Original Article

Determination of prevalence of cardiovascular complications in end-stage renal failure patients

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ABSTRACT

Introduction: It is estimated that about 40–50% of all deaths in the end-stage renal disease patients are of cardiovascular origin. Myocardial infarction (MI), congestive heart failure (CHF), and angina are the three major cardiovascular diseases associated with end-stage renal failure. The aim of this study is to determine the prevalence of cardiovascular complications in end-stage renal failure patients.

Subjects and Methods: A retrospective cohort study was designed to determine the development of complications in end-stage renal failure patients admitted to a tertiary care hospital in Andhra Pradesh, India from January 2012 to June 2015. The mean standard deviation was determined for all categorical variables, and further data analysis was carried out using SPSS software version 20.

Results: A total of 190 chronic kidney disease (CKD) patients were included in this study. Of 190 patients, 38.42% were smokers while 66.32%, 69.67%, and 56.48% of them had diabetes, hypertension, and hyperlipidemia, respectively. The percentage of end-stage renal failure patients who developed MI, CHF, and angina were 40%, 21.58%, and 12.11%, respectively while a Framingham risk score ≥30% was recorded in 38.42% patients.

Conclusion: This study shows that chronic renal failure accelerates cardiovascular complications, and it is more prominent in patients who have predetermined traditional risk factors such as hypertension, dyslipidemia, and smoking. Prevention and treatment of cardiovascular complications are major considerations in the management of individuals with CKD.

Key words: Cardiovascular complications, chronic kidney disease, diabetes, Framingham risk score, hyperlipidemia, smoking cessation

INTRODUCTION

The National Kidney foundation guidelines define individuals with compromised estimated glomerular filtration rate (e-GFR) <60 ml/min/1.73 m^2 for >3 months as chronic kidney disease (CKD) patients.[1] CKD is one of the irreversible clinical conditions, which poses main public health crisis worldwide. A large population is entering the transition phase toward end-stage renal disease (ESRD) due to CKD. The CKD incidences are estimated to be around 16.8% in the US alone and 12.1–17.5% in Asia.[2] Many community-based studies proved that renal insufficiency also been shown to be interwoven with cardiovascular disease (CVD).[1] CKD and CVDs are directly related. The declination of kidney

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function triggers the cardiovascular complications more severely. The mortality and morbidity rates of patients having CKD increase when they are further threatened by the CVD complications. Evidence shows that the pathophysiology and manifestation of CVD in renal patients are different from the nonrenal failure patients. CVDs frequently begins before the end-stage renal failure and about 40–50% of deaths occur due to cardiovascular complications in CKD patients before developing ESRD. Such complications mainly affect the predialysis and dialysis individuals and are the leading cause of death.[3,4] It was also found that the dialysis patients have about 30-folds of risk for CVD when compared to normal non-CKD patients. Besides, the national kidney foundation reveals that the annual CVD mortality rates are much higher in dialysis patients than risk factors such as sex, race, or age group. Whereas junior dialysis patients have a 500-fold increased risk for CVD mortality when compared with general populations.[5,6]

Cardiovascular complications are highly prevalent in CKD and accounts for the majority of morbidity and mortality conditions.[7,8] These multiple comorbidities are classified as traditional coronary risk factors where they are well-established predictors for renal disease progressions. These risk factors can be classified as the Framingham predictive instrument to estimate individual chance for getting coronary heart diseases. The Framingham predictive tool was validated in various racial populations such as Atherosclerosis Risk in Communities trials and Cardiovascular Health Study (CHS).[9-11] Hypertension, diabetes, smoking, and hyperlipidemia are the four most dangerous risk factors in CKD patient that elevate the CVD complications.[12]

This retrospective cohort study aimed to verify that smoking, hypertension, diabetes, and hyperlipidemia are the risk factors for the development of cardiovascular complications in CKD patients. Moreover, we also aimed to show cigarette smoking as the leading cause of CVD in CKD patients. The information gathered from the patients was utilized to calculate the Framingham risk score to assess their chance of getting coronary events in the next 10 years. The assessment tools that were used to calculate the Framingham risk score are age, gender, total cholesterol, high-density lipoprotein (HDL) level, smoking, and systolic blood pressure.

SUBJECTS AND METHODS

Study population

The patients involved in this study were Stage-5 (GFR value <15 ml/min/1.73 m^2) renal disease patients (National Kidney Foundation). The cohort comprised patients diagnosed with end-stage renal failure and was on either hemodialysis or peritoneal dialysis (PD).

Data collection

The data were collected from January 2012 to June 2015 in a tertiary care hospital in Andhra Pradesh, India. The study was approved by the Hospital's Ethical Committee, and the CKD was confirmed for each patient by assessing the kidney function for more than 3 months before they were enrolled in this study.

The data were collected from the patient's detail entry. Basic details such as age, gender, and body weight were collected. Of 190 patients, there were 138 males and 52 females with an age group of 22–83 years. All the patients were on either hemodialysis or PD, and some were on the transplantation list.

Statistical analysis

The patients characteristics, the risk factors associated with the development of the CVDs and other findings were reported using the percentages for categorical variables and mean ± standard deviation for continuous variables as stated in Table 1. The study mainly focuses on the categorical variables and between three types of cardiovascular events that are myocardial infarction (MI), congestive heart failure (CHF), and angina. Logistic regression analysis was applied to determine the odds ratio (OR) for the development of cardiovascular complications. These categorical variable's linear trends were determined using the Chi-square test. All analyses were performed using the SPSS software version 20.[13,14]

RESULTS

The baseline characteristics and the essential laboratory data were presented in Table 1. A total of 190 patients in this study had clinic visits to the hospital during the study period. The mean age of the patients was 58.94 ± 12.38 years with the mean body weight of 65.8 ± 12.47 kg. The clinical data were categorized according to their gender and age as illustrated in Table 1. Among the total number of patients, males (n = 136) who fall into the age group of 60–79 years are mostly affected with CKD.

Table 1: Baseline characteristics, clinical, and laboratory data of Stage-5 chronic kidney disease study participants' accordance to gender and age group

	Total (*n*=190)	By sex		By age group				*P*
		20-39 years (*n*=20)	40-59 years (*n*=69)	60-79 years (*n*=95)	≥80 years (*n*=4)	60-79 years (*n*=95)	≥80 years (*n*=4)	
Age (years)	58.94±12.38	58.96±13.15	58.89±10.28	-	-	-	-	0.035
Weight	65.8±12.47	68.06±12.52	60.11±10.46	59.70±9.06	63.94±13.19	68.02±12.54	62.50±12.29	0.001
Smoker	38.42	52.94	47.06	25	33.33	45.26	33.33	0.006
Diabetes	69.47	61.27	38.73	65	62.32	75.79	66.67	0.001
Hypertension (≥140/90 mmHg)	66.32	76.47	23.53	40	65.22	73.68	50.00	0.002
Total cholesterol	56.84	62.50	37.50	45	55.07	60.00	66.67	0.052
HDL	56.84	62.50	37.50	45	55.07	60.00	66.67	0.012
LDL	56.84	62.50	37.50	45	55.07	60.00	66.67	0.001
Catheter thrombus	35.79	77.94	22.06	50	33.33	33.68	50.00	0.026
Infections	49.47	81.91	18.09	75	47.83	44.21	66.67	0.003
On antibiotics	53.16	78.22	21.78	65	49.28	53.68	50.00	0.016
Myocardial infarction	40.00	93.42	6.58	40	55.07	30.53	16.67	0.042
Congestive heart failure	21.58	80.49	19.51	20	24.64	16.84	33.33	0.046
Angina pectoris	12.11	91.30	8.70	5	21.74	7.37	0.00	0.004
Framingham risk score (>30%)	38.42	76.94	23.06	35	40.58	36.84	50.00	0.003
Hemodialysis	61.58	66.91	48.15	70	62.32	60.00	66.67	0.024
Peritoneal dialysis	28.42	16.18	59.26	35	20.29	32.63	33.33	0.038

HDL=High-density lipoprotein, LDL=Low-density lipoprotein

Of 190 patients, 38.42% were smokers, 66.32% were hypertensive, 69.67% were diabetic, and 56.84% patients had higher levels of total cholesterol, HDL, and low-density lipoprotein. To get the clear picture of the study, we analyze our data according to the risk factors relationship with MI, CHF, and angina pectoris [Table 2]. The percentage of patients getting any type of cardiovascular complications due to the risk factors and the type of complications associated with dialysis is shown in Figures 1 and 2. The number of patients whose Framingham risk scores above 30% was also presented in Table 1.

Table 2 illustrates the most common risk factors for the development of cardiovascular complications in renal failure patients. A logistic regression analysis was applied to determine the effect of independent variables (hypertension, smoking, diabetes, and hyperlipidemia) on dependent variables (angina, CHF, and MI). The frequency and percentage of patients who developed the complications due to the major risk factors are mentioned in the table. The results showed that hypertension and a history of smoking has high tendency of developing MI (OR = 3.67, $P < 0.05$) and angina (OR = 3.12, $P < 0.05$) while patients with diabetes (OR = 2.73, $P < 0.05$), renal failure (OR = 2.24, $P < 0.05$), and poor blood glucose control (OR = 2.94, $P < 0.05$) had higher tendency to develop CHF than the referent group. As presented in Figure 1, smoking was the most vulnerable risk factor in causing any of the cardiovascular complications among all other risk factors as stated in this study. It scores 95.83% in causing the cardiovascular complications, which is followed by hyperlipidemia which accounts about 93.68%. Besides 81.82% and 71.21% patients with hypertension and diabetes were affected with cardiovascular complications. Of 190 patients, 61.58% were on hemodialysis, and 28.42% were on PD. Hemodialysis patients are mostly affected with catheter-related thrombus which was noticed in 53 males and 15 females in this study. Among PD patients, development of severe peritonitis is the major complication which was noted to be 49.47%. On the other hand, 77 males and 17 females were diagnosed with infections and 101 of them were on antibiotics for the infection treatment as stated in Figure 2.

DISCUSSION

We found that CKD has the greatest risk gradient for cardiovascular complications. Patients are more prone to MI, angina pectoris, and CHF, especially when the risk factors such as smoking, hypertension, and diabetes were not addressed and treated promptly. The results show that smoking, hyperlipidemia, hypertension, and diabetes are the four risk factors which reveal a positive feedback toward the

development of cardiovascular complications in ESRD patients. The results of our study were similar to the study conducted by Orth and Hallan, Yacoub *et al.*, Longenecker *et al.*,[9,10,15] The event of CVDs does not occur by itself in CKD patients but by the presence of existing risk factors which fasten the development of the cardiovascular complication than expected. This was proven with the calculated Framingham risk score which was done along with this study. Moreover, our focus on revealing complications associated with hemodialysis and PD such as catheter-related infections and thrombus formation were also successful. 35.79% patients are affected with catheter thrombus, and 49.47% patients are affected with infections which further led to sepsis.

Table 2: Risk factors for the development of Cardiovascular complications

Risk factors	Development (%)	*P*	Adjusted value* OR (95% CI)
Development of MI			
Nonhypertensive	56	0.002	1.00
Hypertensive			**3.67** (1.23-5.78)
Nondiabetic	34	0.013	1.00
Diabetic			2.73 (0.87-4.32)
Nonsmokers	45	0.004	1.00
Smoking			**3.12** (1.13-5.48)
Normal lipid level	26	0.143	1.00
Hyperlipidemia			1.93 (0.84-2.63)
Development of angina			
Nonhypertensive	37	0.003	1.00
Hypertensive			**2.93** (1.06-4.98)
Nondiabetic	38	0.096	1.00
Diabetic			2.24 (0.43-2.94)
Nonsmokers	26	0.031	1.00
Smoking			1.64 (0.73-2.98)
Normal lipid level	18	0.735	1.00
Hyperlipidemia			0.72 (0.09-1.86)
Development of CHF			
Nonhypertensive	32	0.326	1.00
Hypertensive			1.17 (0.35-2.16)
Nondiabetic	55	0.042	1.00
Diabetic			**2.94** (1.24-4.63)
Nonsmokers	32	0.319	1.00
Smoking			1.26 (0.85-3.12)
Normal lipid level	12	0.874	1.00
Hyperlipidemia			0.78 (0.19-1.35)

Overall, predictive accuracy of the model is 76.5% omnibus tests of model coefficients: χ^2=245.840, *P*<0.001-2 log likelihood=232.756, Nagelkerke R^2=0.543. Significance (*P*<0.05), statistically significant variables are in bold. OR=Odds ratio, CI=Confidence interval, CHF=Congestive heart failure, MI=Myocardial infarction

Declination of GFR leads to the incidence of various types of cardiovascular complications which were proven in angiographic studies showing that the CVD events involve more than 50% of stage 5 CKD patients.[16-21] Out of the 16 standard cardiovascular risk factors in renal failure patients, the prevalence of mortality by MI and other complications proven to be caused by the four major risk factors.[11,15,22,23] The risk factors that we mainly focus are the traditional risk factors as those in Framingham Heart Study to estimate the risk of developing heart diseases. The traditional risk factors that we used in this study were highly prevalent in CKD patients and largely parallels the relationships described comparing with general populations.[6,24,25]

In this study, the percentage of developing cardiovascular complications such as MI, CHF, and angina due to smoking was found to be 64.47%, 43.9%, and 52.17%, respectively. This value is higher than the Case Mix Study (45%), Canadian Study (15%), and the DMMS Wave 2 Study (40%).[15,26,27] Besides, in another study, it was illustrated that this rise will

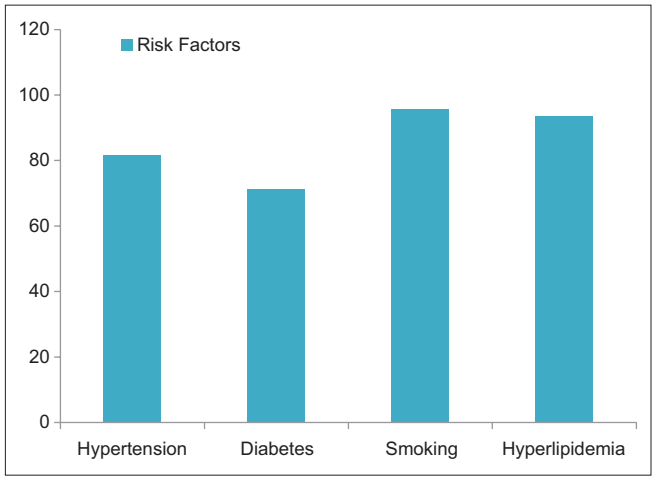

Figure 1: Percentage of risk factors leading to cardiovascular complications

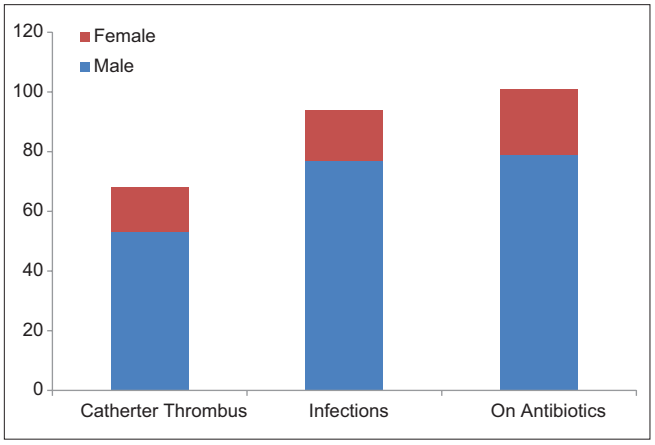

Figure 2: Number of people with infections, catheter thrombus, and on antibiotics

continue to grow in developing countries where smoking habits are increasing substantially and will be directly proportional with CKD problems.[28-32] The effect of tobacco smoking could be severe, distressing both the progression of CKD and CVD. However, this scenario does not click either physician or patient's awareness during treating the CKD conditions. In one of the studies which were documented from the year 2000 to 2005 found that health-care professionals need to improve smoking cessation rates among patients who are undergoing renal therapy.[9] In another prospective cohort study, it was found that cumulative smoking exposure has been recorded to be associated with fatal cardiovascular accidents. This was proven in CHS involving 5808 patients, who were 65 years and also confirmed that smoking causes the largest risk for cardiovascular deaths among patients with CKD.[9,33,34] Therefore, reducing or stopping the smoking habits would be a wise choice to curb the further development of CVD complications in renal failure patients.

The frequency of hyperlipidemia in CKD patients is higher than in general population but differs depending on the type of lipid, target population, cause of renal disease, and level of renal function.[17,35] The hyperlipidemia conditions among the CKD patients in our study were third highest risk factors to develop CVDs. Most of the CKD patients are affected with malnutrition and inflammation that will have lipid unbalancing property. That is the reason why most with deteriorated renal function will have lipid abnormalities.[36] As a consequence of these lipid abnormalities, a patient with ESRD has been described to be at increased risk for atherosclerotic coronary artery disease and its complications.

Hypertension and diabetes are well-established risk factors for coronary problems accounted about 81.72% and 71.21% outcomes in this study, respectively. The target range of hypertension in renal failure patients should be <140/90 mmHg (if urine albumin is <30 mg/24 h). In a research article by Middleton and Pun in 2010, commented that hypertension is one of the consistent risk factors for cardiovascular complications in the absence of discernible kidney function. They also added that in many large clinical trials researchers have mentioned lowering the systemic blood pressure can decrease the cardiovascular morbidity whereby taking certain antihypertensive drugs can be best cardioprotective and renal protective.[37] Patients with CKD will have different pathogenesis for hypertension. They are more likely to develop salt sensitivity which will be a dangerous elevator for the development of the abnormal ventricular structure. Therefore, it would be the reason that hypertension is one of the reasons in the prognosis of CKD-related cardiac and vascular diseases.[14,38] Multidisciplinary care may provide the optimal system for maximizing care of these complex patients.[39]

Despite these complications, catheter-related thrombosis is a never ending problem in the majority of hemodialysis patients. In our study, 35.59% patients are affected with catheter thrombosis. Even though there were a lot of innovations done in making best catheter, yet complications in the form of thrombosis still occur, particularly in the right atrium. Most of the thrombosis occurs in response to intraluminal clot formation or endothelial damage in the right atrium caused by the constant friction between the catheter and right atrial wall.[40] Therefore, selecting a right site placement is essential in minimizing the risk. For example, the right internal jugular site is preferred access for cuffed tunneled catheter, whereas the left internal jugular is a less desirable access due to the development of stenosis and high-malfunction rate.[41] Peritonitis is the major complications with PD. In our study, it was found that 49.47% of PD patients encountered this problem. Worldwide, around 18% of infection leads to mortality in PD patients due to prolong infections in the peritoneal membrane which tend to fail to function and can cause technique failure.[42] Hence, PD needs a careful monitoring to solve the rapid inflammation and damage to the peritoneal membrane which may lead to cause sepsis.

CONCLUSION

Traditional risk factors play an important role in determining a person's risk to get the cardiovascular events. The Framingham risk score supports our study by proving that traditional risk factors are predictors of cardiovascular complications among CKD patients in 10 years' time. This study is important because it documents that CAD risk factors that are known from studies in the general population remain predictive among patients with CKD. We met the goal that smoking is the leading risk factor in CKD patients to rule out the cardiovascular complications. Smoking cessation programs are an essential tool in decreasing the cardiovascular events among CKD patients. As CKD patients are highly prone to many complications, the clinical pharmacist can contribute toward the care of these patients through educating the health-care professionals regarding the rational

use of drugs, optimize medications, and educate the patients to monitor the risk factors frequently. This study confirms the need of proper pharmaceutical care services for CKD.

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Conflicts of interest
There are no conflicts of interest.

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