(9), while acute kidney injury was classified into 3 stages based on the Acute Kidney Injury Network (AKIN) criteria (10). CKD was diagnosed according to K-DOQI guidelines (11). Renal functions were evaluated by the estimated glomerular filtration rate (GFR).

Statistical Analysis

Data were summarized in mean \pm SD for quantitative data and frequencies for qualitative data. A two-sided P-value of < 0.05 was considered statistically significant. We used SPSS 25 software for data analyses.

Results

We included 100 participants, with average age 58.73 ± 14.81 . Of the included participants 54.0% aged 50-70 years, while 23.0% of them aged more than or equal 70 years. Half of the studied patients were male (50.0%). The most common chronic diseases were hypertension (74.0%), and diabetes mellitus (63.0%) (

Table 1). Moreover, the comorbidities in each CRS subtypes are reported in Table 2. Also, there were 15 patients with CKD Grade V were on dialysis, 10 of them were CRS type IV and 5 were CRS type V. Of the 100 included participants, type I, II, III, IV and V included 10, 33, 25, 19 and 13, respectively

Table 6: vital signs and laboratory finds
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	Type I	Type II	Type III	Type IV	Type V
Vitals signs					
Systolic BP	130 ± 49	119 ± 50	123 ± 45	143 ± 50	139 ± 45
Diastolic BP	76 ± 30	75 ± 36	73 ± 24	77 ± 22	84 ± 25
HR	105 ± 26	111 ± 30	93 ± 22	97 ± 21	113 ± 33
CBC					
WBC	12.28 ± 3.2	12.68 ± 5.8	17.1 ± 9.7	17.8 ± 9.2	18.7 ± 10.6
HB	10.6 ± 3.7	10.4 ± 2.4	13.1 ± 17.2	10.1 ± 2.3	9.3 ± 2.5
PLT	344 ± 148	223 ± 112	293 ± 146	249 ± 114	212 ± 123
Electrolytes					
Na	141 ± 5	136 ± 8	136 ± 8	138 ± 5	138 ± 11
K	4.6 ± 0.6	4.3 ± 0.8	4.4 ± 0.9	7.4 ± 0.9	4.5 ± 1.3
Ca	8.8 ± 0.6	7.7 ± 2.2	7.7 ± 2.1	8.5 ± 2.5	7.1 ± 2.1
Renal chemistry					
Phosphate	4.5 ± 1.5	4.2 ± 1.2	4 ± 0.9	4.2 ± 1.1	4.3 ± 1.1
Uric acid	5.8 ± 2.9	5.9 ± 2.9	5.5 ± 3	6.9 ± 3.5	6.5 ± 2.9
Urea	140 ± 32	153 ± 55	182 ± 51	180 ± 42	119 ± 48
Creatinine	2.9 ± 1.2	3.6 ± 2	6.1 ± 3.5	6.6 ± 2.7	4.7 ± 4.3

Table 1: Personal data of the studied patients

	No. (%)
Age: (years) Mean ± SD	58.73 ± 14.81
< 50	23 (23%)
50 - 70	54 (54%)
> 70	23 (23%)
Gender:	Male
	Female
	50 (50%)
	50 (50%)

Table 2: comorbidities according of CRS subtypes

	Type I	Type II	Type III	Type IV	Type V	
DM	6	23	14	13	7	63
HTN	6	24	18	16	10	74
CKD	0	10	7	10	5	32
IHD	3	12	8	4	3	30
COPD	0	4	3	3	5	15

In Pelvi-abdominal sonography, 22 patients were free, and the most frequent findings were bilateral grade I, II, and III nephritis, in 37, 15 and 13, respectively. Moreover, back pressure was reported 4 times in type II, and cancer bladder founded in a grade V case. Also, bilateral G IV N reported once in type IV, cirrhotic liver reported twice, one in type II and one in type III. Thirteen patients found to be normal in ECHO. TR plus MR were the most common reported finding in echo 47, and diastolic dysfunction was reported in 28 cases (Table 3).

Table 3: Relation between type of CRS and radiology

	Type I	Type II	Type III	Type IV	Type V	Total
Pelvi-abdominal:						
Normal	9	9	4	0	0	22
Single Kidney G I N	0	1	0	0	0	1
Single Kidney G II N	0	1	1	0	0	2
Bilateral G I N	1	13	11	5	7	37
Bilateral G II N	0	2	6	3	4	15
Bilateral G III N	0	1	2	9	1	13
ECHO:						
Normal	4	0	6	2	1	13
Diastolic Dysfunction	2	7	6	7	6	28
Dilated ventricle	1	2	0	0	1	4
IHD	2	2	2	0	1	7
Impaired	0	3	2	0	0	5
LVH	0	2	0	0	0	2
MR	0	0	2	1	1	4
Pulmonary HTN	0	1	1	0	1	3
TR & MR	3	15	7	12	10	47
Aortic dissection	0	2	0	0	0	2
TR	0	1	1	0	0	2
Valvular heart disease	0	0	0	0	1	1
Vegetation	0	0	0	1	0	1
AF	0	0	0	1	0	1
Calcified AV	0	1	0	0	0	1
Dilated both atrium	1	0	0	0	0	1
Cardiac tamponade	0	0	0	1	0	1

There was statistically significant relation between types of CRS, CKD (P= 0.011*) and COPD (P= 0.034*). While there were no statistically significant relations with DM (P= 0.643), or IHD (P= 0.625). (Table 4)

Table 4: Relation between type of CRS and general condition

General condition	Type I & II	Type III & IV	Type V	P-value
DM	29	27	7	0.643
HTN	30	34	10	0.704
CKD	10	24	6	0.011*
IHD	15	12	3	0.625
COPD	4	6	5	0.034*

Infection was responsible for about 25 % of occurrence of CRS (UTI, Pneumonia, diabetic foot and bed sores abscess). Also, MI, AKI, shock, uremic fits, arrhythmia, and nephrogenic pulmonary edema were leading causes of CRS (Table 5).

Table 5: Causes of CRS

	Type I	Type II	Type III	Type IV	Type V	Total
UTI	0	3	9	0	0	12
AKI	0	1	6	0	4	11
MI	5	4	1	0	1	11
Pneumonia	0	1	8	1	1	11
Shock	1	7	2	0	1	11
Arrhythmia	0	7	0	0	1	8
Nephrogenic pulmonary edema	0	1	0	7	0	8
Uremic fits	0	1	3	4	0	8
Cardiac tamponade	1	2	0	2	0	5
Pulmonary edema	0	3	1	0	1	5
COPD exacerbation	0	0	1	2	2	5
HTN	0	3	0	1	0	4
Cardiogenic pulmonary edema	1	2	0	0	0	3
HF	1	2	0	0	0	3
DKA	0	0	2	0	0	2
Unstable angina	1	1	0	0	0	2

Systolic blood pressure ranged from 40 to 250 while the diastolic ranged from 20 to 60 and HR ranged from 60 to 190. Laboratory findings were reported in Table 6.

Table 6: vital signs and laboratory finds

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Uric acid	5.8 ± 2.9	5.9 ± 2.9	5.5 ± 3	6.9 ± 3.5	6.5 ± 2.9
Urea	140 ± 32	153 ± 55	182 ± 51	180 ± 42	119 ± 48
Creatinine	2.9 ± 1.2	3.6 ± 2	6.1 ± 3.5	6.6 ± 2.7	4.7 ± 4.3

The severity of CRS was weakly positively correlated with creatinine, and weakly negatively correlated with Ca, rho= 0.23 and -0.227 respectively, p-value < 0.05. while the severity wasn't correlated with other variables Table 7.

Table 7: correlation between CRS & other variables

	Spearman's Rho	p-value	N
Systolic BP	0.144	0.159	97
Diastolic BP	0.098	0.341	97
HR	-0.087	0.409	93
WBC	.131	0.07	100
HB	-0.175	0.081	100
PLT	-0.075	0.461	100
Urea	0.047	0.644	100
Creatinine	.353	0*	100
Na	0.024	0.813	100
K	0.095	0.345	100
Ca	-.227	0.026 *	97
Phosphate	-0.025	0.809	97
Uric acid	0.097	0.344	97

Discussion

Cardiorenal syndrome lacked a universally accepted definition for long, and numerous related key questions yet remain unanswered. Clinical guidelines have classically treated cardiac and renal failure separately, but the characteristics of CRS need to be elucidated more comprehensively to enhance the integrative clinical management of the syndrome (12). More than 50% of CRS cases were aged from 50 :70 years. On the other hand, Abdullah et al., showed that the incidence of CRS among 61-70 years was 18% and 71- 80 years was 8% (13). While Reddy et al., found that 80% of patients with CRS aged between 40-80. (14)

According to type of CRS, we found that the prevalence of type I CRS was 10%, type II was 33.0%, type III was 25.0%, type IV was 19.0%, and type V was only 13.0%. Shah et al., showed that the most common type of CRS was type I CRS by

46%, while 22% presented with type II CRS and there were no individual came under the category of type III CRS (15). Also, Gigante et al., found that the most common CRS is type V 38.4%, while CRS type I represents 32.1% and CRS type II represents (15.8%). CRS was more common in males (68.9% of patients) (16).

We found that the most common chronic diseases among the CRS patients were HTN (74.0%), and diabetes mellitus (63.0%) and CKD were 32%. This was in line with Abdullah et al., results, they found that the most common risk factor was HTN (75%) followed by diabetes (44%) (13). Moreover, Hu et al., showed that 71.30% has HTN, 42.70% with diabetes, 24.7% patients were with a history of chronic kidney disease and 9.80% with COPD (17). Shah et al., (15) showed that among the study population, 39 (78%) patients were hypertensive and 32 (64%) were diabetic. Whereas 25 (50%) had underlying chronic kidney disease, 24 (48%) patients had CAD and 22 (44%) had dyslipidaemia.

We found that multisystem diseases were a leading cause (Table 5), which elicits the relationship between decompensated heart failure and acute kidney injury as CRS increases with patients with multi system affection. There was statistically significant relation between type of CRS and CKD ($P= 0.011^*$). On the other hand, there were no statistically significant relations with DM ($P= 0.643$), or IHD ($P= 0.625$). In agreement to our results Gigante et al., showed that diabetes mellitus ($p = 0.45$), HTN ($p = 0.27$), ischemic heart disease ($p = 0.1$) and COPD ($p = 0.21$) are not significant risk factors for the onset of CRS (16). Also, Shah et al., showed that the association of co-morbidities HTN, DM, COPD and CAD with outcome were found to be statistically insignificant (15). On the other hand Reddy et al., showed that there is a significant association between CRS and DM ($P = 0.030$), COPD ($P = 0.016$), and CKD ($P > 0.001$) with CRS (14).

Limitations

The present study has some limitations; sample size is one of them, as our sample was comparatively less. Future studies with larger sample size and more comprehensive and longer follow-up are required to validate the findings. In addition, the study was conducted in a tertiary care hospital in a city. Thus, the findings cannot be extrapolated to the general population, including rural citizens. Nevertheless, the present study provides a basis for future studies to study the subtypes of CRS and their individual pathophysiology (18).

Conclusion

Current study suggests that CRS type II had the highest prevalence of the CRS subtypes. Moreover, types of CRS are related to chronic diseases, CRS is associated with CKD.

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