eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: <u>www.bioscmed.com</u>

# Factors Affecting Chronic Heart Failure in Patients with End-Stage Renal Disease at Bhayangkara Hospital Denpasar

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### ARTICLE INFO

#### **Keywords**:

Factors Chronic heart failure End-Stage renal disease Prevention

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v6i7.545

# ABSTRACT

Background: Patients with end-stage renal disease (ESRD) have a twofold risk of developing heart failure. A number of factors in ESRD patients are related to chronic heart failure (CHF). The intervention of cardiovascular risk factors in the early stages of chronic kidney disease (CKD) can reduce mortality from heart disease and slow the severity of kidney deterioration. This study aims to examine the factors that affect CHF in patients with ESRD. Methods: This study was a cross-sectional analytic observational study of 49 patients with ESRD based on consecutive sampling. The data collected were primary and secondary data on ESRD patients at the Cardiac Polyclinic, Internal Medicine Polyclinic, and the Medical Records Unit Bhayangkara Hospital Denpasar. Results: In this study, it was found that most patients were in the age group  $\geq$ 40 years (92%) and male gender (63%). From the chi-square test analysis, it was found that the factors affecting CHF in patients with ESRD are hypertension (HT) (p-value < 0.001) with prevalence ratio (PR) 11.19 (1.69-73.92), type 2 diabetes mellitus (T2DM) (pvalue = 0.008) with PR 1.72 (1.18-2.51), obesity (p-value < 0.001) with PR 6.67 (2.34-18.92), and smoking (p-value = 0.027) with PR 1.6 (1.02-2.49). Conclusion: It can be concluded that the factors affecting CHF in patients with ESRD are HT, T2DM, obesity, and smoking. The results of this study are expected to be used as an illustration so that in the future, prevention can be made for factors affecting CHF in ESRD patients.

#### 1. Introduction

Chronic kidney disease (CKD) and heart failure are two chronic diseases that have become epidemics worldwide. The incidence and prevalence of these two diseases have increased the most in the elderly population as well as the population with comorbid diseases such as hypertension (HT) and diabetes mellitus (DM). CKD is a disease in the form of a gradual decrease in kidney function due to damage to the kidneys. Kidney damage can include pathological conditions in the kidney, persistent proteinuria, and abnormalities during urination such as hematuria, as well as a decrease in the glomerular filtration rate (GFR) to below 60 mL/minute / 1.73m2 on two measurements in a range of > 90 days and, is not associated with reversible conditions such as depletion of body fluid volume.<sup>1,2</sup>

End-stage renal disease (ESRD) is chronic kidney disease with the uremic syndrome, which is categorized as stage 5 in the classification of chronic kidney disease according to the National Kidney Foundation, with a glomerular filtration rate (LFG) <15 ml/minute / 1.73 m<sup>2.3</sup> ESRD is currently one of the most recent health problems, given its increasing incidence recently. Centers Disease Control (CDC) reports that in the period 1999-2004 there were 16.8% of the population over 20 years of age experienced CKD, with 0.4% of the population suffering from stage 4 and/or stage 5.4. Indonesia is a country with a high rate of kidney failure patients. It is estimated that the number is 100 sufferers per one million population in a year. Based on data from the Indonesian Health Profile in 2006, ESRD ranks the 6<sup>th</sup> as the cause of death for patients hospitalized throughout Indonesia, with a Proportional Mortality Rate (PMR) of 2.99%.<sup>5</sup>

ESRD is often accompanied by other pathological conditions (comorbid conditions). Cardiovascular disease is a major cause of premature death in CKD patients.<sup>6</sup> The prevalence of cardiomyopathy, ischemic heart disease, and heart failure was found to be quite high in ESRD patients on dialysis. Data by echocardiography in Canada showed that only 16% of patients on dialysis had a normal heart, the remaining 75% had left ventricular hypertrophy, concentric left ventricular hypertrophy as much as 41%, and systolic dysfunction in 16%. In ESRD patients undergoing dialysis therapy, 38% were found to have ischemic heart disease, and 35% had heart failure. The high prevalence of heart failure in ESRD patients undergoing dialysis indicates that the predialitic phase in CKD patients is a condition with a high risk of heart disease.7,8,9

Patients with ESRD have a twofold risk of developing heart failure. Heart failure is defined as a syndrome caused by a disturbance in the structure and function of the heart that causes the heart to fail to pump blood.<sup>10</sup> Each year, among patients who have just undergone hemodialysis, 36% have CHF, and as

many as 7% experience CHF while undergoing hemodialysis. CHF is a major contributor to death from heart disease in ESRD patients undergoing hemodialysis. In a prospective study by Damman, et al. (2016), patients with CHF had an average life expectancy of only 36 months compared to patients without CHF who had an average life expectancy of 62 months.<sup>11</sup> A number of factors in ESRD patients are related to CHF. These factors include age, male gender, the presence of hypertension, diabetes mellitus, atherosclerosis, and structural abnormalities of the heart.<sup>12,13</sup>

The occurrence of heart failure in patients with ESRD is closely related to the occurrence of cardiorenal syndrome (CRS). Cardiorenal Syndrome (CRS) is a condition, both acute and chronic, in which the heart or kidneys fail to compensate for impaired function and have an impact on other organ function disorders or secondary to systemic diseases that interfere with both, resulting in a dangerous cycle that causes circulatory system failure.14,15 An increase in the filling load of the heart is associated with an increase in renal venous pressure. Renal perfusion pressure is proportional to mean arterial pressure minus left atrial pressure as an index of renal venous pressure. An increase in central venous pressure indicates a decrease in the glomerular filtration rate, which in turn leads to water and sodium retention as well as stimulation of the renin-angiotensinaldosterone (RAAS) system. Therefore, the increase of left and right ventricular end-diastolic pressures not only interferes with cardiac output but also causes renal dysfunction with increased renal venous pressure.<sup>16,17</sup> The occurrence of CHF in patients with ESRD is included in type 4 CRS according to the Ronco classification as follows:

Type 1	Acute cardiorenal syndrome			
	Acute heart disorders impact kidney function			
Type 2	Chronic cardiorenal syndrome			
	Chronic heart disorders have an impact on kidney function			
Туре З	Acute renocardial syndrome			
	Acute kidney disorders have an impact on heart function			
Туре 4	Chronic renocardial syndrome			
	Chronic kidney disorders have an impact on heart function			
Туре 5	Secondary cardiorenal syndrome			
	Systemic disorders impact the function of the heart and kidneys			
	simultaneously.			

CKD and heart disease are closely related. Therefore it is important to identify risk factors for CHF in the CKD patient population to provide early intervention. The intervention of cardiovascular risk factors in the early stages of CKD patients can reduce mortality from heart disease and slow the severity of kidney deterioration. The primary objective of this study was to examine the factors that affect CHF in patients with ESRD

#### 2. Methods

# Study design and data collection

This study is an analytic observational study with a cross-sectional design to prove the effect of age, gender, education level, occupation, smoking, alcohol consumption, obesity, hypertension (HT), diabetes mellitus (DM), and anemia on the occurrence of CHF in patients with ESRD. The data collected were primary and secondary data on ESRD patients from March 1st, 2020, to March 31st, 2021, at the Cardiac Polyclinic, Internal Medicine Polyclinic, and the Medical Records Unit Bhayangkara Hospital Denpasar. 49 participants' samples aged 18 and older were taken consecutively using the non-random sampling method, in which all subjects who came and met the eligibility criteria were included in the study until the required sample size was met. The study began with the preparation of a research proposal, sampling and recording of research data, and finally, analyzing and compiling the research results.

Pediatric patients, patients with pregnancy conditions, autoimmune diseases, or incomplete medical records according to the required variables were excluded. This research has been approved by the local ethical committee.

# Statistical analysis

The data obtained in this study were processed with computer software. All data obtained were entered in Excel and transferred to the SPSS (a statistical program) version 25 for Windows to be analyzed. The data entry on patient characteristics was performed using Microsoft Excel. A descriptive analysis was carried out after it to obtain the basic characteristics of the research subjects and the distribution of the independent variables in the form of age, gender, education level, occupation, smoking, alcohol consumption, height, weight, diagnosis of hypertension and diabetes mellitus and anemia in patients with the ESRD. A descriptive analysis was also carried out to see the frequency of CHF in patients with ESRD.

Variables of gender, education level, occupation, alcohol consumption, smoking, obesity, hypertension, diabetes mellitus, and anemia were stated in nominal variables. In contrast, the age variable is expressed in two types of variables, namely numerical, to see the mean ± SD and nominal. The hemoglobin level of the research subjects was also expressed in numerical variables to see the mean ± SD. Furthermore, a bivariate analysis was carried out to see the effect of age, gender, education level, occupation, smoking, alcohol consumption, height, weight, diagnosis of HT and DM, and anemia on the occurrence of CHF in ESRD patients undergoing treatment at Bhayangkara Hospital Denpasar. The analysis was carried out by using the chi-square test with a bivariate table description according to table 4.2. Fisher's test is performed when the expected value is more than 2 cells in the contingency table. It has an expected value of less than 5. The variable is declared to have a significant relationship if it has a value of pvalue <0.05 with a 95% confidence interval. In addition to the analysis to find the p-value, an analysis was also carried out to find the prevalence ratio value to determine the strength of the relationship with the 95% confidence interval.

# 3. Results

The subjects in this study were patients with ESRD at Bhayangkara Hospital Denpasar, which in the period March 1st, 2020, to March 31st, 2021, were obtained as many as 49 samples. Data were collected from medical records, laboratory results, and patient statements, and obtained the characteristics of the study sample as listed in Table 2 below.

Variable	Frequency (%)		
Age (Mean±SD)	54 ± 13 yo		
<u>≥</u> 40 yo	45 (92%)		
< 40 yo	4 (8%)		
Gender			
Male	31 (63%)		
Female	18 (37%)		
Education Level			
Not taking education	4 (8%)		
Elementary school	14 (29%)		
Junior high school	1 (2%)		
Senior high school	21 (43%)		
Bachelor/Diploma	9 (18%)		
Occupation/Working status			
Working	39 (80%)		
Not working	10 (20%)		
Smoking			
Yes	25 (51%)		
No	24 (49%)		
Alcohol Consumption			
Yes	20 (41%)		
No	29 (59%)		
Obese			
Yes	29 (59%)		
No	20 (41%)		
Hypertension			
Yes	36 (73%)		
No	13 (27%)		
Diabetes Mellitus			
Yes	18 (37%)		
No	31 (63%)		
Anemia			
Yes	38 (78%)		
No	11 (22%)		

Table 2. The basic characteristics of ESRD patients at Bhayangkara Hospital Denpasar

The majority of the patient was > 40 years old (92%) with an average age of 54 years and male gender (63%). In terms of education level, it is found that the majority have graduated from high school education level (43%). As many as 80% of the sample were working before experiencing illness. The comparison of study samples who had smoking and non-smoking habits did not differ much (51% vs. 49%), but in terms of alcohol consumption, more samples had no history of

alcohol consumption (59%). In terms of clinical characteristics, it was found that more samples were obese (59%), had hypertension (73%), did not have diabetes (63%), and as many as 78% of the samples had anemia. Of the 49 study samples, it was found that more patients had CHF than those who did not experience CHF, as listed in Table 3 below.

Table 3	Comparison	of the number	er of patier	ts with ESRD	who have	CHF and who do not
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	CHF (%)	Not CHF (%)	Total (%)
ESRD patients	32 (65,3)	17 (34,7)	49 (100%)

After the univariate analysis was carried out to see the basic characteristics of the sample, then bivariate analysis was carried out to look for factors that influence the occurrence of CHF in patients with ESRD at Bhayangkara Hospital Denpasar. In terms of age, the majority of ESRD patients with CHF were > 40 years old (97%), male (63%), had a higher education level, namely graduated from high school or undergraduate (63%), and had a working status (78%).

Table 4. Table	bivariate analysis	of factors	affecting	CHF in	patients with ESRD.

Variable	ESRD Patients with CHF n (%)	ESRD Patients without CHF n (%)	P-value	PR (CI95%)
Age (Mean±SD)	50,64 ±13,66 yo	54,31 ±12,80 yo		2,75
<u>&gt;</u> 40 yo	31 (97%)	14 (82%)	0,114	(0,49-5,21)
<40 yo	1 (3%)	3 (18%)		(0,49-3,21)
Gender				0,96
Male	20 (63%)	11 (65%)	0,879	(0,63-1,47)
Female	12 (37%)	6 (35%)		(0,03-1,47)
Education Level				
Low-level education (None,	12 (37%)	7 (41%)	0,801	
Elementary school, Junior high				1,05
school)				
High-level education (Senior high				(0,68-1,61)
school, Bachelor/Diploma)				
	20 (63%)	10 (59%)		
Occupation/Working Status				0.91
Not working	7 (22%)	3 (18%)	0,727	
Working	25 (78%)	14 (82%)		(0,57-1,46)
Smoking				1.6
Yes	20 (63%)	5 (29%)	0,027*	1,6
No	12 (37%)	12 (71%)		(1,02-2,49)
Alcohol Consumption				0.91
Yes	16 (50%)	4 (24%)	0,073	
No	16 (50%)	13 (76%)		(0,57-1,46)
Obese				6.67
Yes	29 (91%)	0 (0%)	0,000*	6,67 (2,34-18,92)
No	3 (9%)	17 (100%)		(2,34-18,92)
Hypertension				11,19
Yes	31 (97%)	5 (29%)	0,000*	
No	1 (3%)	12 (71%)		(1,69-73,92)
Diabetes		1		1.70
Yes	16 (50%)	2 (12%)	0,008*	1,72
No	16 (50%)	15 (88%)		(1,18-2,51)
Anemia		1		1.54
Yes	27 (84%)	11 (65%)	0,116	1,56
No	5 (16%)	6 (35%)		(0,79-3,08)

\*significant variable if p value < 0,05 ; CI= confidence interval; PR=prevalence ratio

In terms of clinical characteristics, the majority of patients with ESRD who experienced CHF were in the obese group (91%) and had hypertension (97%) and anemia (84%). Meanwhile, the comparison of ESRD patients with CHF from the diabetes profile (had diabetes and did not have diabetes) was found to be the same, as shown in Table 4.

Of the ten variables carried out by bivariate analysis, the results showed that four variables were significantly associated with affecting CHF in patients with ESRD at Bhayangkara Hospital Denpasar. These variables include smoking (p = 0,027) with a PR value of 1,6 (1,02-2,49), obesity (p = 0,00) with a PR value of 6,67 (2,34-18,92), hypertension (p = 0,00) with a PR value of 11,19 (1,69-73,92) and diabetes mellitus (p =0,008) with a PR value of 1,72 (1,18-2,51). Meanwhile, six other variables, namely age, gender, education level, occupation, alcohol consumption, and anemia, were found to have no significant affecting CHF in patients with ESRD.

# 4. Discussion

This study is a cross-sectional analytical study that examines the effect of 10 sociodemographic variables and clinical characteristics affecting CHF in patients with ESRD at Bhayangkara Hospital Denpasar. In terms of age, the majority of patients with ESRD who experience CHF are more than 40 years old and male gender. These findings are similar to a study by Smith, et al. (2013), who conducted a cohort study to assess the characteristics of 24.331 adult patients with heart failure and CKD. The study stated that more male patients who had ESRD and also experienced heart failure than the female (54.6% vs. 45.4%). Another study also found similar results, namely by Dhingra, et al. (2011) using a multivariate analysis model on 10.181 samples where it was stated that male patients with LFG <60 miles/minute had a twofold greater risk of developing heart failure.<sup>19</sup> These results are similar to the findings in our study, which also found that the cases of ESRD with heart failure were more common in the male sex group (63%), but our study showed no significant relationship between gender and the occurrence of CHF in patients with ESRD. In terms of age, the mean age of patients with ESRD in this study was 54 years. The average age of ESRD patients who had CHF was found to be younger, namely 50,64 years, compared to the group of patients who did not have CHF, namely 54,31 years. Our findings are slightly different from the study by Smith, et al. (2013) where the mean age of ESRD patients with CHF was found to be 68,3 years old.<sup>20</sup> Meanwhile, a study by He, et al. (2017) found that the mean age of ESRD patients with CHF was similar to the findings of our study, namely 58,2 years old.<sup>13</sup>

There is no significant relationship between education level and employment/working status affecting CHF in our study results. Research by He, et al. (2017) found different results, where the level of education was stated to be significantly associated with an increased risk of heart failure. This can be attributed to higher levels of education and decent work status leading to better access to health care by patients taking medication. For the smoking habit variable, this study found a significant relationship between smoking habits affecting heart failure in patients with ESRD.13 In our study also found that smoking increased the risk of heart failure by 1,6 times greater than that of non-smoking patients with ESRD. Smoking habit is one of the traditional risk factors for cardiovascular disease and increased mortality in ESRD patients. Approximately 25% of ESRD patients and 50% of patients undergoing dialysis have a history of smoking, according to a study by Curtis, et al. (2005).<sup>21</sup> In 2013, approximately 14% of dialysis patients in the United States had a smoking habit. Smoking is a modifiable risk factor. Smoking cessation can reduce the risk of cardiovascular disease and slow the progression of chronic kidney damage.22,23

A study by Orth, et al. (2008) found that smoking was an independent risk factor for arterial calcification in ESRD patients, which was associated with an increased risk of cardiovascular disease. Coroner heart disease and peripheral artery disease are common in patients undergoing dialysis.<sup>24</sup> In a prospective study by Horwich, et al. (2001) found that as many as 14% of patients initiating hemodialysis had coronary heart disease and limb ischemia disease. Associated with the condition of heart failure, the presence of coronary heart disease and peripheral arteries is an early clinical condition before the occurrence of heart failure.<sup>25</sup> Another study that supports the findings in our study is the study by Foley, et al. (2005) which found that smoking was independently associated with CHF with a risk of 1,59 times and a greater mortality rate of 1,37 times higher than non-smokers.<sup>26</sup>

Apart from smoking, alcohol consumption and obesity are also basic risk factors for cardiovascular disease. The condition of obesity is associated with hyperlipidemia, which also plays a role as a factor in atherosclerosis in heart disease. This study found that obesity was significantly associated with heart failure in ESRD patients, which increased the risk of heart failure by 6,67 times. The findings in our study are in line with the results of a study by Horwich, et al. (2001), who found that obesity and overweight were significantly associated with heart failure. Obesity causes changes in the hemodynamic profile in the form of neurohormonal changes. In obese patients, changes in cytokines and neuroendocrine profiles modulate the progression of heart failure. In obese patients, changes in proinflammatory cytokines such tumor necrosis factor-alpha (TNF-α) were as observed.25

Adipose tissue produces pro-inflammatory cytokines, particularly TNF-a, which are more abundant in inducing cardiac muscle damage through its pro-apoptotic and negative inotropic effects. Obesity is also associated with changes in the sympathetic nervous system and the reninangiotensin Cohort data from the system. Framingham Heart Study Offspring Cohort showed a 68% increase in relative risk for CKD with a large BMI of > 30 kg / m2 to develop heart failure compared to the group of patients with normal BMI.27 It also mentions anatomical changes in the heart caused by obesity are left ventricular hypertrophy, diastolic dysfunction, and increased left ventricular dimension at the end of the diastolic. The mechanisms that occur in the heart due to obesity are referred to as cardiomyopathy associated with obesity.<sup>1,27</sup>

Our study did not find a significant association between alcohol consumption and heart failure. Research by Bryson, et al. (2006) stated that alcohol consumption has a complex association with CHF and other heart diseases, especially since former drinkers had an increased risk of CHF compared with nondrinkers. The habit of consuming alcohol can cause cardiomyopathy, which is a precursor to heart failure.<sup>28</sup> Another study by Joo, et al. (2019) found that compared to a group of patients who did not consume alcohol, patients with regular alcohol consumption had a 2,2-fold risk of developing ESRD progression and heart failure with a relative risk of 1.38-3.46 and 95% CI.<sup>29</sup>

The results of this study are in line with a study conducted by House, et al. (2019) which also states that hypertension has an effect on affecting CHF in ESRD patients. In patients with ESRD with uncontrolled hypertension where salt and water retention can cause left ventricular hypertrophy, fibrosis, and increased afterload due to increased arterial stiffness. Vasoconstriction and water retention will temporarily increase blood pressure, whereas an increase in preload increases heart contraction through Starling's law.<sup>30</sup> In addition, hypertension patients will often encounter left ventricular hypertrophy, which can cause an imbalance between oxygen supply and demand, resulting in ischemia in heart muscle cells. This ischemic process causes apoptosis of heart cells, accumulation of collagen and extracellular matrix, and leads to interstitial fibrosis. This results in left ventricular stiffness, increased left ventricular filling pressure, impaired diastolic filling, and diastolic dysfunction. These structural and functional abnormalities cause the heart's pumping ability to be impaired and can lead to heart failure.7,8,20 In this study, it was found that the presence of hypertension increases the risk of CHF in patients with ESRD by 11,19 times greater than in patients

without hypertension comorbidities.

Our study found a significant relationship between type 2 diabetes mellitus (T2DM) with CHF in patients with ESRD, with a large risk of 1,72 times compared to the group of patients who did not have T2DM. The results of the study that also support our findings are researched by He, et al. (2017) in a cohort study of chronic renal insufficiency (CRIC) with an average study time of 6,3 years and involving 452 study participants found that conditions of insulin resistance and HbA1c levels were significantly associated with heart failure in patients with chronic renal insufficiency, where insulin resistance causes heart failure 1,16 times higher and high HbA1c levels increase the risk of heart failure 1, 27 times higher.<sup>13</sup> The relationship between T2DM and heart failure was also mentioned by Goyal, et al (2010) where DM is known to increase the risk of heart failure two to six times greater than conditions without diabetes.<sup>22</sup> The cohort population study by Vardeny, et al. (2013) also stated that the condition of insulin resistance which was calculated from random blood sugar levels and HbA1c, found a relationship between them and heart failure conditions.<sup>31</sup>

The association of DM or insulin resistance conditions with the development of heart failure was described by the study by Banerjee, et al. (2013). It is stated that there is strong evidence of a biological effect of high fasting blood sugar levels, which induces heart failure. During periods of myocardial stress, the heart changes to fetal gene programming, inducing an increase in the relative use of glucose for energy instead of using free fatty acids. In conditions of insulin resistance, these changes are also found to be ineffective due to impaired glucose use. As a result, the heart continues to experience a lack of energy which can worsen the condition of heart failure. Another mechanism is that insulin resistance also has a direct effect on the myocardial muscle and its vasculature in the form of chronic adrenergic stimulation, cellular apoptosis, and endothelial dysfunction. Other indirect effects are a disruption in myocardial energy metabolism, hypertension, and dyslipidemia. Further additional evidence is that the condition of insulin resistance causes structural abnormalities of the heart that contribute to heart failure, namely diastolic dysfunction in the form of increased left ventricular mass and left ventricular hypertrophy.<sup>12</sup>

Our study found no significant association between anemia and CHF in patients with ESRD, even though from the clinical characteristics, most of the ESRD patients with heart failure in our study had anemia. Our study findings differ from the findings of several studies and also differ from existing theories. A study by He, et al (2017) stated that anemia is common in the ESRD patient population and increases the risk of cardiovascular disease in ESRD patients.<sup>13</sup> However, several clinical trials have stated that the management of anemia in ESRD patients does not reduce the risk of cardiovascular disease.13,19 Patients with ESRD have low levels of the hormone erythropoietin, which causes anemia. A decrease in hemoglobin concentration is significantly associated with an increase in left ventricular mass, which is an anatomical change that contributes to heart failure.19

In this study, it was found that more patients with ESRD had CHF than those who did not. This finding has important clinical significance because the current condition of ESRD has an increasing prevalence in the general population, and cardiovascular disease, including heart failure, is the leading cause of death in patients with CKD, especially ESRD.13 In the Framingham heart study conducted in the period 1971-1996, it was stated that the incidence of heart failure was 4.7 per 1000 population per year of 3,757 men and 4,472 women aged 40 to 94 years who were included in the cohort study.<sup>32</sup> Research by The Cardiovascular Lifetime Risk Pooling Project involving 39.578 samples of adults aged over 45 years reported the incidence of heart failure was 8,3 per 1000 population per year.<sup>33</sup> Another study about the Multi-Ethnic Study of Atherosclerosis found that the incidence of heart failure was 3,1 per 1000 population per year among 6.814 samples studied aged 48-84.34 Another study by Dhingra, et al. (2011) reported that individuals with an LFG <60 mL/minute per 1.73 m2 had a twofold higher risk of developing heart failure compared with individuals who had an LFG  $\geq$  60 mL/minute in a cohort study involving 10.181 research samples and were observed for 10 years.<sup>19</sup>

There are several mechanisms that may be associated with an increased risk of heart failure in ESRD patients. First, individuals with ESRD have a higher prevalence of comorbid diseases such as hypertension, diabetes mellitus, a higher BMI, and other coronary risk factors. These risk factors have been found to increase the risk of developing heart failure. In addition, some researchers evaluating cardiovascular risk in ESRD patients claim that ESRD patients also have a higher traditional risk of coronary abnormalities. These traditional risk factors include hypertension, diabetes mellitus, poor lipid profile, obesity, smoking habits, alcohol consumption, lack of left ventricular physical activity, and hypertrophy.19,23,35

The second cause, damage to the nephrons in ESRD, causes an increase in blood pressure through some mechanisms such as plasma volume expansion, increased activity of the sympathetic nervous system, and the renin-angiotensin-aldosterone axis. This mechanism causes blood pressure to increase and leads to enlargement of the left ventricle, which is a precursor to heart failure.<sup>1,19</sup> Therefore, one of the main components of the management of ESRD is reducing cardiovascular risk. The recommendation is that patients with ESRD who are 50 years of age or older are given therapy in the form of low to mediumdose statins, even though they have low LDL levels. Another thing that must be done is motivation to reduce smoking habits. The JNC VII and KDIGO guidelines have recommended a systolic and diastolic blood pressure target of less than 140/90 mmHg for the group of patients with chronic kidney disease.<sup>3,36</sup> The latest recommendation is the results of the study, the Systolic Blood Pressure Intervention Trial (SPRINT), showing that in individuals with a high risk of cardiovascular disease but without comorbid diabetes, a more intensive blood pressure control is recommended, which is <120 mmHg for systolic blood pressure associated with the risk of cardiovascular events 25% lower risk of mortality and 27% lower risk of mortality compared to the standard blood pressure target (systolic blood pressure <140 mmHg).<sup>1</sup>

A multidisciplinary approach, prevention, and comprehensive management are required in the management of ESRD patients with CHF or those without CHF. The intervention of cardiac risk factors in the early stages of CKD can reduce mortality from heart disease and slow the severity of deterioration in kidney function. Strict blood pressure control, with a target systolic blood pressure <120 mmHg, can reduce the incidence of heart failure with a left ventricular ejection fraction ≥35%, with or without heart failure.<sup>30</sup> In patients with ESRD and T2DM, control of the patient's glycemic index is associated with a reduced risk of heart failure, particularly using sodium-glucose cotransporter 2 inhibitors (SGLT2 inhibitors) has shown not only to slow the progression of ESRD in these patients but also to reduce the risk of hospitalizing patients with heart failure, lowers blood pressure, body weight, and helps diuresis.<sup>30</sup> Smoking cessation can reduce cardiovascular complications in patients, slow down the progression of ESRD and improve the patient's quality of life.21

The weakness of our study is that our study is still observational with a small sample size. Subsequent research with a superior research design and a larger number of samples will provide more reliable results and conclusions. In addition, the variables assessed in our study are still very limited, especially those related to patient clinical parameters. Important variables such as lipid profile, uric acid, and albumin levels could not be evaluated because of the unavailability of data on medical records.

# 5. Conclusion

It can be concluded that the factors affecting CHF in patients with ESRD are HT, T2DM, obesity, and smoking. The results of this study are expected to be used as an illustration so that in the future, prevention can be made for factors affecting CHF in ESRD patients.

# 6. References

- Chen TK, Knicely DH, Grams ME. Chronic kidney disease diagnosis and management: A Review. JAMA. 2019; 322(13): 1294-304.
- 2. Vaidya SR, Aeddul NR. Chronic renal failure. StatPearls. 2020; 1-7.
- Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney international. 2009. Supplement 113: 1-130.
- Centers for Disease Control and Prevention. Chronic kidney disease in the United States, 2019. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention. 2019.
- Kemenkes RI. Situasi Penyakit Ginjal Kronis. Jakarta: Kementerian Kesehatan RI. InfoDATIN. 2017; 2-10.
- Bhatti NK, Galougahi KK, Paz Y, Nazif T, Moses JW, et al. diagnosis and management of cardiovascular disease in advanced and end-stage renal disease. J Am Heart Assoc. 2016; 5: 1-11,
- Campbell RC, Sui X, Filippatos G, Love TE, Wahle C, et al. Association of chronic kidney disease with outcomes in chronic heart failure: a propensity-matched study. Nephrol Dialysis Transplant. 2009; 24(1): 186-93.
- Bangalore S. Management of coronary disease in patients with advanced kidney disease. New England J Med. 2020; 382(17): 1608-18.
- Kovács Á, Papp Z, Nagy L. Causes and pathophysiology of heart failure with preserved ejection fraction. Heart failure Clin. 2014; 10(3): 389-98.
- Indonesian Cardiovascular Specialist Association (PERKI). Guidelines for The Procedure of Heart Failure. 2020. 12-132.
- Damman K, Perez AC, Anand IS, Komajda M, McKelvie RS, et al. Worsening renal function

and outcome in heart failure patients with reduced and preserved ejection fraction and the impact of angiotensin receptor blocker treatment: data from the CHARM-study programme. Eur J Heart Failure. 2014; 64(11): 1106-12.

- Banerjee D, Biggs ML, Mercer L, Mukamal K, Kaplan R, et al. Insulin resistance and risk of incident heart failure: Cardiovascular Health Study. Circulation: Heart Failure. 2013; 6: 364-70.
- 13. He J, Shlipak M, Anderson A, Roy JA, Feldman HI, et al. Risk factors for heart failure in patients with chronic kidney disease: the CRIC (Chronic Renal Insufficiency Cohort) study. J Am Heart Assoc. 2017; 6(5) :1-8.
- Costanzo MR. The cardiorenal syndrome in heart failure. Heart failure Clin. 2020; 16(1) : 81-97.
- 15. Rangaswami J, Bhalla V, Blair JEA, Chang TI, Costa S, et al. Cardiorenal syndrome: classification, pathophysiology, diagnosis, and treatment strategies: a scientific statement from the American Heart Association. Circulation. 2019; 139(16): 1-29.
- 16. Kumar U, Wettersten N, Garimella PS. Cardiorenal syndrome: pathophysiology. Cardiology clinics. 2019; 37 (3): 251-65.
- Savira F, Magaye R, Liew D, Reid C, Kelly DJ, et al. Cardiorenal syndrome: Multi-organ dysfunction involving the heart, kidney, and vasculature. Br J Pharmacol. 2020; 177: 2906-22.
- Loekman JS. Cardiorenal Syndrome. Bali Uro-Nephrology Scientific Communication. 2017; 2017 : 289-94.
- Dhingra R, Gaziano JM, Djoussé L. Chronic kidney disease and the risk of heart failure in men. Circulation Heart Failure. 2011; 4: 138-44.
- 20. Smith DH, Thorp ML, Gurwitz JH, McManus DD, et al. Chronic kidney disease and

outcomes in heart failure with preserved versus reduced ejection fraction: the Cardiovascular Research Network PRESERVE Study. Circulation: Cardiovascular Quality and Outcomes. 2013; 6: 333-42.

- 21. Curtis BM, Parfrey PS. Congestive heart failure in chronic kidney disease: diseasespecific mechanisms of systolic and diastolic heart failure and management. Cardiology clinics. 2005; 23(2005): 275-84.
- 22. Goyal A. Norton CR, Thomas TN, Davis RL, Butler J, et al. Predictors of incident heart failure in a large insured population: a one million person-year follow-up study. Circulation: Heart Failure. 2010; 3: 698-705.
- 23. Shlipak MG, Fried LF, Cushman M, Manolio TA, Peterson D, et al. Cardiovascular mortality risk in chronic kidney disease: comparison of traditional and novel risk factors. JAMA. 2005 ; 293(14): 1737-45.
- 24. Orth SR, Hallan SI. Smoking: a risk factor for progression of chronic kidney disease and for cardiovascular morbidity and mortality in renal patients—absence of evidence or evidence of absence?. Clin J Am Soc Nephrol. 2008; 3(1): 226-36.
- 25. Horwich TB, Fonarow GC, Hamilton MA, MacLellan WR, Woo MA, et al. The relationship between obesity and mortality in patients with heart failure. J Am College Cardiol. 2001; 38(3): 789-95.
- 26. Foley RN, Murray AM, Li S, Herzog CA, McBean AM, et al. Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare population, 1998 to 1999. Journal Am Society Nephrol. 2005. 16(2): 489-95.
- Hall ME, Carmo JMD, Alexandre ADS, Juncos LA, et al. Obesity, hypertension, and chronic kidney disease. Int J Nephrol Renovascular Dis. 2014; 7: 75-86.

- 28. Bryson CL, Mukamal KJ, Mittleman MA, Fried LP, Hirsch CH, et al. The association of alcohol consumption and incident heart failure: the Cardiovascular Health Study. J Am Col Cardiol. 2006; 48(2): 305-11.
- 29. Joo YS, Koh H, Nam KH, Lee S, Kim J, et al. Alkohol consumption and progression of chronic kidney disease: results from the Korean Cohort Study for Outcome in Patients With Chronic Kidney Disease. Mayo Clinic Proceedings. 2020; 95(2): 1-12.
- 30. House AA, Wanner C, Sarnak MJ, Pina IL, McIntyre CW, et al. Heart failure in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney international. 2019; 95(6): 1304-17.
- 31. Vardeny O, Gupta DK, Claggett B, Burke S, Shah A, et al. Insulin resistance and incident heart failure: the ARIC study (Atherosclerosis Risk in Communities). JACC: Heart Failure. 2013; 1(6): 531-6.
- 32. Lloyd-Jones DM, Larson MG, Leip EP, Beiser A, Agostino RBD, et al. Lifetime risk for developing congestive heart failure: the Framingham Heart Study. Circulation. 2002; 106: 3068-72.
- 33. Huffman MD, Berry JD, Ning H, Dyer AR, Garside DB, et al. Lifetime risk for heart failure among white and black Americans: cardiovascular lifetime risk pooling project. J Am Col Cardiol. 2013; 61(14): 1510-7.
- 34. Bahrami H, Kronmal R, Bluemke DA, Olson J, Shea S, et al. Differences in the incidence of congestive heart failure by ethnicity: the multi-ethnic study of atherosclerosis. Arch Internal Med. 2008; 168(19): 2138-45.
- 35. Garg AX, Clark WF, Haynes B, House AA. Moderate renal insufficiency and the risk of cardiovascular mortality: Results from the NHANES I. Kidney International. 2002; 6: 1486-94.

36. National High Blood Pressure Education Program (JNC VII). The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. NIH Publication. 2004; 4: 1-64.