

# **Medication Adherence Pattern, Associated Factors and outcomes among Hospitalized Heart Failure Patients in a Tertiary Hospital in Tanzania: A Prospective Cohort Study**

**Pedro Pallangyo**

Jakaya Kikwete Cardiac Institute, Tanzania, jalackmilinga2@gmail.com

## **Extended Abstract**

### **Abstract**

Managing heart disease is complex and multifaceted, but adherence to medication remains the cornerstone of avoiding avoidable readmissions, premature deaths, as well as needless costs in health care. Despite the evidence-based effectiveness of anti-fraud drugs, poor adherence is widespread and also remains a significant barrier to improving clinical outcomes in cardiac insufficiency populations. We enrolled 459 patients with established diagnosis of heart failure. Sociodemographic, clinical, laboratory, and echocardiographic data were gathered using a structured questionnaire during the hospital admission of enrollment. The Medication adherence is being assessed using the 8-item Morisky Medication Adherence Scale (MMAS-8). The primary outcome measures were rehospitalization and mortality at 180-days. Linear logistic regression analyses were used to assess for factors associated with adherence and predictors of rehospitalization. Based on their's adherence status, the participants were compared with respect to survival using Cox proportional-hazards regression model. All tests were 2-sided and  $p < 0.05$  was used to denote statistical significance.

### **Introduction**

Cardiovascular disorders (CVD) are responsible for about one-third of all global mortality with over three-quarters of deaths transpiring in the developing world. In spite of the remarkable advances in novel screening techniques and therapeutic directions, the prognosis of heart failure (HF) remains strikingly poor around the globe particularly in the developing nations. Owing to its chronic nature, clinical management of HF necessitate long-term use of several drugs to reduce morbidity and mortality. However, universally low prescription rates of such drugs among patients who require them is observed.

Despite of all developments in HF management, adherence plays a pivotal role in attaining maximal therapeutic benefits. Nevertheless, regardless of the assessment tool used or population studied, adherence rates are consistently suboptimal across studies making it a significant public health issue]. Poor adherence to prescribed regimens is pervasive and results in preventable hospitalizations, premature deaths and unnecessary health care expenditure regardless of the underlying cardiovascular etiology. There is dearth of information regarding medication adherence among heart failure population in Tanzania and Sub-Saharan Africa at large. In this prospective cohort study, we sought to explore the adherence pattern, associated factors and outcomes among hospitalized heart failure patients in a tertiary hospital in Tanzania.

### **Methods**

#### **Recruitment process and definition of terms**

All patients who were hospitalized at Jakaya Kikwete Cardiac Insitute (a tertiary care public teaching hospital) between March and October 2018 with established diagnosis of heart failure (for at least 3 months' prior enrollment) were consecutively enrolled for this study. Sociodemographic, clinical, laboratory, echocardiographic, and adherence data were gathered using a structured questionnaire during the hospital admission of enrollment. Framingham criteria was used to screen participants for heart failure symptoms and a 2-dimensional echocardiography was utilized for diagnosis reconfirmation. Renal functions were estimated using the Modification of Diet in Renal Disease equation and estimated glomerular filtration rate (eGFR) value of  $< 60 \text{ mL/min/1.73 m}^2$  was used to define renal dysfunction. Diagnosis of anemia utilized the WHO criteria i.e. Hemoglobin (Hb) concentration of  $< 13.0 \text{ g/dL}$  and  $< 12.0 \text{ g/dL}$  for males and females respectively.

Diabetes was defined by fasting blood glucose levels  $\geq 7.0$  mmol/L or use of glucose lowering agents. Hypertension was defined as systolic blood pressure (SBP)  $> 140$  mmHg and/or diastolic blood pressure (DBP)  $> 90$  mmHg or use of antihypertensive medications. Total cholesterol level greater than 6.2 mmol/L was used to define dyslipidemia. Hyponatremia, hypokalemia, hypocalcemia, and hypomagnesemia were defined by concentrations  $< 135$  mmol/L,  $< 3.5$  mmol/L,  $< 2.1$  mmol/L and  $< 0.7$  mmol/L respectively. Potassium levels  $> 5.0$  mmol/L was used to denote hyperkalemia. We measured adherence based on the last time a participant took her drugs for heart failure. For the purposes of this analysis, we described good adherence as the intake of all prescribed medications for heart failure within 72 h before recruitment admission.

### Follow-up and study outcomes

Follow-up was conducted through scheduled weekly phone calls and continued through April 2019 with a predetermined stopping point providing a maximum of 180 days of follow-up for each patient after enrollment. Data was censored after completion of follow-up or death, whichever occurred first. A participant was deemed lost to follow-up when despite all attempts couldn't be reached through phone numbers provided. Our primary outcome measures were rehospitalization and all-cause mortality. We defined re-hospitalization as any cardiovascular-related admission to hospital following a successful discharge from the enrollment hospitalization. Early mortality was defined as death during enrollment hospitalisation.

### Statistical analysis

All statistical analyses utilized STATA v11.0 software. Pearson Chi square and Student's T-test were used to compare categorical and continuous variables respectively. Logistic regression analyses was used to assess for factors associated with adherence and predictors of rehospitalization. Factors included in our logistic regression model included age, sex, education level, marital status, employment status, residence, comorbidities and possession of health insurance. Based on their adherence status, the participants were compared with respect to survival using Cox proportional-hazards regression model. Differences in survival between the low- and high-adherence groups were compared using the log-rank test. We report Odds ratio (OR), Relative risk (RR) and Hazard ratio (HR) with 95% confidence intervals (CI) and p-values where appropriate. All tests were 2-sided and  $p < 0.05$  was used to denote statistical significance.

### Discussion

Management of heart failure is complex and multifaceted but adherence to medications remains a fundamental measure to prevent acute exacerbations. Given unclear evidence of the efficacy of anti-fraud medications, poor adherence is widespread and remains a major barrier to improving clinical results in the cardiac insufficiency population. Estimates of nonadherence in heart failure patients have varied widely (22–90%) in the literature. In this present study, less than one-fifth of participants were categorized as having high adherence. Our rate of nonadherence is skewed to the extreme undesired end of the reported range in the literature. With regards to reasons for poor adherence, numerous factors have predominated in various studies. For instance, in studies by Toh et al. (71%) and Mujtaba et al. (72.7%), a poor medication instruction was the most reported factor. On the other hand, studies by Aggarwal et al. and Dickson et al. found forgetfulness and comorbidities respectively as the leading factors for nonadherence. Nearly 90 per cent of nonadherent participants identified the cost of medication as the main obstacle to adherence in this study. These findings are in line with the study by Dunlay et al. in terms of cost being the most reported factor, but it was a barrier in a significantly lower proportion (22 per cent) compared to what we observed. While majority of known risk factors for nonadherence are potentially modifiable, inability to comply due to poverty is not. Owing to this, improving medication adherence in impoverished societies continues to be a very difficult undertaking. It should not be forgotten that these deprived communities and their already strained health systems tend to struggle with the prevention and control of the infectious diseases that are ever present. Several studies have shown the effects of poor adherence on a heart failure prognosis. In addition, several studies have established the prognostic benefits of therapies for improving adhesion. Nearly 60 per cent of participants with poor adherence were rehospitalized within 6 months of enrollment in this present study. Our findings are in line with several other prospective studies resulting in rehospitalization rates ranging from 20 to 69%. Furthermore, intervention studies have consistently shown that enhanced adherence is associated with reduction in readmission risk (3–96 per cent). In addition, systematic reviews and meta-analysis by Ruppert et al. and Unverzagt et al. revealed 21 per cent and 10 per cent lower chances of rehospitalization in the adherence intervention arm, respectively.