Renal Function In Nigerian Patients With Heart Failure.
E Arodiwe, C Ijoma, I Ulasi, O Onodugo

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Abstract
BACKGROUND: Studies have identified abnormal renal function as one of the most important risk factors for morbidity and mortality in patients with heart failure (HF).OBJECTIVES: To determine the prevalence, mortality rate and factors associated with impaired kidney function (IKF) in patients admitted with HF.METHOD: Case notes, admission and discharge records of all patients admitted with a principal diagnosis of HF between January 2007 and January 2008 were studied. IKF was defined as serum creatinine ≥ 124µmol/l for women and ≥ 133µmol/l for men. Chronic kidney disease was defined as eGFR <60 mL/min or presence of markers of kidney disease for 3 months or more. RESULT: A total of ninety two patients were admitted for HF. Forty four (47.3%) had IKF. 19(20.7%) had renal failure. Twenty three of the patients (12 with IKF) died giving a mortality of 25%. SBP r=0.318, p=0.002, DBP, r=0.279, p=0.007, Serum Creatinine , r=0.572, p< 0.001, correlated positively with presence of IKF. There were negative correlation between the presence of IKF and haemoglobin level(r=-0.513, p<0.001) and eGFR(r=-0.840, p<0.001). Linear regression analysis confirmed the eGFR (82%) as the best predictor of IKF. Renal failure appeared not to be independently associated with death among the heart failure patients. CONCLUSION: The prevalence and mortality of IKF in our patients with heart failure is high, 47.3% and 25% respectively. Up to 20.7% were already in kidney failure. It is important that the eGFR of our patients with HF be determined as a guide to identifying those with IKF. Efforts should be intensified at prevention, identification, and appropriate management of hypertension and anaemia in these patients.

INTRODUCTION
Despite recent advances in the medical management of patients with chronic heart failure, morbidity and mortality remain high. A recent study identified eight separate risk factors for death among women with heart failure. Of these, abnormal kidney function was the most common, and it was associated with the greatest increased risk of death. The authors of the study concluded that abnormal kidney function, even when mild, was a major predictor of death among women with heart failure. There are many links between kidney disease and heart disease. High blood pressure, increased serum creatinine levels and diabetes are all factors that increase the risk of both heart disease and kidney disease. Evidence suggests that co morbidities such as kidney disease, anaemia, and diabetes mellitus have a pivotal role in determining the prognosis of patients with different cardiovascular disorders. The prevalence of CKD is even higher among patients with cardiovascular disease. Additionally, CKD is a major and serious risk factor for cardiovascular disease. Death from cardiovascular disease is 10 to 30 times higher in dialysis patients than in the general population. Heart disease is more common in people with even mild to moderate kidney disease than in those of the same age and sex without kidney disease. Recent studies have also confirmed that even early CKD constitutes a significant risk factor for cardiovascular events and death. In addition, CKD is a risk factor for recurrent cardiovascular events, and proper management of cardiovascular disease is different and more complex in patients with CKD. A growing number of patients in the United States have both heart failure and kidney disease. Both of these conditions are costly and burdensome. The same is likely to be the case in our environment. When followed for at least one year, 38 percent of patients with mild renal disease had died, as had as many as 51 percent with moderate to severe disease. These mortality risks are comparable to risks attributed to deadly cancers. We need to understand outcomes in these patients in order to improve treatment strategies. The frequency of cardiovascular complications and the progression of impaired renal function can be ameliorated in these patients by appropriate intervention. This study may provide momentum for future research in sub-Saharan Africa where there is paucity of information on the prevalence, associated factors, outcome and management strategies for patients with heart failure and various stages of kidney impairment. Healthcare providers
should evaluate their patients for the presence of impaired kidney function as part of preventive care and treatment strategies.

What is the prevalence of impaired renal function in our patients admitted with heart failure? What is the mortality rate in these patients? What factors are associated with impaired renal function in our patients admitted with heart failure? These are the questions this study sets out to answer.

SUBJECTS AND METHODS
This was a cross sectional retrospective study covering a period of one year (January 2007 – January 2008). The case notes, admission and discharge records of all patients admitted with a Principal diagnosis of heart failure were examined. Diagnosis of heart failure was made using the modified Framingham criteria. The major criteria were paroxysmal nocturnal dyspnoea, raised jugular venous pressure, clinical cardiomegally, basal crepitations, S₃ gallop, clinical acute pulmonary oedema, pulmonary upper lobe blood diversion on chest radiograph, pulmonary oedema on chest radiograph. Minor criteria – tachycardia, orthopnoea, exertional dyspnoea, nocturnal cough, hepatomegally, pleural effusion, and diuretic use. Heart failure was diagnosed if the patient had two major and one minor or one major and two minor criteria. Demographic and other parameters were documented. Impaired kidney function (IKF) was defined as serum creatinine ≥ 124µmol/l for women and ≥ 133µmol/l for men. CKD was defined as either (1) kidney damage for ≥3 months, as confirmed by kidney biopsy or markers of kidney damage, with or without a decrease in glomerular filtration rate (GFR), or (2) GFR <60 mL • min⁻¹ per 1.73 m² for ≥3 months, with or without kidney damage. The degree of renal impairment was categorized according to the NKDF criteria into stages 1 to 5 and the prevalence of chronic kidney disease (ckd) in each stage noted. The overall prevalence of ckd was also documented. GFR was estimated using the MDRD formula.

Statistical analysis was done using the SPSS version 17.0. For continuous variables, mean values and standard deviation were calculated and the means compared using analysis of variance. Categorical variables were compared using the non parametric test chi-squared. All tests were two-tailed, and p<0.05 taken as statistically significant. Pearson correlation was used to correlate non categorical variables, while Spearman Rho was used for categorical ones. Significant variables were further analyzed using the linear regression analysis to determine variables that predict impaired renal function.

RESULTS
Study characteristics: A total of ninety two patients were hospitalized for heart failure during the period of study. Majority, 73(79.3%) were males. There were no statistically significant differences in the sexes between those that had impaired kidney function (IKF) and those without. The mean age of the patients was 58.4±17.8 years. There were no statistically significant differences between the age of those with and without IKF. The mean estimated GFR was 44.0±27.9mls/min. Those with IKF had lower mean eGFR (19.8±10.4mls/min) compared with those without (66.1±18.9), p<0.001, Table I. The mean systolic blood pressure (SBP), diastolic blood pressure (DBP), haemoglobin (HB) and serum creatinine (S.Cr) were 131.5±35.6 mmHg, 85.8±22.0mmHg, 10.6±2.6g/dl and 232.7±251.1µmol/l respectively. The mean SBP (119.5±29mmHg), DBP (79.3±18.9) and S.Cr (90.5±20.1µmol/l were significantly lower in those without IKF than those with IKF, p<0.05. However, the mean HB was significantly lower in those with IKF (9.1±2.4g/dl) when compared with those without (12±1.9), p<0.05.
Clinical features: Fifty percent (50%) of the patients were clinically pale. More patients with IKF, 28(63.6%) were clinically pale than those without 18 (37.5%), p= 0.012. This was the only clinical feature that was significantly different between the two groups.

Most of the patients presented with NYHA class IV heart failure.
Figure 2: Aetiology of heart failure in the study participants.

Prevalence of impaired renal function: Out of the 92 patients admitted for heart failure, 44 had impaired kidney function giving a mortality rate of 47.3%, Table I. Using the NKDF criteria, seven patients (7.6%) had normal renal function with eGFR ≥ 90ml/min, 21 (22.8%) had mild renal dysfunction with eGFR 60 – 89ml/min, 26 (28.3%) had moderate renal dysfunction with eGFR 30 – 59ml/min, 19 (20.7%) had severe renal dysfunction with eGFR 15 – 29ml/min, while another 19 (20.7%) had kidney failure with eGFR < 15ml/min.

Figure 5
Table III. Staging/Prevalence of renal dysfunction in the patients

<table>
<thead>
<tr>
<th>Stage</th>
<th>Prevalence of CKD(Overall)</th>
<th>Prevalence of CKD in the IGF group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(Normal)</td>
<td>7(7.6)</td>
<td>0</td>
</tr>
<tr>
<td>2(Mild)</td>
<td>21(23.1)</td>
<td>0</td>
</tr>
<tr>
<td>3(Moderate)</td>
<td>26(28.3)</td>
<td>3(18.3)</td>
</tr>
<tr>
<td>4(Severe)</td>
<td>19(20.7)</td>
<td>17(30.6)</td>
</tr>
<tr>
<td>5(Kidney failure)</td>
<td>19(20.7)</td>
<td>19(40.2)</td>
</tr>
<tr>
<td>Total</td>
<td>92(100)</td>
<td>44(40%)</td>
</tr>
</tbody>
</table>

Factors associated with impaired renal function: The following factors: SBP, r = 0.318, p = 0.002, DBP, r = 0.279, p = 0.007, Serum Creatinine level, r = 0.172, p < 0.001, correlated positively with presence of IGF in heart failure patients. There was negative correlation between the presence of IGF and haemoglobin level (r = -0.513, p<0.001) and eGFR (r = -0.840, p <0.001). eGFR showed the strongest correlation, r = 0.840.

Figure 6
Table IV. Correlation analysis for relationship of IKF in heart failure with various variables.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Correlation coefficient</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>0.048</td>
<td>0.650</td>
</tr>
<tr>
<td>Weight(kg)</td>
<td>-0.132</td>
<td>0.208</td>
</tr>
<tr>
<td>SBP(mmHg)</td>
<td>0.318</td>
<td>0.002</td>
</tr>
<tr>
<td>DBP(mmHg)</td>
<td>0.279</td>
<td>0.007</td>
</tr>
<tr>
<td>Hb(g/dl)</td>
<td>-0.513</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>S.Cr(μmol/l)</td>
<td>0.572</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR(ml/min/1.73m²)</td>
<td>0.840</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Multiple linear regression analysis confirmed the eGFR (82%) as the best predictor of impaired renal function in our patients with heart failure.

Figure 7
Table V. Multiple linear regression analysis of variables that correlated with heart failure

<table>
<thead>
<tr>
<th>Model Summary</th>
<th>R</th>
<th>R Square</th>
<th>Adjusted R Square</th>
<th>Standard Error of the Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.842</td>
<td>0.709</td>
<td>0.692</td>
<td>0.279</td>
</tr>
<tr>
<td>a. Predictors</td>
<td>(Constant), gfr, dbp, hbo, creat, ek</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Dependent Variable</td>
<td>impaired kidney function</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: gfr – estimated glomerular filtration rate, dbp – diastolic blood pressure, hbo – haemoglobin level, creat – serum creatinine level, ek – systolic blood pressure
Mortality pattern/outcome: Out of the 92 patients admitted with heart failure, 23 died (12 with impaired kidney function, 11 without) giving a mortality rate of 25%. Four patients (3 with IKF, 1 with normal renal function) were discharged against medical advice, while 65 (30 with IKF, 35 without IKF) were discharged alive, Table VI.

**DISCUSSION**

This study demonstrated a high prevalence of impaired kidney function (47.3%) in our patients admitted with a diagnosis of heart failure. The blood pressure (both systolic and diastolic) as well as the serum creatinine level showed positive correlation with the presence of IKF in these patients. Heart failure patients with higher blood pressure on admission as well as those with higher serum creatinine levels are more likely to have IKF than those with lower values. Haemoglobin level and eGFR demonstrated negative correlation with the presence of IKF in the patients. The patients admitted with lower haemoglobin levels and eGFR levels were more likely to have IKF. eGFR was the best predictor of IKF. The study also demonstrated a mortality rate of 25%. Presence of impaired renal function appeared not to be associated with a higher mortality, $X^2 = 1.626$, df = 2, $p = 0.443$. Renal failure independently appeared not to be associated with death among the heart failure patients, Table VII. This is difficult to explain though some studies are in support of this. The prevalence of renal impairment increased progressively in these patients with heart failure as
the kidney function deteriorated, Table III.

Various studies have shown a high prevalence of kidney dysfunction in heart failure patients ranging between 30% to about 50% \(^{16-19}\). Over 50% of patients with heart failure were found to have kidney disease and this unstable combination resulted in poor survival \(^{15}\). When these patients were followed for at least one year, 38% of those with disease had died, as had as many as 51% with moderate to severe disease. These mortality risks are comparable to risks attributed to deathly cancers \(^{15}\).

Hypertension, increased serum creatinine levels and anaemia are factors that increase the risk of both heart disease and kidney disease \(^{16-19}\). Hypertension is the commonest cause of heart failure in Sub-Saharan Africa \(^{20,21}\) and in most studies in our environment the second commonest cause of chronic kidney disease (CKD) \(^{22,23}\). These findings were collaborated by the present study- hypertension being associated with IKF in the patients and also the commonest cause of heart failure in these patients. Rising creatinine level is a telltale sign that the kidneys are failing. Increased serum creatinine level is also a risk factor for heart disease. Anaemia is very common in chronic heart failure (CHF) patients \(^{24-26}\). CKD can cause or worsen both anaemia and CHF \(^{24-26}\), CHF can cause or worsen anaemia and CKD \(^{24-26}\), and anaemia can cause or worsen CKD and CHF \(^{24-26}\). This interaction between the three conditions is called the cardiorenal anaemia syndrome \(^{24}\). The implication of this interaction is that adequate management of CHF and anaemia would prevent the progression of both CHF and CKD.

Mortality and morbidity of CHF is still very high, although it is said to have improved slightly over the years \(^{37}\). The mortality is even higher with the presence of kidney failure \(^{15}\). Although there appeared to be no difference between death in those with IKF and those without in this study, could anaemia be the culprit? Many patients with CHF are anaemic. Anaemia is associated with more severe CHF and higher mortality, hospitalization and morbidity rates \(^{28}\). Majority of our patients were in Stage IV NYHA functional class and anaemic. Many published works, but not all, show a positive effect of erythropoietin or its derivatives when co administered with oral or intravenous (IV) iron, with improvements in left and right ventricular systolic and diastolic function, dilation, hypertrophy, renal function, New York Heart Association class, exercise capacity, oxygen utilization, caloric intake, quality of life, and the activity of endothelial progenitor cells \(^{24-26,28,29}\).

Renal failure independently appeared not to be associated with death among the heart failure patients, Table VII. This is difficult to explain though some studies are in support of this \(^{14}\). Some of these may be cases of transient rather than persisting worsening of renal function.

In conclusion, the prevalence and mortality of IKF in our patients with heart failure is high, 47.3% and 25% respectively. Up to 20.7% were already in kidney failure at presentation. It is important to have a high index of suspicion of renal impairment in patients with heart failure, especially those that are not responding to treatment. It is equally important that the eGFR of our patients with HF be determined as a guide to identifying those with IKF and renal failure. Efforts should be intensified at prevention, identification, and appropriate management of hypertension and anaemia in these patients.

References

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