Medical Science

25(109), March, 2021

Prevalence of chronic kidney disease among heart failure patients, single center study, Saudi Arabia

Raneem A Alraheili[1]✉, Bayan S Alalawi[1], Khalid A Alsaedi[2], Naif N Alajmi[3], Fisal M Haobani[4], Zainab A Alsinan[5], Fayez D Althobaiti[6], Ahmad R Alnadri[4], Mohammed A Alburi[4], Ali B Alaithan[4], Abdullah S Alfayez[7], Raghad A Alshareef [8], Alaa A Alraheili[9]

To Cite:
Alraheili RA, Alalawi BS, Alsaedi KA, Alajmi NN, Haobani FM, Alsinan ZA, Althobaiti FD, Alnadri AR, Alburi MA, Alaithan AB, Alfayez AS, Alshareef RA , Alraheili AA. Prevalence of chronic kidney disease among heart failure patients, single center study, Saudi Arabia. *Medical Science*, 2021, 25(109), 662-670

Author Affiliation:
[1]Medical Intern, College of Medicine, Taibah University, Madinah, Saudi Arabia
[2]PharmD, King Abdullah Medical City, Mecca, Saudi Arabia
[3]Medical Student, College of Medicine, Al Maarefa University, Riyadh, Saudi Arabia
[4]Medical Student, College of Medicine, Vision Colleges, Riyadh, Saudi Arabia
[5]Medical Intern, College of Medicine, Imam Abdulrahman bin Faisal University, Dammam, Saudi Arabia
[6]Medical Student, College of Medicine, Taif University, Taif, Saudi Arabia
[7]Medical Intern, College of Medicine, Sulaiman AlRajhi University, Al Qassim, Saudi Arabia
[8]Medical Student, College of Medicine, Hail University, Hail, Saudi Arabia
[9]Internal Medicine Resident, Internal Medicine Department, Prince Mohammed Bin Abdulaziz Hospital, Madinah, Saudi Arabia

✉**Corresponding author**
Medical Intern, College of Medicine, Taibah University, Madinah,
Saudi Arabia;
Email: dr.raneemalraheili@gmail.com

Peer-Review History
Received: 03 February 2021
Reviewed & Revised: 04/February/2021 to 08/March/2021
Accepted: 09 March 2021
Published: March 2021

Peer-review Method
External peer-review was done through double-blind method.

ABSTRACT

Background: The interaction between heart and kidneys has increased, and parts of the pathophysiological background for the cardiorenal syndrome have been established. This study aimed to determine the prevalence of Chronic Kidney Disease (CKD) among Heart Failure (HF) patients. *Methods:* This is a cross-sectional study included 1559 patients, who were admitted with a diagnosis of HF during the period from 1-March-2011 till 20-June-2019 at Madinah cardiac center. All patients were divided into five renal function categories based on the estimated glomerular filtration rate. *Results*: Of the total of 1559 patients, 67.2% were males, 51.3% were hypertensive, 56.1% were diabetic and 49.1% were anemic. About 9.8% of HF patients had stage I CKD, 29.6% had stage II, 41.9% had stage III, 15% had stage IV, and 3.9% had stage V. Patients with CKD were significantly had valvular heart diseases ($p<0.001$), history of ACS ($p=0.002$), rheumatic heart diseases ($p=0.043$), anemia ($p<0.001$), hypertension ($p<0.001$), diabetes mellitus ($p<0.001$), stroke ($p=0.003$) and smoking ($p<0.001$). *Conclusion*: About 9.8% of HF patients had stage I CKD, 29.6% had stage II, 41.9% had stage III, 15% had stage IV and 3.9% had end stage renal disease.

Keywords: Heart Failure, Chronic Kidney Diseases, Glomerular Filtration Rate

1. INTRODUCTION

Heart Failure (HF) is defined as an abnormality in cardiac structure or function that leads to the inability of the heart to maintain sufficient blood flow to meet the physiological requirements of the metabolizing tissues or can do so at the expense of high filling pressure (AlHabeeb et al., 2019). HF has become a high priority health issue due to its high prevalence particularly among the older age group, and the high rates of associated morbidity and

mortality (Sánchez-Torrijos et al., 2006; Löfman et al., 2016). Chronic Kidney Disease (CKD) is a disorder of gradual or permanent loss of renal function, resulting in renal failure (Silverberg et al., 2000). The diagnosis of CKD is often made based on estimated Glomerular Filtration Rate (eGFR) which provides a more precise approximation of renal function than elevated serum creatininealone (Heywood, 2007).

Our knowledge about the interaction between kidneys and heart has increased over the years, and many parts of the pathophysiological background of the cardiorenal syndrome have been recognized (Pai, 2015). The heart and renal function are closely linked together by the sympathetic nervous system, hemodynamic, and neurohormones. The cardiorenal syndrome is complex, as renal diseases and HF share the same risk factors, which work together and potentiate each other (Löfman et al., 2016). HF is associated with a reduction in renal blood flow and a further decrease in eGFR (Pai, 2015; Alamoudi et al. 2021). Progressive renal ischemia leads to activation of the Renin Angiotensin Aldosterone System (RAAS) and an increase in sympathetic activity; both have toxic effects on the renal tissues (Yu, 2003). Angiotensin Converting Enzyme Inhibitors (ACEIs) is pivotal in the management of systolic HF, by blocking the RAAS which preserves renal function and decreases mortality rate (Smith et al., 2006).

The presence of CKD in HF patients has a critical role in the pathophysiology and progression of HF over time (Ärnlöv, 2009). HF patients had volume overload which leads to an increase in the central venous pressure in their blood vessels with low systemic pressure, which leads to compromise in the renal perfusion pressure (Afsar et al., 2015). Also, there is an activation of intrarenal sensors and arterial baroreceptors leading to the activation of the sympathoadrenal system, the RAAS, and intravascular volume. These factors will lead to intrarenal and peripheral vasoconstriction, which causing a further decrease in the renal blood flow and eGFR, leading to RD (Valente et al., 2014). Given the growing incidences of CKD among HF patients, this study aimed to determine the prevalence of CKD in hospitalized HF patients in Madinah cardiac center, Saudi Arabia.

2. MATERIALS AND METHODS

Study Design, Study Setting, and Study Period

This is a cross-sectional study conducted at Madinah cardiac center involving patients with HF registered in the Health Management Information System (HMIS) database during the period from 1-March-2011 to 20-June-2019.

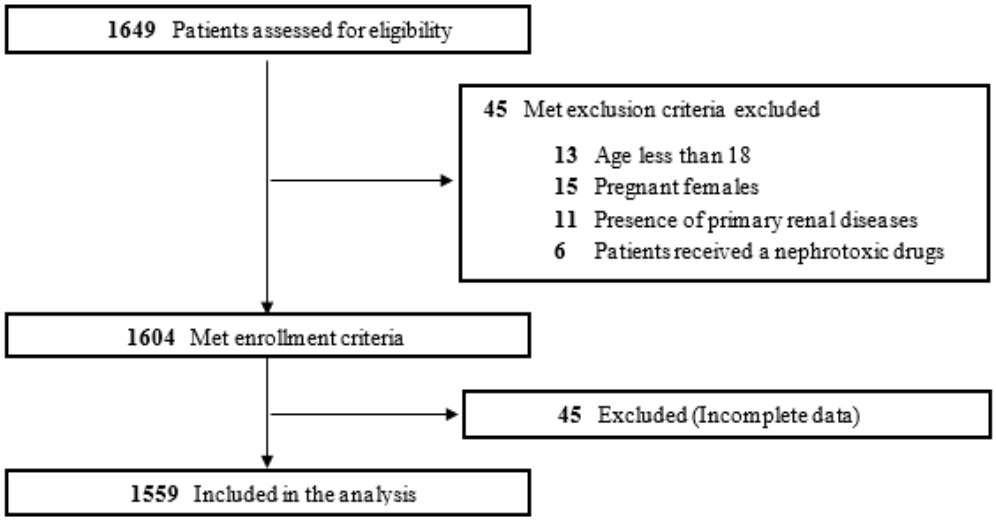

Figure 1 Flow chart of the study population

Study Population

We reviewed the electronic medical records from the HMIS. A total of 1649 patients were identified as having a documented clinical diagnosis of HF. The diagnosis of HF was also confirmed through chart review for symptoms and radiographic findings consistent with the diagnosis. Patients with Left Ventricular Ejection Fraction (LVEF) ≤40% were classified as HF with Reduced Ejection Fraction (HFREF), and those with an LVEF >40% were classified as HF with Preserved Ejection Fraction (HFPEF) as determined by echocardiography were included in the study. Age less than 18 years old, pregnant females, and patients who received nephrotoxic agents during hospitalization were excluded from the study. The presence of primary renal diseases was set as exclusion criteria as well. Of the remaining 1604 patients, we excluded 45 patients with incomplete data, yielding 1559 patients for analysis (Figure 1).

GFR estimation

GFRwas estimated depending on the equation made by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) as the following: eGFR = 141 × min (Scr / κ, 1)α × max (Scr / κ, 1)-1.209 × 0.993Age × 1.018 [if female] × 1.159 [if black] where: Scr is serum creatinine in mg/dL, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males. All patients were divided according to the current National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) recommendations into five renal function categories with eGFR (mL/min/ 1.73 m2): Stage I (eGFR ≥90, normal function), Stage II (eGFR 60–89, mild dysfunction), Stage III (eGFR 30–59, moderate dysfunction), Stage IV (eGFR 15–29, severe dysfunction) and Stage V (eGFR <15, End Stage Renal Disease [ESRD]) (Myers et al., 2006). These categories are only considered as renal function strata and not CKD stages due to lacking data on albuminuria.

Ethical Approval

The research ethics committee of Madinah cardiac center approved this study protocol (approval number: IRB00010413). All study parts were conforming to the declaration of Helsinki Ethical Principles for medical research involving human subjects as revised in 1975.

Statistical Analysis

Data were analyzed using the Statistical Package for Social Science software version 23. Continuous data were presented as median (minimum - maximum) as they were not normally distributed when tested by the Shapiro-Wilk test, while the categorical data were presented as frequencies and percentages. Baseline demographic and clinical variables were compared between the five stages of CKD using the Pearson Chi-squared test for categorical variables and the Kruskal–Wallis test for continuous variables. P value was considered significant if it is ≤ 0.05.

3. RESULTS

Out of 1559 patients included in the analysis, 1047 (67.2%) were males, 585 (37.5%) had a history of Acute Coronary Syndrome (ACS), 799 (51.3%) were hypertensive, 874 (56.1%) were diabetic, 280 (18.0%) were smokers, 766 (49.1%) were anemic at the time of admission, and 188 (12.1%) were on Angiotensin Converting Enzyme Inhibitors (ACEIs) (Table 1).

Table 1 Sociodemographic and clinical characteristics of the study population

Variables	Number (n=1559)	(%)
Gender		
Male	1047	(67.2)
Female	512	(32.8)
Cardiac History		
Myocardial infarction	122	(7.8)
Atrial fibrillation	208	(13.3)
Arrhythmias	96	(6.2)
Valvular heart disease	344	(22.1)
Acute coronary syndrome	585	(37.5)
Rheumatic heart diseases	34	(2.2)
Family history of CAD	41	(2.6)
Percutaneous coronary interventions	142	(9.1)
Coronary artery bypass grafting	91	(5.8)
Valve replacement	35	(2.2)
Cardiac device	96	(6.2)
Cardiac arrest	47	(3.0)
Noncardiac History		
Smoking	280	(18.0)
Anemia	766	(49.1)
Hypertension	799	(51.3)

Diabetes Mellitus	874	(56.1)
Stroke	100	(6.4)
Peripheral vascular disease	20	(1.3)
Hyperlipidemia	117	(7.5)
Preadmission Medications		
Aspirin	69	(4.4)
Clopidogrel	224	(14.4)
Angiotensin converting enzyme inhibitors	188	(12.1)
Calcium channel blockers	31	(2.0)
Beta blockers	264	(16.9)
Digoxin	143	(9.2)
Anticoagulants	96	(6.2)
Diuretics	107	(6.9)
Statin	179	(11.5)
Iron supplements	87	(5.6)

About 9.8% of HF patients had stage I CKD, 29.6% had stage II, 41.9% had stage III, 15% had stage IV and 3.9% had ESRD. (Figure 2) showed the prevalence of five stages of CKD regarding age categories, type of HF, HTN, and DM. Patients with CKD were significantly older. Median (minimum - maximum) of age was 62 (18-99) years in patients with stage II CKD compared to 73 (26-102) years in patients with stage V CKD ($p<0.001$). Patients with CKD were significantly had valvular heart diseases ($p<0.001$), a history of ACS ($p=0.002$), rheumatic heart diseases ($p=0.043$), anemia ($p<0.001$), Hypertension (HTN) ($p<0.001$), Diabetes Mellitus (DM) ($p<0.001$), stroke ($p=0.003$) and smoking ($p<0.001$). There was no significant association in atrial fibrillation, myocardial infarction, prior percutaneous coronary interventions, or coronary artery bypass grafting. Other baseline clinical characteristics are displayed in (Table 2).

Table 2 Baseline clinical characteristic stratified by CKD stages (n=1559)

Variable	CKD Stages										P value
	I (n=149)(9.6%)		II (n=461)(29.6%)		III (n=654)(41.9%)		IV (n=234)(15.0%)		V (n=61)(3.9%)		
	Number (%) / Median (Minimum - Maximum)										
Age	47	(18-87)	62	(18-99)	71	(32-108)	73	(24-110)	73	(26-102)	<0.001
Gender											
Male	103	(69.1)	343	(74.4)	444	(67.9)	120	(51.3)	37	(60.7)	<0.001
Female	46	(30.9)	118	(25.6)	210	(32.1)	114	(48.7)	24	(39.3)	<0.001
Cardiac History											
Myocardial Infarction	5	(3.4)	36	(7.8)	58	(8.9)	19	(8.1)	4	(6.6)	0.260
Atrial Fibrillation	17	(11.4)	55	(11.9)	93	(14.2)	34	(14.5)	9	(14.8)	0.717
Arrhythmias	14	(9.4)	28	(6.1)	40	(6.1)	12	(5.1)	2	(3.3)	0.404
Valvular heart disease	50	(33.6)	99	(21.5)	128	(19.6)	47	(20.1)	20	(32.8)	<0.001
ACS	37	(24.8)	163	(35.4)	274	(41.9)	90	(38.5)	21	(34.4)	0.002
Rheumatic heart diseases	12	(8.1)	7	(1.5)	12	(1.8)	3	(1.3)	0	(0.0)	<0.001
Family history of CAD	4	(2.7)	12	(2.6)	18	(2.8)	7	(3.0)	0	(0.0)	0.771
PCI	7	(4.7)	41	(8.9)	71	(10.9)	18	(7.7)	5	(8.2)	0.161
CABG	4	(2.7)	24	(5.2)	41	(6.3)	17	(7.3)	5	(8.2)	0.315
Valve replacement	9	(6.0)	8	(1.7)	11	(1.7)	5	(2.1)	2	(3.3)	0.021
Cardiac device	10	(6.7)	23	(5.0)	43	(6.6)	15	(6.4)	5	(8.2)	0.767
Cardiac arrest	3	(2.0)	6	(1.3)	26	(4.0)	11	(4.7)	1	(1.6)	0.043

Noncardiac History											
Current smoker	39	(26.2)	104	(22.6)	106	(16.2)	24	(10.3)	7	(11.5)	<0.001
Anemia	61	(40.9)	179	(38.8)	325	(49.7)	154	(65.8)	47	(77.0)	<0.001
Hypertension	40	(26.8)	189	(41.0)	375	(57.3)	156	(66.7)	39	(63.9)	<0.001
Diabetes mellitus	52	(34.9)	215	(46.6)	392	(59.9)	173	(73.9)	42	(68.9)	<0.001
Stroke	5	(3.4)	20	(4.3)	49	(7.5)	20	(8.5)	6	(9.8)	0.043
PVD	0	(0.0)	4	(0.9)	10	(1.5)	4	(1.7)	2	(3.3)	0.274
Hyperlipidemia	3	(2.0)	36	(7.8)	56	(8.6)	18	(7.7)	4	(6.6)	0.104
Medications											
Aspirin	8	(5.4)	19	(4.1)	27	(4.1)	10	(4.3)	5	(8.2)	0.624
Clopidogrel	13	(8.7)	65	(14.1)	91	(13.9)	46	(19.7)	9	(14.8)	0.054
ACEIs	32	(21.5)	51	(11.1)	83	(12.7)	19	(8.1)	3	(4.9)	<0.001
CCB	0	(0.0)	7	(1.5)	12	(1.8)	8	(3.4)	4	(6.6)	0.013
Beta blockers	33	(22.1)	92	(20.0)	98	(15.0)	34	(14.5)	7	(11.5)	0.042
Digoxin	20	(13.4)	44	(9.5)	57	(8.7)	18	(7.7)	4	(6.6)	0.332
Anticoagulants	8	(5.4)	26	(5.6)	43	(6.6)	18	(7.7)	1	(1.6)	0.451
Diuretics	11	(7.4)	40	(8.7)	38	(5.8)	13	(5.6)	5	(8.2)	0.359
Statin	18	(12.1)	45	(9.8)	88	(13.5)	25	(10.7)	3	(4.9)	0.157
Iron supplements	9	(6.0)	30	(6.5)	28	(4.3)	16	(6.8)	4	(6.6)	0.445
ACS; Acute Coronary Syndrome, CAD; Coronary Artery Disease, PCI; Percutaneous Coronary Interventions, CABG; Coronary Artery Bypass Grafting, PVD; Peripheral Vascular Disease, ACEIs; Angiotensin Converting Enzyme Inhibitors, CCB; Calcium Channel Blockers											

Table 3 laboratory tests results stratified by CKD stages (n=1559)

Variable	CKD Stages										P value
	I (n=149)(9.6%)		II (n=461)(29.6%)		III (n=654)(41.9%)		IV (n=234)(15.0%)		V (n=61)(3.9%)		
	Median (Minimum - Maximum)										
CBC											
Hemoglobin (g/dl)	14.0	(7 -19)	14.0	(5-19)	13.0	(7-18)	11.0	(7-17)	11.0	(7-15)	<0.001
HCT%	42.1	(24-55)	40.8	(19-56)	38.5	(22-52)	34.9	(20-51)	33.0	(22-46)	<0.001
RBC $\times 10^{12}/\mu L$	4.8	(3-6)	4.7	(3-12)	4.42	(3-7)	4.1	(2-7)	3.6	(0-5)	<0.001
MCV fL	86.1	(59-99)	87.1	(61-108)	87.9	(39-105)	87.2	(66-106)	88.9	(73-108)	0.201
WBC $\times 10^3/\mu L$	8.4	(3-20)	7.9	(3-27)	8.9	(1-87)	9.1	(3-32)	10.3	(4-39)	<0.001
Platelet count $\times 10^3/\mu L$	251.0	(112-587)	243.0	(65-69)	244.0	(79-632)	243.0	(56-813)	201.0	(114-577)	0.079
Kidney Function Test											
eGFR	100.0	(90-257)	71	(90-60)	46	(30-60)	24	(15-30)	12	(5-15)	<0.001
Creatinine (μmol/L)	73.0	(34-93)	94.0	(49-139)	126.5	(78-206)	203.0	(135-361)	392.0	(234-641)	<0.001
BUN (mmol/L)	4.6	(1-11)	6.3	(2-21)	8.8	(2-29)	16.5	(6-55)	28.4	(10-67)	<0.001
Lipid Profile (mmol/L)											
LDL	2.3	(1-7)	2.2	(0-11)	2.1	(0-7)	1.6	(1-7)	1.7	(1-4)	<0.001
HDL	0.9	(0-2)	0.9	(0-8)	0.9	(0-2)	0.9	(0-2)	0.9	(0-2)	0.395
Triglycerides	1.2	(0-3)	1.1	(0-4)	1.0	(0-5)	1.0	(0-4)	1.1	(0-5)	0.476
Total cholesterol	3.8	(2-9)	3.7	(1-8)	3.7	(1-9)	3.2	(1-9)	3.3	(2-6)	<0.001
CBC, Complete blood count; HCT%, Hematocrit; RBC, Red Blood Cells; MCV, Mean Corpuscular Volume; WBC, White Blood Cells; eGFR,estimated glomerular filtration rate; BUN, Blood Urea Nitrogen; LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein.											

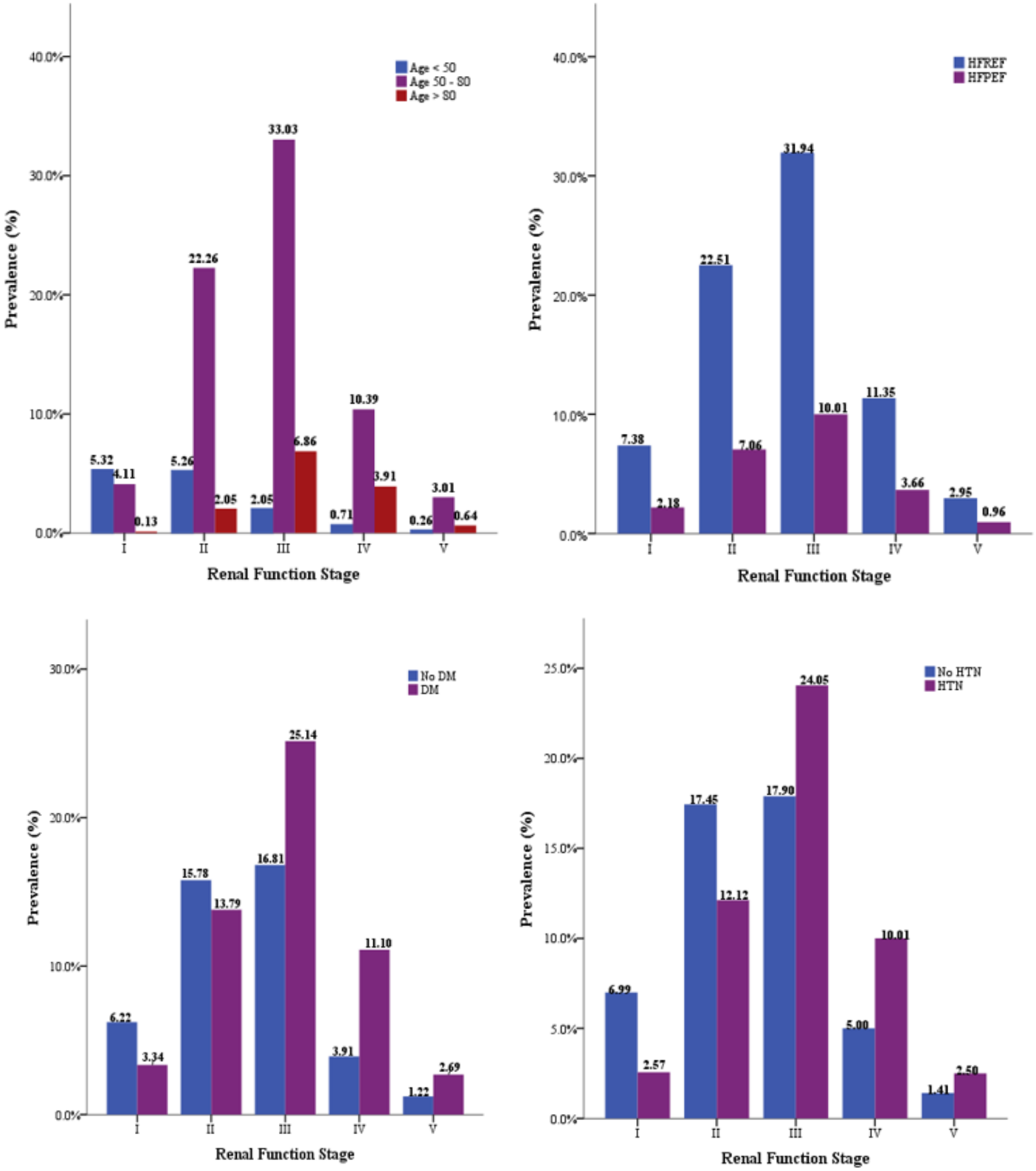

Figure 2 Prevalence of chronic kidney disease stages in heart failure patients in relation to: (A) age categories, (B) heart failure type, (C) diabetes mellitus, (D) hypertension

Figure 2 showed the prevalence of five stages of CKD regarding age categories, type of HF, HTN, and DM. The use of medical therapy was differed by renal function stages. The use of ACEIs decreased markedly with increasing the degree of renal impairment (21.5%, 11.1%, 12.7%, 8.1%, and 4.9% respectively for patients with stage I through V) ($p<0.001$). Beta blockers were used in 22.1% of patients with stage I CKD, other stages from II to V respectively were 20.0%, 15.0%, 14.5%, and 11.5% ($p=0.042$). The use of calcium channel blockers was higher in patients with severe renal impairment compared to others; however, diuretics and digoxin using were not substantially different.

Regarding laboratory data, patients with CKD exhibited a significantly lower hematological profile. The median Hb level was 14 g/dl and 11 g/dl in patients with stage II and stage IV-V, respectively ($p<0.001$). Median eGFR was 100, 71, 46, 24, and 12 mL/min/1.73 m^2 in patients with stage I, II, III, IV, and V, respectively. Also, patients with advanced renal impairment more often exhibited a lower level of total cholesterol and low density lipoprotein ($p<0.001$). Other clinical variables are displayed in (Table 3).

4. DISCUSSION

Renal impairment in HF patients is becoming more frequent and severedespite significant advances in the treatment of HF (Ahmed & Campbell, 2008). Clinical HF is largely a disease of the elderly and it is often accompanied by HTN and DM, so it is not surprising that CKD is frequently coexisting with HF (Costanzo, 2019). In the current study, we found that about 9.8% of HF patients had stage I CKD, 29.6% had stage II, 41.9% had stage III, 15% had stage IV and 3.9% had ESRD. Previous studies have reported a relatively high prevalence of renal impairment among patients hospitalized with HF. In accordance with the results of the current study, a recent retrospective cohort study done on 47716 patients in the Swedish HF registry found the prevalence of CKD was 11%, 38.2%, 40.1%, 8.9%, and 1.7% for those with stage I to V) (Löfman et al., 2016).

Similarly, a past meta-analysis evaluated the association between renal impairment and HF revealed that 63% of patients had CKD (defined as eGFR <60) (Liu, 2011). A recent study reported that 45-63% of systolic HF patients had CKD (Ronco & Di Lullo, 2016). Moreover, Baydemir et al. (2017) showed that 81% of HF patients had stage III CKDand 19% had stage IV. It was also reported that more than 50% of all HF patients have moderate to severe CKD. It found that CKD was present in 64% of patients, of whom 44%, 13%, and 7% of patients, respectively had stage III, IV, and VCKD (Sarnak, 2014). However, in a study conducted on 1301 patients registered in a systolic HF disease management program, just 26% were found to have CKD (Hebert et al., 2010).

HF can cause renal impairment through different pathophysiological mechanisms. This finding of the high prevalence of CKD among HF patients may be due to an underlying severe cardiac disease, the presence of multiple comorbidities, or due to medication (Verdiani et al., 2010; Aradhey et al. 2020; Kaur et al. 2020). HF is usually associated with volume overload and high central venous pressure with low systemic pressure which decreases the renal perfusion pressure (Kottgen et al., 2007). Also, activation of arterial baroreceptors and intrarenal sensors cause the activation of RAAS and the sympathoadrenal system. All these factors will lead to peripheral and intrarenal vasoconstriction, which further decreases the renal blood flow and eGFR. With time, the presence of all these changes can cause CKD (Matsushita et al., 2017).

5. CONCLUSION

Renal impairment is common in HF patient. About 9.8% of HF patients had stage I CKD, 29.6% had stage II, 41.9% had stage III, 15% had stage IV and 3.9% had ESRD. The presence of renal impairment has a critical role in the progression of HF over time. Strategies on identification and early treatment of cardiorenal syndrome in this clinical setting are necessary to improve the prognosis of HF patients.

Informed consent

Written and oral informed consent was obtained from all individual participants included in the study.

Ethical approval

The research ethics committee of Madinah cardiac center approved this study protocol (approval number: IRB00010413).

Author's contributions

All authors contributed to the research and/or preparation of the manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

We are grateful to Engineer. Mohammed Yousef Mahrous, head of E-health department at Madinah cardiac center for providing the study data.

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. Afsar B, Ortiz A, Covic A, Solak Y, Goldsmith D, Kanbay M. Focus on renal congestion in heart failure. Clinical Kidney Journal 2015; 9(1):39-47.
2. Ahmed A, Campbell RC et.al. Epidemiology of chronic kidney disease in heart failure. Heart Fail Clin 2008;4(4):387–399.
3. Alamoudi HA, Alzahrani RM, Hawsa AA, Lary SO, Awlia AM, Alothmani HH, Zaher NA, Mosli RH, Alhozali HM, Mosli HH, Merdad MA. The immediate effect of hemodialysis on thyroid function. Med Sci, 2021, 25(107), 112-119
4. AlHabeeb W, Al-Ayoubi F, AIGhalayini K, Al Ghofaili F, Al Hebaishi Y, Al-Jazairi A. Saudi Heart Association (SHA) guidelines for the management of heart failure. J Saudi Hear Assoc 2019; 31(4): 204-253.
5. Aradhey P, Bakre A, Kumar S, Acharya S. Clinical profile of Uremic polyneuropathy in Chronic Kidney Disease patients. Med Sci, 2020, 24(102), 945-951
6. Ärnlöv J. Diminished renal function and the incidence of heart failure. Curr Cardiol Rev 2009; 5(3): 223–227.
7. Baydemir C, Ural D, Karaüzüm K, Balci S, Argan O, Karaüzüm I. Predictors of long-term mortality and frequent re-hospitalization in patients with acute decompensated heart failure and kidney dysfunction treated with renin-angiotensin system blockers. Med Sci Monit 2017;23:3335–3344.
8. Costanzo MR. Cardiorenal syndrome in heart failure patients I . Cardiorenal Syndrome : What every physician needs to know . II . Diagnostic confirmation : are you sure your patient has cardiorenal syndrome? 2019;1–33.
9. Hebert K, Dias A, Delgado MC, Franco E, Tamariz L, Steen D. Epidemiology and survival of the five stages of chronic kidney disease in a systolic heart failure population. Eur J Heart Fail 2010;12(8):861–865.
10. Heywood JT, Fonarow GC, Costanzo MR, Mathur VS, Wigneswaran JR, Wynne J. 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(6): 422–430.
11. Kaur B, Marwaha S, Agrawal BK. Study of Anemia in Chronic Heart Failure. Med Sci, 2020, 24(102), 891-896
12. Kottgen A, Russell SD, Loehr LR, Crainiceanu CM, Rosamond WD, Chang PP. Reduced kidney function as a risk factor for incident heart failure: The Atherosclerosis Risk in Communities (ARIC) study. J Am Soc Nephrol 2007;18(4):1307–1315.
13. Liu PP. Cardiorenal syndrome in heart failure: A cardiologist's perspective. Can J Cardiol 2011;24(7):25-29.
14. Löfman I, Szummer K, Hagerman I, Dahlström U, Lund LH, Jernberg T. Prevalence and prognostic impact of kidney disease on heart failure patients. Open Hear 2016; 3(1): e000324.
15. Matsushita K, Kwak L, Hyun N, Bessel M, Agarwal SK, Loehr LR. Community burden and prognostic impact of reduced kidney function among patients hospitalized with acute decompensated heart failure: The Atherosclerosis Risk in Communities (ARIC) study community surveillance. PLoS One 2017;12(8).
16. Myers GL, Miller WG, Coresh J, Fleming J, Greenberg N, Greene T. Recommendations for improving serum creatinine measurement: A report from the laboratory working group of the national kidney disease education program. Clin Chem 2006; 52(1): 5–18.
17. Pai P. Cardiorenal syndrome. Hong Kong J Nephrol 2015; 17(2): 36–45.
18. Ronco C, Di Lullo L.Cardiorenal syndrome in western countries: epidemiology, diagnosis and management approaches. Kidney Dis 2016;2(4):151–163.
19. Sánchez-Torrijos J, Gudín-Uriel M, Nadal-Barangé M, Jacas-Osborn V, Trigo-Bautista A, Giménez-Alcalá M. Prognostic Value of discharge hemoglobin level in patients hospitalized for acute heart failure. Rev Esp Cardiol 2006; 59(12): 1276–1282.

20. Sarnak M. A patient with heart failure and worsening kidney function. Clinical Journal of the American Society of Nephrology 2014;9(10):1790-1798.
21. Silverberg DS, Wexler D, Blum M, Keren G, Sheps D, Leibovitch E. The use of subcutaneous erythropoietin and intravenous iron for the treatment of the anemia of severe, resistant congestive heart failure improves cardiac and renal function and functional cardiac class, and markedly reduces hospitalizations. J Am Coll Cardiol 2000; 35(7): 1737–1744.
22. Smith GL, Lichtman JH, Bracken MB, Shlipak MG, Phillips CO, DiCapua P. Renal impairment and outcomes in heart failure. systematic review and meta-analysis. J Am Coll Cardiol 2006; 47(10): 1987–1996.
23. Valente MAE, Hillege HL, Navis G, Voors AA, Dunselman PHJM, Van Veldhuisen DJ. The chronic kidney disease epidemiology collaboration equation outperforms the modification of diet in renal disease equation for estimating glomerular filtration rate in chronic systolic heart failure. Eur J Heart Fail 2014;16(1):86–94.
24. Verdiani V, Lastrucci V, Nozzoli C. Worsening renal function in patients hospitalized with acute heart failure: risk factors and prognostic significances. Int J Nephrol 2010;2011:1–5.
25. Yu HT. Progression of chronic renal failure. Arch Intern Med 2003; 163(12): 1417–1429.

 ISSN 2321–7359 EISSN 2321–7367 I OPEN ACCESS