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Clinical Pharmacist Led-Educational Intervention to Promote Medications' Adherence for Sudanese Patients with Heart Failure: A Prospective Study

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Abstract Clinical pharmacists are in a suitable position to improve medications adherence for chronic diseases, including heart failure (HF). This study aimed to identify if the structured educational intervention by the clinical pharmacist can improve adherence to HF medications in a specialized HF clinic. Methods: A quasi-interventional study was implemented in an outpatient HF clinic for six months at Ahmed Gasim Cardiac Surgery and Renal Transplantation Center, Khartoum, Sudan. Adherence was assessed by using Morisky-4 Medication Adherence Scale (MMAS-4). Clinical pharmacist intervention using verbal and written materials composed of different aspects to promote medications adherence for HF were performed during the study period. Results: Among 110 patients, 97.3% were non-adherent to HF medications at baseline, with the exception of receiving education about HF; all sociodemographic and clinical characteristics of patients were not associated with the non-adherence status. Significant improvement in medication adherence was reported after clinical pharmacist intervention by different views of MMAS-4. There was a reduction in the total mean MMAS-4 score (2.64 ±1.1 vs. 0.67 ±0.9, P=0.001), and a significant increase in the percentage of patients having high adherence (2.7% vs. 56.4%, P=0.001) before and after clinical pharmacist intervention. By contrast, the proportion of patients with medium and low adherence was significantly reduced after intervention (42.7% vs. 37.3%, P=0.001) and (54.5% vs. 6.4%, P=0.001), respectively. Conclusion: Non-adherence was highly prevalent among Sudanese patients with HF; the clinical pharmacist led-educational intervention can improve medication adherence for HF medications.

Keywords Heart Failure, Medication's Adherence, Education, Clinical Pharmacist, Sudan, Prospective Study

1. Introduction

Heart failure (HF) disease has poor prognosis, despite

advancements in medical and devise therapy in real-world settings. For patients with HF and reduced ejection fraction (HFrEF), mortality and hospitalization were significantly improved by adherence to Guideline Directed Medical Therapy (GDMT), including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), β-blockers (BBs), angiotensin II receptor blocker-Neprilysin-inhibitor (ARNi), and mineralocorticoid receptor antagonists (MRAs), sodium-glucose co-transporter 2 (SGLT2) inhibitors, in addition to digoxin and diuretics [1]. Poor medication adherence is considered as one of the logical reasons that explain the lack of improvement in outcomes [2]. Adherence is defined as "the extent to which a person's behavior, taking medication, following a prescribed diet, and/or executing lifestyle changes corresponds with agreed recommendations from the health care provider" [3].

Non-adherence of patients is considered as one of the best documented, but one of the least understood health-related behaviors. The World Health Organization described medications' non-adherence as "a new pharmacological problem." Moreover, substantially increasing the effectiveness of measures and interventions designed to increase patients' medications' adherence and recommendations may impact people's health far better than any other progress made in the therapeutic arena [4].

In the developed countries, data on medications adherence for patients with HF were available. These data include the rate of adherence, prevalence, reasons for non-adherence, and the strategies to improve medication adherence [5]. In contrast, information is scarce regarding medication adherence among the HF population in developing countries [6]. Management of patients in a specialized HF clinic has been associated with improved medication adherence and HF outcomes. These clinics are either run by a single provider or by a multidisciplinary (MD) HF team [3]. Pharmacists as drug experts are well equipped to optimize drug regimens, identify, and overcome barriers to medication adherence through education to the patients and the health care team about medication-related topics [7].

The adherence rates of Sudanese patients with cardiac diseases are generally low. For instance, analysis of adherence among cardiac patients revealed that more than half (51% (95% CI: 45.9–56.1) had poor adherence to their treatment [8]. Another study conducted in a rural area in Sudan among patients with hypertension and/or diabetes had an adherence rate of 39.6% [3]. Regarding HF in Sudan, only one published study assessed medication adherence among 76 heart failure patients admitted to the Sudan Heart Institute in Khartoum, which indicated that 75% of the respondents adhered to their medications [8].

Data about medication adherence among Sudanese patients with HF was scarce. To our knowledge was the first interventional study that utilized a clinical pharmacist. The main objective was to identify if the structured educational intervention by the clinical pharmacist could improve adherence to HF medications.

2. Materials and Methods

2.1. Study Design and Area

A quasi-experimental study, using pre-test and post-test was implemented in outpatient MD-HF clinic at Ahmed Gasim Cardiac Surgery and Renal Transplantation Centre, Khartoum, Sudan. The study was conducted through 2018-2019. The MD-HF clinic was the first MD clinic in Sudan established in parallel with study enrolment; different specialties with synchronized roles are taking care of HF Patients. The major responsibilities of clinical pharmacists were: 1) medications' adherence-related interventions in terms of assessment and barriers resolving, and 2) followed by patients education, which led to HF patients to take their active role in their management process.

2.2. Study Population

Patients were eligible for the study if; they were aged 18 years and above, documented EF ≤ 40%, using at least one HF medication, and committed to 6 months follow up. Those who were newly diagnosed with HF (less than four months), and patients with diagnosed cognitive impairment or psychiatric illnesses were excluded from the study.

2.3. Data Collection Tools

Data were collected by interviewing the patients using a pre-tested questionnaire composed of patients and medications data. Medication adherence was assessed using a validated Morisky-4 Medication Adherence Scale (MMAS-4) [9]. The MMAS-4 was translated to Arabic language by the research investigator and validated by two bilingual experts who made minor changes. The reliability of the scale was evaluated by internal consistency and reliability (Cronbach's alpha= 0.667). The Morisky Scale asks patients 4 'yes/no' questions regarding patterns of medicine use. Based on calculating the number of yes answers ('1' for each 'no' and '0' for each 'yes' response), patients were classified to high, medium, and low adherence, if the total scores were '0','1-2', and '3-4', respectively. Further, for the purpose of the present analysis, the patients were divided into 2 groups: those scoring 0 were considered adherent, and those scoring 1-4 were deemed non-adherent.

2.4. Educational Intervention by the Clinical Pharmacist to Improve Medication Adherence

Baseline information about adherence to HF medications (ACEIs, ARBs, ARNi, BBs, spironolactone, digoxin, and diuretics) was recorded at the beginning of the study using MMAS-4. Then the clinical pharmacist performed a face-to-face educational intervention at the MD-HF clinic that suited the patient's individual need. The clinical pharmacist used information about each HF medication collected from the European Society of Cardiology (ESC) web addenda, which was delivered in a simple way to HF patients [10]. The educational session took 20-30 minutes after the patient agreed to participate at days 0, 30, 60, and 90 using verbal and written material to highlight (1) the significance of medication adherence, (2) dose and frequency of medications, (3) differentiate between drugs used to reduce the HF symptoms/hospitalization and those used to reduce the mortality, (4) common side effects of each medication with advises to report early deterioration, (5) motivation to live with HF, and when to seek medical help. Patients were given chances to ask the clinical pharmacist questions regarding their drug therapy and to be provided with a telephone number for additional explanations, or in case a new problem/s. Each patient was followed up for a period of six months. The education was carried for the first three months only then to test the understanding and durability of clinical pharmacist intervention, finally medication adherence was reassessed for each patient at six months.

2.5. Data Analysis

Data were processed using Statistical Package for Social Sciences (SPSS), version 25 (IBM Corp., Armonk, New York, USA). Sociodemographic and HF characteristics were presented as the number of patients (%) for categorical variables and as mean ± standard deviation (SD) for continuous variables. Chi-square and Fisher exact tests were used to test the association between adherence and categorical variables, whereas as Mann-Whitney test was applied to test the association between adherence and continuous variables. For the primary outcome of medication adherence, the McNemar test was performed to examine a reduction of percentages (Yes) answers to MMAS-4 and the adherence category. Wilcoxon signed rank test was used to evaluate the total Morisky score at the baseline and after six months of clinical pharmacist intervention. P-value of less than 0.05 was considered statistically significant.

2.6. Ethics Statement

The ethical approval for this study was obtained from Medical Ethical Committee, Ministry of Health, Khartoum State (Serial Number: KMOH-REC-2020-NO.3), which followed the ethical criteria of the 1975 Declaration of Helsinki. All eligible patients were asked to participate in this study after obtaining written informed consent. To maintain confidentiality throughout the study, all collected data were coded.

3. Results

At six months, 110 participants completed the study with a mean age of 55.8 ±12.6 years. Near half of patients (44.5%) who belonged to the 60 years or over age group, more than half of the participants (57.3%) were males, the vast majority (90%) were married, and 70% had low-intermediate school education. About 70% of patients were unemployed, and nearly three-quarters (74.5%) had low monthly income. When studying cohort; if they received any specific education about HF, the vast majority 92.7% of them were answered negatively (Table 1). The means (SD) of the comorbid diseases and number of medications among the study participants were 1.42 ± 0.9 and 5.37 ± 1.71, respectively. On analysis of hospitalization history in the last year, the mean was found to be 1.65 ±0.9 (Table 1).

Figure 1 shows the analysis of the prescription pattern of medications at baseline. About 85.5% of patients were on drugs that act on renin-angiotensin system, 93.6% on BBs, 58.2% were on spironolactone, 5.5% on digoxin, and 75.5% were using furosemide.

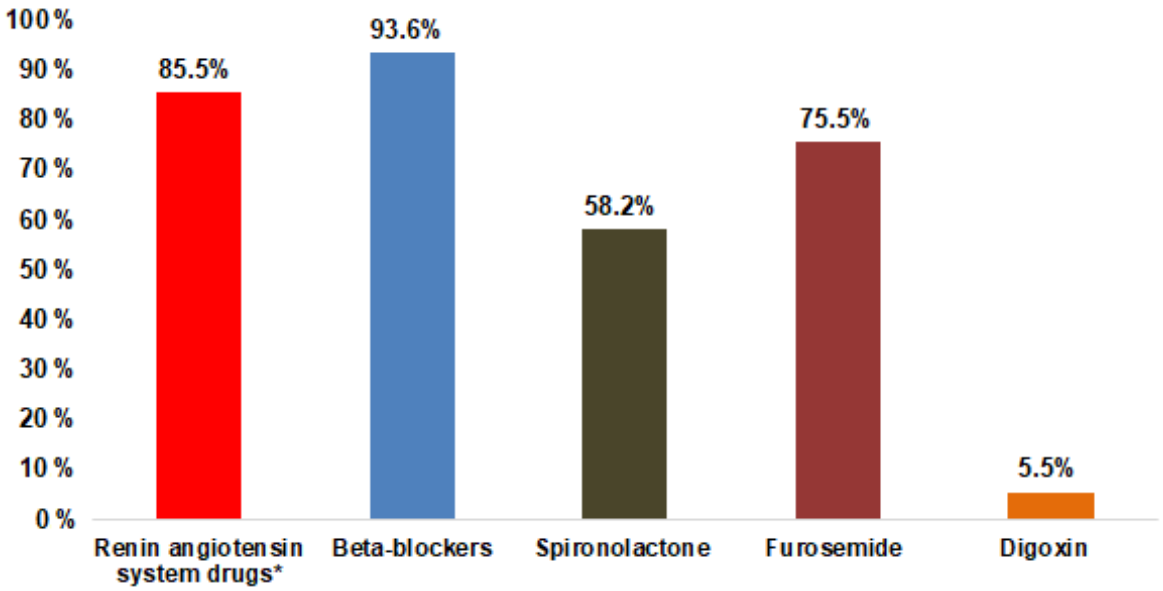
At the beginning of the study, the medication adherence measured by MMAS-4 showed that only 3 patients were adherent to HF medication. With exception of receiving education about HF, all socio-demographics and clinical characteristics of patients were not statistically associated with the non-adherence status of patients (Table 1).

Table 2 shows that, there was a significant reduction ($P<0.001$) in the number of patients answering (YES) after clinical pharmacist intervention as follows; 95.5% vs. 40% reported that they did ever forget to take their HF medications, 48.2% vs. 10.9% were careless at times about taking their HF medications, 66.4% vs. 10.9% sometimes stop taking HF medications if they feel worse, 52.7% vs. 10% sometimes stop taking their HF medications, if they feel better before and after clinical pharmacist intervention.

On investigation of medication adherence by categories of MMAS-4 (high, medium, low), the study revealed a significant increase in the percentage of patients having high adherence (2.7% vs. 56.4%) before and after clinical pharmacist intervention. By contrast, the proportion of patients reported as having medium and low adherence was significantly reduced after intervention (42.7% vs. 37.3%) and (54.5% vs. 6.4%), respectively. Similarly, there was a significant reduction in total Morisky score at the baseline and after 6 months of intervention, as shown in Table 3.

Table 1. Distribution of baseline characteristics and adherence to heart failure medications among heart failure patients (n=110)

Characteristics	All Frequency (%)	Adherent Frequency (%)	Non-adherent Frequency (%)	P value
Gender				
Male	63 (57.3)	2 (1.8)	61 (55.5)	0.609
Female	47 (42.7)	1 (0.9)	46 (31.8)	
Age group (years)				
18-39	10 (9.1)	0 (0.0)	10 (9.1)	
40-49	19 (17.3)	1 (0.9)	18 (16.4)	
50-59	32 (29.1)	2 (1.8)	30 (27.3)	0.494
≥60	49 (44.5)	0 (0.0)	49 (44.5)	
Marital status				
Single	11 (10)	1 (0.9)	10 (9.1)	0.727
Married	99 (90)	2 (1.8)	97 (88.2)	
Education Level				
Low – intermediate education	77 (70)	1 (0.9)	76 (69.1)	0.661
High Education	33 (30)	2 (1.8)	31 (28.2)	
Employment				
Employed	33 (30)	2 (1.8)	31 (28.2)	0.59
Unemployed	77 (70)	1 (0.9)	76 (69.1)	
Monthly income				
Low	82 (74.5)	2 (1.8)	80 (72.7)	
Middle	14 (12.7)	1 (0.9)	13 (11.8)	0.485
High	14 (12.7)	0 (0.0)	14 (12.7)	
Heart Failure Education				
Yes	8 (7.3)	2 (1.8)	6 (5.5)	0.019
No	102 (92.7)	1 (0.9)	101 (91.8)	
Number of comorbid diseases, mean ± SD	1.42 ± 0.9	0.67 ± 0.58	1.44 ± 0.67	0.125
Hospitalization (number/year), mean ± SD	1.65 ± 0.9	1.67 ± 1.53	1.65 ± 0.89	0.837
Number of medications, mean ± SD	5.37 ± 1.71	5.33 ± 1.15	5.37 ± 1.73	0.985



* Renin angiotensin system drugs: Angiotensin converting enzyme inhibitors (ACEIs), Angiotensin receptor blockers (ARBs), and Angiotensin receptor-neprilysin inhibitors (ARNi).

Figure 1. Prescription pattern of heart failure medications at baseline (n=110)

Table 2. Comparison of patients answers (YES) on MMAS-4 baseline and at 6 months of clinical pharmacist intervention

Questions		Frequency (%)	% Reduction	P value
Do you ever forget to take your HF medications?	Before Intervention After Intervention	105 (95.5) 44 (40)	55.5%	0.001
Are you careless at times about taking your HF medications?	Before Intervention After Intervention	53 (48.2) 12 (10.9)	37.3%	0.001
Sometimes if you feel worse when you take the HF medications, do you stop taking it?	Before Intervention After Intervention	73 (66.4) 12 (10.9)	55.5%	0.001
When you feel better, do you sometimes stop taking your HF medications?	Before Intervention After Intervention	58 (52.7) 11 (10)	42.7%	0.001

Table 3. Comparison of patients' total MMAS-4 score before and after clinical pharmacist intervention

Characteristics	Before intervention Frequency (%)	After intervention Frequency (%)	P value
High adherence (0) Medium adherence (1-2) Low adherence (3-4)	3 (2.7) 47 (42.7) 60 (54.5)	62 (56.4) 41 (37.3) 7 (6.4)	0.001 0.001 0.001
Dherent patient	3 (2.7)	62 (56.4)	0.001
	Before intervention	After intervention	P value
Adherence score (Mean ± SD)	2.64 ± 1.1	0.67 ± 0.9	0.001

4. Discussion

To the best of our knowledge, this is the first interventional study in Sudan that highlights the value of clinical pharmacist-led educational intervention on medication adherence for patients with HF. Even those two Sudanese studies that previously evaluated adherence were cross-sectional or observational without considering clinical pharmacist intervention. Moreover, one study assessed adherence to all cardiovascular diseases without concentrating on HF patients as in our study [8]. On the other hand, the only study that considered HF patients did not use a validated tool for adherence assessment or pharmacist intervention [11].

Although poor medication adherence represents a major problem, however, it also provides a major opportunity to improve outcomes in patients with HF [12]. It was found that, regardless of the assessment tool used or population studied, adherence rates are consistently suboptimal worldwide despite advances in HF management. Previous reports estimated that non-adherence in HF patients ranged from 22%–90% [6].

At baseline, the non-adherence to HF medications was 97.3%, which was high compared to studies conducted in Ethiopia (26.2%), Yemen (54.2%), Pakistan (72.7%), and Tanzania (74.7%) [6,13-15]. At the same line, our result was higher than two studies conducted in Khartoum, 25% and 51%. The contrary findings might be due to methods used to assess adherence and the cut-off point between adherence and non-adherence; for example, AL-khadher et al., evaluated adherence towards HF in Sudan Heart Institute by asking only one question [11]. Furthermore, another Sudanese study used MMAS-8, which has different definitions for non-adherence than ours (MMAS-4) [8].

Educational intervention is a cost-effective and achievable tactic to improve medication adherence, particularly in the context of the increasing cost of HF medications in nations with limited resources in terms of chronic disease [3]. Furthermore, when that intervention was performed by a drug expert as the clinical pharmacist in a specialized HF clinic and followed patients for 6 months, this could help tackle all patients' barriers, which ultimately improved medication adherence in HF. Literature reviews have emphasized the positive role of pharmacists' interventions on adherence to cardiovascular medications including HF medications [5,7].

In this study, we found that clinical pharmacists played a quintessential role in initiating such an education to patients who significantly improved the mean adherence score (2.64 SD±1.1 vs. 0.67 SD± 0.9 P<0.001) for HF medications after six months. These findings were in agreement with other studies evaluating the role of pharmacists' interventions to promote medication adherence in HF [5]. A study done in Japan showed that regular intervention by pharmacists to outpatients with HF significantly improved medication adherence (0.8 SD±0.91 vs. 0.63 SD± 0.49 P=0.013) compared with non-intervention group (1.08 SD±0.49 vs. 0.92 SD± 0.49 P=0.212) [15].

Furthermore, our findings showed a significant increase in the percentage of patients having high adherence (2.7%

vs. 56.4%) before and after clinical pharmacist intervention. Similarly, a study conducted in Israel revealed that direct pharmacist counselling for HF patients prior to hospital discharge led to improve the adherence percentage (77.83%) compared with non-interventional group (62.46%), and significantly reduced the number of hospital readmission for the pharmacist-intervention group [17].

The findings of our study also highlighted the importance of pharmaceutical care in enhancing the adherence through providing education to patients regarding their medications, as there was a significant increase in the number of adherent patients (3 vs. 62) following pharmacist intervention (Table 3). These findings are in line with a randomized clinical trial conducted in the United Arab Emirates that indicated utilization of pharmaceutical care for HF patients through combined intervention of treatment algorithm and patient education led to significant increase in the number of individuals who adhered to medications (85 vs. 35) and lifestyle advise (75 vs. 29) compared to non-intervention group [18]. In consistent, a randomized trial showed that pharmaceutical care for outpatients with HF improved medications adherence, and decreased the use and cost of health care by decreasing the number of emergency department visits and hospital admission [19].

There were some limitations to this study; it was a single-centre, nonrandomized study that only used questionnaire to assess adherence, which depends mainly on memory and the trustworthiness of patients. This may lead to over-or underestimation of the results. Moreover, the study was not testing the relationship between medication adherence and HF hospitalization or mortality, due to the fact that patients were relatively stable, which may lead to biased results. So, multicentre randomized studies, using different methods (subjective and objective) to assess adherence, and including a large number of clinical pharmacists, are urgently needed.

Despite the aforementioned limitations, this study had some strengths; we moved from theoretical to interventional, giving HF patients' chances to contribute to their treatment actively. Furthermore, in Sudan as a low to middle income country, we can utilize clinical pharmacists to promote medications' adherence for HF and other chronic diseases by adding adherence assessment and educational intervention into routine work, this will help the patients and health system with economically feasible tools.

5. Conclusions

Clinical pharmacist through educational intervention was improving medication adherence for Sudanese patients with heart failure in outpatient MD-HF clinic. The positive findings of the current study will encourage other hospitals in Sudan to establish their specialized MD clinic for HF and other cardiovascular diseases. In addition, it will let policymakers in Sudan pay more attention to clinical pharmacists' roles in taking national projects for medication adherence for chronic diseases and establishing an adherence assessment tool that suits our society's needs.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Author Contribution

K.O. Ahmed, A. B. Babiker, E.M. Taj Eldin, M. A. Yousif, A.A. Albarraq involved in study concept and design, analysed and interpreted the data, had full access to all of the data in the study, and took responsibility for the integrity of the data and the accuracy of the data analysis. K.O. Ahmed, B.A.Yousef, N.E. Ahmed acquired data. All authors contributed to the drafting and editing of the article and have granted their approval of the submitted manuscript. A. B. Babiker, E.M. Taj Eldin supervised the study.

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