Research Article

Treatment of chronic heart failure in adults at a referral hospital in Kenya: adverse drug reactions and determinants of adherence

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Background: Chronic Heart Failure is a major health problem with a prevalence of between 1 and 12% in USA and Europe, and approximately 5.7% in Sub-Saharan Africa, and has socio-economic relevance owing to its high prevalence, mortality and impact on young economically active individuals. In 1999 chronic heart failure constituted 3.3% of all medical admissions at Kenyatta National Hospital.

Objective: The purpose of the current study was to determine factors that affect adherence to treatment among patients with Chronic Heart Failure at Kenyatta National Hospital and assess any association between any such factors

Methodology: This was a descriptive cross-sectional study involving patients >18 years diagnosed with Chronic Heart Failure at Kenyatta National Hospital. Eighty three eligible and consenting study participants were recruited into the study using a convenient sampling technique. Data were collected by means of an interviewer administered questionnaire adapted from the Revised HF Adherence Questionnaire.

Results: Data from 83 patients was analyzed majority (n=51, 61.4%) of whom were women. The age of the patients ranged from 18 to 80 years with the majority (n= 37, 44.6%), between 21-40 years. Majority (n=58, 68.9%) of the patients considered appointment keeping, compliance to medication (n= 64, 77.1%), dietary restriction (n=59, 72%), regular exercise (n=49 59.0%), smoking cessation (n=59, 71%), and alcohol cessation (n=58, 69.9%) as very important. Fifty three (63.9%) respondents had not failed to take their medicines at any time. Majority (n=72, 86.8%) of the study participants were aware of the disease condition they were suffering from while valvular heart disease was the commonest comorbidity (n= 17 27.9%). The study revealed an association between sex and some adverse drug reactions using Pearson χ^2 test through bivariate analysis. Sleep disturbances and nausea occurred more in males than females while headache and drowsiness were more prevalent in females and in both cases the relationships were statistically significant ($p< 0.05$)

Conclusions: Adherence to medicines among patients with Chronic Heart Failure is reasonably high at Kenyatta National Hospital despite patients' knowledge level about the condition being generally low. Valvular heart disease was the most common comorbidity while hyponatremia was the most prevalent electrolyte disturbance, and tachycardia, vomiting and rash the most common adverse drug effects.

Key words

Chronic heart failure; adherence; compliance; adverse drug reactions.

1. Introduction

Chronic heart failure (CHF) is a clinical condition in which the heart is unable to provide adequate blood for the metabolic needs of the body (Whang et al, 2013). This is characterized by shortness of breath and fatigue at rest or with exertion in the presence of underlying structural and/or functional heart disease which results in diminished ability to increase cardiac output or cardiac work in response to an increase in pre-load (Katz et al, 2009).

Although the hemodynamic abnormalities may explain the symptoms of CHF, they do not adequately explain the disease progression and researchers have reported that activation of the sympathetic and the Renin Angiotensin Aldosterone System (RAAS) exerts a direct deleterious effect on the heart that is independent of their hemodynamic effects, and interventions targeting these neurohumoral systems favorably alter the natural history of the disease (Packer et al, 1999).Other researchers have similarly reported that the interplay between diverse organ systems contributing to CHF is mediated by the activation of various counteracting neurohormonal pathways geared to re-establishing hemodynamic homeostasis(Buglioni et al, 2015).

The exact prevalence of CHF is currently estimated to be between 1% and 12% in USA and Europe. Mann et al, 2008 estimated a prevalence of 2% and rising while in an earlier study, Mosterd et al, 1998 had estimated the overall prevalence to be 3.9%. Tantchou et al, 2011, in a study to determine occurrence, etiology and challenges in the management of CHF reported an occurrence of 5.7%, while among all admissions at Kenyatta National Hospital (KNH), CHF constituted 3.3% of cases and rheumatic heart disease was the commonest cause (Oyoo et al, 1999). Recent studies indicate that although CHF is still predominantly non-ischemic, coronary heart disease has assumed greater prominence in the last 15 years (Ogeng'o et al, 2014).The disease is the leading cause of hospitalization in patients over 65 years and represents a significant clinical and economic burden (Azad et al, 2014).

There is need for the healthcare professional to be equipped with the knowledge and tools to assure comprehensive care not only addressing the heart failure, but the individual as a whole especially the older patients (Azad et al, 2014). The patients also need to be informed of the complexity of the management regimens and the importance of adherence to the management plans.

Patients fail to adhere to medicines due to several reasons including, adverse effects of drugs, forgetfulness**,** and inadequate communication between the healthcare provider and the patient, emotional factors, occupation, cost of the medications and poor accessibility to prescribed medicines. These barriers to adherence could be the result of complex regimens, failure of the healthcare provider to adequately explain the benefits and adverse effects of the medicines, as well as failure to take into consideration the patient's occupation or the cost of the drugs, and a poor therapeutic relationship between healthcare provider and the patient. Non-adherence to a therapeutic regimen may result in negative outcomes and may be compounded in patients with multiple comorbidities which require multiple drug therapy (Hughes et al, 2004).

Non-adherence to medications, diet and fluid restriction in management of CHF decreases the efficacy of prescribed treatment and exposes the patient to clinical destabilization, which can lead to worsening of CHF symptoms (Hughes et al, 2004). Thus non-adherence may result in: poor clinical outcomes, poor health related quality of life and additional economic burden to the healthcare system.

While data on adherence is available in developed countries, there is paucity of data from local studies conducted in the developing countries. The purpose of the study was to determine the factors that affect adherence to medicines among patients with CHF at KNH and assess any association between any such factors

2. Methodology

2.1 Study design

The study design was descriptive cross-sectional. The purpose of the current study was to descriptively shed light on the factors affecting adherence among patients with CHF attending the cardiology clinic as well as those admitted in KNH with the condition.

2.2 Study area

This study was carried out at Kenyatta National Hospital (KNH). The hospital conducts a cardiology clinic once a week with approximately 80 patients per clinic day and an average of 30 new patients per month. KNH is a Teaching and National Referral Hospital with a bed capacity of 1800. Its choice as the study site was based on the availability of a sizeable number patients presenting with CHF.

2.3 Study population

The study population was patients aged above 18 years presenting with CHF admitted into Kenyatta National Hospital and those attending the cardiology clinic.

Eligibility criteria

Consenting male and female patients above the age of 18 years diagnosed with CHF were included in the study, while uncooperative patients due to dementia or psychosis and patients unable to participate in the study due to their disease condition were excluded.

2.4 Sampling

The sample size was determined using the Fisher and Van Bell formula (Le, 2003), applying the estimated prevalence of 5.7% (Tantchou et al, 2011).

Eighty three participants who meet the inclusion criteria were recruited into the study using convenient sampling.

2.5 Data collection

An interviewer administered questionnaire adapted from the Revised HF adherence Questionnaire was used

for purposes of collecting demographic data, responses with respect to adherence, level of knowledge about CHF, and types of adverse drug reactions experienced while on treatment for CHF (van der Wal et al, 2006).

Patients file records were reviewed to capture clinical data, treatment regimen, comorbidities associated with CHF, blood urea, creatinine and electrolyte levels.

2.6 Data analysis

Data were coded to ensure confidentiality, entered into the data base and double checked to ensure accuracy and cleaning. Descriptive data analysis was carried out on all variables using STATA V.12.

Bivariate analysis was used to establish the association between each of the predictor variables and the dependent variable, and multivariable regression to establish the association between several variables using a linear regression model.

2.7 Ethical considerations

Approval (**KNH-ERC/A/396**) was obtained from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UON-ERC), before the commencement of the study.

3. Results

3.1 Sociodemographic characteristics

Among 83 respondents, 51(61.4%) were female, and the age of the patients ranged from 18 to 80 years with the majority (n= 37, 44.6%), between 21-40 years, an important economically active age group.

Sixty one (73.5%), were married, and only 17(20.5%) had attained tertiary level of education.

Majority (n=38, 45.8%) were self-employed and 17 (20.7%) admitted having taken alcohol at some point in their lives and of those 17, 8 (47.1%), had taken it for more than 10 years. Thirteen (15.7%) reported having smoked at some point in their lives.

3.2 The proportion of patients with CHF that adhere to drugs

Indicators of adherence to management protocol

Patients were requested to report on their adherence to management protocol through several questions on the various indicators of adherence; these included follow-up with appointments, medication compliance, dietary restrictions, regular exercise, smoking cessation and alcohol cessation (**Table 1**). Majority (n=58, 68.9%) of the patients considered follow-up, acquiescence to medication (n= 64, 77.1%), dietary restriction (n=59, 72%), regular exercise (n=49, 59.0%), smoking cessation (n=59, 71.0%), and alcohol cessation (n=58, 69.9%) as very important. Between 0-1.2% considered these indicators as not important.

Non-adherence to medicines

Majority (n=53, 63.9%) of study participants reported having not failed to comply in taking their medicines at any time, with 28(33.7%) reporting having failed to take their medicine rarely, while 1(1.2%) reported having failed to take his medicines most of the time (**Table 2**). Seventeen (60.7%) of the respondents failed to take their medicine due to forgetfulness while 6(21.4 %) was because the instructions were too complicated.

Accessibility to medicines

Sixty eight (81.9%) of the respondents had no difficulty obtaining medicines prescribed for them while 15 (18.1%) found it difficult. Sixty three (75.9%) of the study participants had been informed by the healthcare provider as to why they were taking the prescribed medicines, while 20 (24.1%) denied having received such a communication.

3.3 Drugs prescribed for patients with CHF

Seventy five (90.4%) of the study participant were on a diuretic, while 45 (54.2%) were on a β-adrenergic receptor antagonist.   The most commonly prescribed drug combination was, a diuretic + ACE inhibitor + β-blocker+ cardiac glycoside (n=15, 19.0%).

Table 1: Indicators of adherence to management protocol

Indicator	Not important n (%)	Not very important n (%)	Important n (%)	Very important n (%)
Follow up	1 (1.2%)	2 (2.4%)	22(26.5%)	58 (68.9%)
Medication	0 (0%)	1(1.2%)	18 (21.7%)	64(77.1%)
Diet restrictions	1(1.2%)	3(3.7%)	19(23.2%)	59(72.0%)
Regular exercise	2(2.4%)	10(12.1%)	22(26.5%)	49(59.0%)
Smoking cessation	0 (0%)	2 (2.4%)	22(26.5%)	59 (71.0)
Alcohol cessation	1(1.4%)	1(1.2%)	23(27.7%)	58 (69.9%)

Table 2: Non-adherence to required use of medicines

Characteristic	Frequency (n)	Percentage (%)
Failure to take medicines		
Most of the time	1	1.2
Half the time	1	1.2
Rarely	28	33.7
None of the time	53	63.9
Reasons for failing to take medicines		
Side effects	1	3.6
Frequency of dosing	1	3.6
Medicines not working	1	3.6
Forgetfulness	17	60.7
Instructions are too complicated	6	21.4
Too many drugs	2	7.1

Table 3: Relationship between sex and adverse drug reactions

Adverse drug reaction	Males (n, %)	Females (n, %)	P-value
Sleep disturbances			
Yes	13(15.7%)	10(12%)	0.037
No	19(22.9%)	41(49.4%	
Headache			
Yes	9(10.8%)	27(32.5%)	0.026
No	23(27.7%)	24(28.9%)	
Drowsiness			
Yes	6(7.2%)	28(33.7%)	0.001
No	26(31.3%)	23(27.7%)	
Nausea			
Yes	13(15.7%)	9(10.8%)	0.021
No	19(22.9%)	42(50.6%)	

3.4 Patient knowledge about CHF

Majority (n=72, 86.8%) of the study participants were aware of the disease condition they were suffering from and 65(85.5%) had suffered from the condition for less than 5 years.

Fifty one (61.4%) had been admitted to a hospital for the condition, and of those who had been admitted to hospital, 18(35.8%) had been admitted once. While 40(48.2%) participants had been advised on the expected outcome of their condition 43(51.8%) were not aware of the outcome. Fifty six (67.5%) had been advised on lifestyle changes requisite to ensure that symptoms of CHF did not worsen and 29(34.9%) of the respondents understood a little regarding the requisite lifestyle changes.

3.5 Comorbidities associated with CHF

Valvular heart disease (VHD) presented as the commonest comorbidity (n=17, 27.9%) in patients with CHF.

3.6 Prevalence of adverse drug reactions used in the treatment of CHF

Fifty six (67.5%) of the study participants experienced tachycardia, while 54(65.1%) skin rash and 48(57.8%) vomiting during the course of treatment for CHF.

Others experienced various adverse drug reactions as shown in **Table 3**.

3.7 Serum levels of blood urea, creatinine and electrolytes

Majority (n=43, 51.8%) of the participants were hyponatremic and 11 (13.3%) had elevated levels of potassium. Twelve (14.5%) had elevated urea levels, and 10(12%) had elevated creatinine levels.

3.8 Association between sex and adverse drug reactions

Our study revealed a relationship between sex and some adverse drug reactions using Pearson chi square test through bivariate analysis (**Table 3**). Sleep disturbances and nausea occurred more in males than females while headache and drowsiness were more prevalent in females. Among the side effects explored less than half of the patients experienced them.

4. Discussion

The prevalence of CHF is slightly higher among women than men which does not concur with an earlier study by Ogeng'o et al, 2014 which reported a male:female ratio of 1:1 without a difference in age groups. Majority of the study participants were between 21-40 years, which is an important economically active age group (Tantchou et al, 2011). This shows an earlier onset of CHF compared to Caucasian populations probably due to the fact that the predominant cause of CHF in the Kenyan population is still rheumatic heart disease (Oyoo et al, 1999, Ogeng'o et al, 2014).

Adherence has been defined as the extent to which the patient's medication taking behavior corresponds with an agreed upon medication regimen (Riegel et al, 2012). This entails taking the correct medicine, the correct dose, at the right time, and avoiding missing a dose for more than a specified period of time. The six indicators of adherence assessed, included follow-up on appointments, compliance to medication, dietary restrictions, recommended regular exercise, smoking cessation and alcohol cessation. Majority of the study participant reported that they considered all the six indicators to be very important. Sixty nine percent of the study participants reported not failing to take their prescribed medicines at any time which is higher compared with adherence rate reported by Riegel et al (2012). Forgetfulness was the reason given by the majority of the participants for failing to take their medicines.

Accessibility to medicine is an important determinant of adherence and it is imperative to ensure that medicines are accessible to those who need them. Our study revealed that majority of the study participants did not find it difficult to access medicines prescribed for them. Non-adherence increases the cost of healthcare (Bagchi et al, 2007). This could be due to poor communication between the healthcare provider and the patient, but in our study we found that 79.5% of the participants had been informed as to why they were taking the prescribed medicines.

Majority of the patients diagnosed with CHF at KNH were on a diuretic with the most frequently prescribed diuretics being frusemide alone or in combination with an aldosterone receptor antagonist, invariably spironolactone. The other commonly used drugs in the treatment of CHF at KNH included beta adrenergic receptor antagonists, and cardiac glycosides. The most commonly prescribed combination at KNH was; diuretic + ACE inhibitor +beta-blocker +cardiac glycoside.

ACE inhibitors are indicated as first line therapy in patients with left ventricular systolic dysfunction with a reduced ejection fraction because they reduce both preload and afterload (peripheral resistance) without causing a reflex sympathetic activation (Swedberg et al, 2005, Bennett and Brown 2008). ARBs are indicated in patients who cannot tolerate ACE inhibitors (Granger et al, 2003, Pfeffer et al, 2003, Maggioni et al, 2002, Cohn et al, 2003) and Cardiac glycosides are indicated in any degree of symptomatic CHF (Coletta et al, 2003). Diuretics are essential in symptomatic management of CHF especially in the presence of pulmonary congestion and pulmonary edema.

Studies have shown that patients' education is a key component in comprehensive CHF management. There is however a gap between patients receiving and absorbing or retaining information on self-care (Ni et al, 1999). Other studies indicate that health literacy is independently related to disease knowledge, which underscores the need to improve patients' knowledge of their chronic diseases (Gazmararian et al, 2003).

Majority of the study participants were aware of the condition they suffer from, although the majority had suffered from the condition for less than five years. A small proportion had suffered for more than ten years and some had been hospitalized for more than seven times. The level of understanding of CHF was generally poor with only about one third of the participants reporting that they understood most things in respect of the lifestyle changes requisite to ensure that symptoms of CHF did not get worse.

Telemonitoring (TM) and structured telephone support (STS) have been used to improve outcomes in CHF and self-management programs have been shown to decrease readmission for CHF (Inglis et al, 2011, Ezekowitz et al, 2003), but there is still need for continuous education of both healthcare providers and patients (Achelrod et al, 2014). Effective communication is essential in management of chronic diseases and there is need for continuous education of both the health care providers and patients with respect to adherence and self-care in the comprehensive management of CHF.

Valvular heart disease was the most common comorbidity among CHF patients at KNH followed by hypertension, anemia and diabetes mellitus. Other comorbidities noted included, ulcers, ischemic heart disease, hyperthyroidism, dilated cardiomyopathy and restrictive cardiomyopathy. Ho et al, 2014 observed that comorbidities are common and result in increased hospital stay in patient with CHF. They reported anemia to be a common and independent prognostic factor for mortality, while other studies reported that renal failure, heart failure and anemia cause or worsen each other (Silverberg et al, 2005)

The most common adverse drug effects reported in our study are tachycardia, skin rash, vomiting, bradycardia,

renal dysfunction and hyponatremia. ACE inhibitors cause cough and are associated with compromising the renal function and should be withdrawn when serum creatinine increases by 100%, but ARBs have been reported to contribute to the risk of cancer (Sipahi et al, 2010)

Loop diuretics cause hypokalemia, hypomagnesemia and hyponatremia, while potassium sparing diuretics are associated with hyperkalemia, and digoxin which has a low therapeutic index causes bradycardia, nausea and vomiting (Bennett and Brown 2008). On their part beta-blockers cause fatigue and sleep disturbances and affect carbohydrate metabolism and may cause hypoglycemia and hyperglycemia in patients with or without diabetes (Svensson et al, 2003).

5. Conclusion

Adherence to medicines among patients with CHF is reasonably high at KNH, but patients' knowledge level about CHF was generally low. Valvular heart disease was the most common comorbidity while hyponatremia was the most prevalent electrolyte disturbance, and tachycardia, vomiting and rash the most common adverse drug effects. The study did not assess healthcare provider related factors that affect adherence.

Continuous education of both the healthcare provider and the patient should be done to build a strong therapeutic relationship. This will improve adherence to medicines, improve the patient's quality of life and ameliorate the economic burden to the healthcare system by reducing morbidity and mortality.

Conflict of Interest Declaration

The authors declare no conflict of interest.

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