

# Patient Medication Adherence and Physician Prescribing among Congestive Heart Failure Patients of Yemen

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Alakhali, *et al.*: Medication Adherence and Prescribing among Congestive Heart Failure Patients

Congestive heart failure has been associated with high morbidity and mortality requiring hospitalisation and is further complicated by noncompliance and under prescriptions. We aim to determine medication adherence and percentage deviation among Asians population in general and Yemenis in particular. A cross-sectional, prospective observational study with purposive sampling was conducted at two cardiac outpatient centers in 70 congestive heart failure patients for a period of 3 months. An Arabic translated Morisky 4 item scale assessed the adherence of patients. Deviation in prescribing was determined by chart review. All 70 patients had mean age of  $56.6 \pm 16$  years. Morisky 4 item scale predicted low adherence ( $n=33$ ; 47.1%) and overall nonadherencerate ( $n=38$ ; 54.2%) was slightly higher than adherence. Percentage nonadherence versus adherence was high with diuretics (53 vs. 46%) and, digoxin (40 vs. 29%). The adherence percentage of angiotensin receptor blockers (9%) and beta blockers (8%) was low. Diuretics were the most prescribed drugs ( $n=69$ ; 99%), followed by angiotensin converting enzyme inhibitors ( $n=51$ ; 73%), cardiac glycoside ( $n=48$ ; 69%), few patients were on angiotensin receptor blockers ( $n=8$ ; 11%) and ( $n=9$ ; 13%) beta blockers. The maximum prescribing rate deviation was seen with angiotensin receptor blockers (-89%) and beta blockers (-87%) followed by nitrates (-77%). Digoxin (-31%) and angiotensin converting enzymes (-27%) deviated comparatively less. Prescribing as well as utilisation rates generally were low resulting in nonachievement of therapeutic goals which could be resolved using multimodel approach.

**Key words:** Adherence, Arabic 4 item Morisky scale, congestive heart failure, deviation in prescribing

Congestive heart failure (CHF) is a progressive syndrome with a significantly shortened life expectancy, debilitating symptoms resulting in frequent hospitalisation, altogether constituting an important medical, social, and economic problem. In longstanding heart failure, prognosis appears to be worse than that seen with the majority of cancers, with 50% mortality after 4 years<sup>[1,2]</sup>. Approximately 2-3% of adult population has CHF, with rising prevalence of 10% or more among aged<sup>[3]</sup>.

Adherence rates of patients in various observational studies were observed to be between 61 and 80% for all heart failure medications<sup>[4]</sup>. One of the leading causes of hospital readmission and mortality among patients with CHF is nonadherence<sup>[5]</sup>. Nonadherence significantly contributes to morbidity and mortality, and wastes scarce health resource<sup>[6]</sup>.

Hospitalisation accounts for almost 70% of total costs, which is the greatest contributor to the costs of treatment and care for CHF patients<sup>[7]</sup>. Drug nonadherence of patients not only leads to treatment inefficacy, but also increases the risk of recurrence, pain and unwanted suffering and increase of the cost of therapy<sup>[8]</sup>.

In CHF quality of life observed has been less when compared to any other chronic conditions of lung disease, arthritis or diabetes<sup>[9]</sup>. As per the guidelines of European Society of Cardiology (ESC)<sup>[10]</sup> and the American Heart Association/American College of Cardiology (AHA/ACC)<sup>[11]</sup>, it has been recommended to prescribe multiple medications like loop diuretics, angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), beta blockers, aldosterone antagonist like spironolactone, and ionotropics like digoxin for beneficial effects in cardiac failure patients. Specific classes of medications are known to decrease the risk of hospitalisation and death in heart failure patients. Evidence based drug

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therapy in heart failure improves symptoms over time, and increase patient's quality of life<sup>[1]</sup>.

The majority of heart failure patients receiving these medications do not continue this therapy for the long term which offsets the full mortality benefit that might result from improved prescribing rates. Considering the superior survival advantage observed in clinical trials, nonadherence to these agents is the likely cause of preventable deaths and is correctable<sup>[12]</sup>.

Despite the reasonable adherence of prescribing in line with the guidelines, the success of drug therapy is far from achieving target, due to the prevailing nonadherence which continues to remain as major clinical problem in management of CHF patients<sup>[13]</sup>. In a systemic review, medication adherence had been assessed using different methods of adherence, in which adherence varied among CHF patients<sup>[14]</sup>.

Availability of data on adherence of CHF medications and the prescribing pattern among Asian patients in general and Yemenis population in particular are scarce. Our aim in this study was to determine the adherence among the CHF outpatients using a questionnaire; so that our prevalence of nonadherence could be assessed and to determine the percentage of deviation observed in actual prescribing and recommended guidelines<sup>[1]</sup>.

## MATERIALS AND METHODS

A cross-sectional, observational study with purposive sampling was conducted at cardiac outpatient department of two Government Hospitals, Sana'a, Al-Thawrah and Thamar's, Al-Wahdah, Yemen. Patients were enrolled prospectively for a period of 3 months. A validated standard questionnaire was used for patient interviewing after its translation to Arabic language which assessed the adherence of patients.

A total of 70 patients with CHF were interviewed personally and related data were collected after medical chart review. Diagnosis of heart failure was established on the basis of history, physical examination, and echocardiography. Patients above 18 years, who were confirmed with the diagnosis of heart failure and were classified as having NYHA (New York Heart Association) class (III-IV)<sup>[15]</sup> were included in study. Patients who were having heart failure associated with valvular heart disease, recent myocardial infarction,

referred for heart transplantation, life threatening comorbidities such as severe renal failure, liver failure, severe COPD, and advanced malignancy were excluded. Appropriate ethical approvals were obtained from the concerned hospitals.

Patients were assessed for adherence using a validated 4 item questionnaire of Morisky scale<sup>[16]</sup> (Table 1). This questionnaire was offered in Arabic. Patients adherence to prescribed CHF medications were assessed through interview and were graded as low, medium and high adherence, if the total score obtained were '0', '1-2', and '3-4', respectively, by assigning score '1' for each 'no' and '0' for each 'yes' response. Patients were also assumed to be noncompliant, if the total score obtained was below 2. Prescribing of CHF medications was assessed against the recommendations of AHA<sup>[1]</sup>, and percentage deviation was derived.

A data collection form was prepared to collect the patient related data (age, gender, marital status, work status, residential status, risk factors, causes of heart failure, drugs prescribed). Data were entered and analysed in Microsoft Excel-2007 for Windows. Continuous data were analysed statistically using student's *t*-test, and categorical data were analysed by Chi-square test. Descriptive analysis was used to summarise the data. Level of significance was assigned at,  $P < 0.05$ .

## RESULTS AND DISCUSSION

All 70 patients enrolled had mean ( $\pm$ SD) age of  $56.6 \pm 16$  years. Out of them majority were male ( $n=46$ ; 65.7%) patients. The demographic characteristic of the study patients are presented in Table 2. More than three-fourth of the patients were married ( $n=63$ ; 90%) and work status of patients in terms of employee was more than employer ( $n=54$ ; 77%). Patients resided more in villages ( $n=43$ ; 61%) than town. Hypertension ( $n=63$ ; 47%) was major risk factor as well as single etiology ( $n=36$ ; 51%) responsible for the development of CHF. Other risk factors associated were smoking ( $n=28$ ; 21%) followed by diabetes ( $n=15$ ; 11%).

Using Morisky scale<sup>[16]</sup>, it was determined that, the percentage of patients having low adherence ( $n=33$ ; 47.1%) were more as compared to patients having high adherence ( $n=28$ ; 40%) and those having medium adherence ( $n=9$ ; 12.9%). Assuming that,

if the mean Morisky score was  $<2$ , patient was considered as nonadherent and the total number of nonadherent patients exceeded ( $n=38$ ; 54.2%) the adherent patients. It was found that age ( $P=0.3$ ) and gender ( $P=0.6$ ) played no role in influencing the adherence behaviour, as in Table 3.

The percentage of adherence and nonadherence with regard to different drug classes are presented in fig. 1. With diuretics drug group, the percentage nonadherence (53%) was higher than adherence (46%), while percentages for ACEI were almost equal. The adherence percentage associated with ARB (9%) and beta blockers (8%) was more than nonadherence. Digoxin had nonadherence percentage (40%) more than adherence (29%).

**TABLE 1: MORISKY SCALE**

	No	Yes
Do you ever forget to take your medications?	(1)	(0)
Are you careless at times about taking your medications?	(1)	(0)
When you feel better, do you sometimes stop taking your medications?	(1)	(1)
Sometimes, if you feel worse when you take your medicines, do you stop taking them?	(1)	(1)

**TABLE 2: POPULATION CHARACTERISTICS AND DISEASE STATUS OF HEART FAILURE PATIENTS**

Characteristics	Number (%)
Age (yrs), mean ( $\pm$ SD)	56.6 ( $\pm$ 16)
Gender	
Male	46 (65.7)
Marital status	
Married	63 (90)
Work status	
Employee	54 (77)
Employer	16 (23)
Location of patients	
Village	43 (61)
Town	27 (39)
Risk factors	
Hypertension	63 (47)
Smoking	28 (21)
Diabetes	15 (11)
Hyperlipidemia	14 (11)
Family history	13 (10)
Etiology	
Hypertension	36 (51)
Hypertension/Ischemic heart disease	18 (26)
Dilated cardiac myopathy	6 (9)
Rheumatic heart disease	5 (7)
Hypertension/Rheumatic heart disease	3 (4)
Ischemic heart disease	2 (3)

Yrs=years; SD=standard deviation of ( $N=70$ ) patient sample

On analysis of prescription pattern of major CHF medications, it was found that diuretics were the most prescribed drugs ( $n=69$ ; 99%), followed by ACEI ( $n=51$ ; 73%) and cardiac glycoside ( $n=48$ ; 69%). ARB ( $n=8$ ; 11%) and beta blockers ( $n=9$ ; 13%) had been found in few prescriptions. Specific drugs under various classes of drugs recommended for CHF patients are presented in Table 4. Among the diuretics, combination of furosemide/spironolactone ( $n=46$ ; 66%) were commonly prescribed than furosemide alone ( $n=23$ ; 33%). In the class of ACEI, lisinopril ( $n=22$ ; 31%) and captopril ( $n=21$ ; 30%) had been almost equally prescribed. Among ARB, candesartan ( $n=5$ ; 7%) has been used slightly more than losartan ( $n=3$ ; 4%). Among beta blockers carvedilol ( $n=5$ ; 7%) and bisoprolol ( $n=4$ ; 6%) have been prescribed with almost equal frequency.

The prescribing of the recommended drugs for the management of CHF differed from the ideal prescribing recommendations as shown in fig. 2. The maximum deviation in prescribing rate was observed with the drug class of ARB ( $-89\%$ ) and

**TABLE 3: DISTRIBUTION AND INFLUENCE OF AGE AND GENDER AMONG ADHERENT AND NONADHERENT GROUPS**

Factors	Adherence ( $n=32$ )	Nonadherence ( $n=38$ )
*Age, mean ( $\pm$ SD)	54.8 ( $\pm$ 17.6)	58.3 ( $\pm$ 15.1)
†Gender		
Male ( $n=46$ )	20	26
Female ( $n=24$ )	12	12

\*Age ( $p=0.3$ ) and †Gender ( $p=0.6$ ); SD=standard deviation of ( $N=70$ ) patient sample

**TABLE 4: FREQUENCY OF DRUG CLASS AND SPECIFIC DRUGS PRESCRIBED IN HEART FAILURE PATIENTS**

Drug groups	Drug	Frequency (%)
Angiotensin converting enzyme inhibitors	Lisinopril	22 (31)
	Captopril	21 (30)
	Ramipril	6 (9)
Beta blockers	Enalapril	2 (3)
	Carvedilol	5 (7)
Angiotensin receptor blockers	Bisoprolol	4 (6)
	Candesartan	5 (7)
Cardiac glycoside	Lorasartan	3 (4)
	Digoxin	48 (69)
Diuretics	Furosemide+spironolactone	46 (66)
	Furosemide	23 (33)
Nitrates	Isosorbide dinitrate	12 (17)
	Glyceryl trinitrate	4 (6)
Calcium channel blockers	Amlodipine	3 (4)
	Diltiazem	1 (1)
Anticoagulants	Warfarin	9 (13)
Antiplatelet	Aspirin	46 (66)

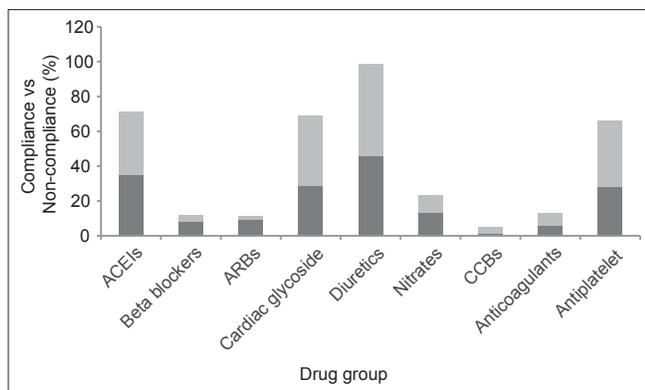


Fig. 1: Percentage of adherence and nonadherence observed with CHF medications in heart failure patients.

■ Nonadherence; ■ adherence. CHF stands for congestive heart failure.

beta blockers (-87%) followed by nitrates (-77%). Digoxin (-31%), ACEI (-27%) were the preferred drugs with less comparative deviation. Spironolactone had not been prescribed as a single drug but it had been used in combination as diuretics with furosemide, still spironolactone showed an individual deviation of -34%.

The overall nonadherence percentage observed in our study was 54.2%, which was measured using Morisky scale through patient interviewing. Similarly, by using questionnaire method, Ni *et al.* found a nonadherence of 23%<sup>[17]</sup>, Evangelista *et al.* found a nonadherence of only 4%<sup>[18]</sup>, whereas Artinian *et al.* recorded a 7% nonadherence rate<sup>[19]</sup>. On comparing nonadherence of our study with the similar studies our nonadherence rate recorded was found to be highest. There are different methods to assess adherence of medications, and various studies have used different adherence assessment methods which use different procedures in different patient population so comparison between them may not be accurate; this could be a partial reason for variation in adherence rate.

Data on Asian population studied Sayed *et al.* showed nonadherence of 72.7% which is higher when compared to our study as the method of adherence assessment was different. Maximum adherence was observed for diuretics (60%) followed by beta blockers (50%) and spironolactone (43.4%), while in our study maximum adherence was observed with diuretics (46%), followed by ACEI (35%), cardiac glycoside (29%), spironolactone and furosemide in combination for diuresis (29%) and found no effect of gender on adherence, as seen in our study<sup>[20]</sup>.

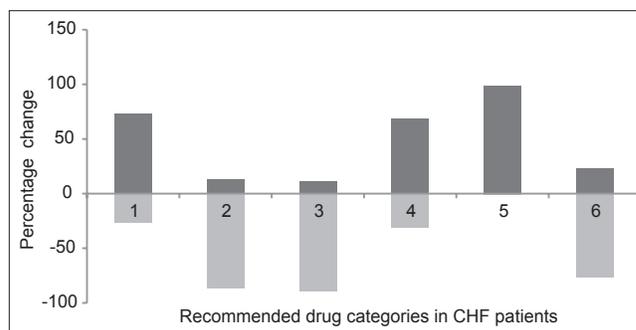


Fig. 2: Percentage deviation of CHF medications in terms of actual prescribing rate.

■ % actually prescribed; ■ % deviation observed in prescribing. CHF stands for congestive heart failure; 1=Angiotensin converting enzyme inhibitors; 2=Beta blockers; 3=Angiotensin receptor blocker; 4=Cardiac glycoside; 5=Diuretics; 6=Nitrates.

Adherence percentage of patients to medication for ACEI alone was 35%, which is low when compared to average adherence rate for ACEI which range from 67 to 92.9% in various studies<sup>[21]</sup>. Utilisation rates of continued therapy of beta blockers at 6, 12 and 24 months were 69, 70 and 74%, respectively<sup>[22]</sup>, whereas in our case it was just 8% when measured cross-sectionally. Digoxin adherence in heart failure patients was found to be 29% which was relatively higher than reported by Monane *et al.* (10%)<sup>[23]</sup>.

Combined utilisation rates of ACEI and beta blockers in this study was found to be 43% which is lower in contrast to median adherence 91.6 and 92.9% for beta blockers and ACEI, respectively<sup>[5]</sup>. The adherence percentage of patients for ACEI and ARB both combined was 44%, though ARB have been studied as alternative agents to ACEI and also as add-on therapy<sup>[24]</sup>, some benefit has been shown when an ARB is added to ACEI therapy<sup>[25]</sup>. The low adherence rate could be attributed to the lack of knowledge regarding disease process and importance of drug therapy.

Prescription containing medications for CHF in our study had diuretics (99%) in almost all prescriptions, followed by (73%) ACEI, (69%) cardiac glycoside, (13%) beta blockers and (11%) ARB. In a similar study by Sayed *et al.* showed prescription rate of 60.2% for diuretics, 56.1% for ACEI, 38.2% for digoxin which were relatively lower than our study, except with beta blockers (45.3%) which were comparatively higher than our prescription rate. Spironolactone was found in 43.0% of prescriptions. In our study, the prescriptions did not contain

spironolactone as single aldosterone antagonist, as recommended in guidelines, the use of spironolactone in addition to usual heart failure medication decreases mortality by 30%<sup>[26]</sup>, except that spironolactone had been prescribed for diuresis as combination therapy with furosemide, this could be attributed to lack of awareness on the advantage of spironolactone. In our study, the prescription rate of drugs as recommended by guidelines were more in comparison to the above study, but the adherence rate observed was far low<sup>[27]</sup>.

According to the reports of European, American and Canadian studies 28 to 75% of heart failure patients are prescribed an ACEI and only 11.8 to 41% are prescribed beta blockers<sup>[28-32]</sup>. Beta blockers prescribing rates for elderly patients are still lower<sup>[22]</sup>. In our study frequency of ACEI prescribed was 73%, and for beta blockers it was only 13%, with 27% of study patients above 65 years, which conveys that ACEI falls within the range mentioned in other studies.

In the present study combined prescriptions of ACEI and ARB add up to 84% which was marginally higher than other studies (61.7 to 82%)<sup>[28]</sup>. Guidelines recommend the routine use of ACEI or ARB, and beta blockers in heart failure patients due to their proven improvement in morbidity, mortality and hospitalisation rates<sup>[1]</sup>. Our study indicates that these recommended medications had been underprescribed (fig. 2), where deviation in prescribing rate with the drug class of ARB (-89%), beta blockers (-87%) followed by nitrates (-77%) were more prominently observed and less so with digoxin and ACEI. Nitrates are required to be prescribed in combination with hydralazine in selected severe cases<sup>[1]</sup>. With regard to ARB, current recommendations suggest it is used only when ACEI is contraindicated, so the percentage deviation observed could be exaggerated. Though the reason is unclear, inadequacy in prescribing rate could be attributed to the lack of updation on newer drug therapy and their advantages, unaware of guidelines or do not agree with evidence based therapy and in certain cases patient resists medication change.

From the observations of utilisation data and drugs prescribed, it can be established that there exists a wide variation in prescribing and adherence rate. Physician under-prescribing along with poor adherence rates of ACEI and beta blockers are the

glaring under-utilisation, which highlights the need for bridging the gap in optimal care to patients. Limitations in this study are: Translated Arabic Morisky 4 item scale has not been validated as it's assumed that the responses observed in either of the versions are same. Non-use of CHF medications due to contraindications was not recorded.

Nonadherence is very common among heart failure patients. Despite the evidence-based drug therapy showing a benefit for neurohormonal blockers in patients with heart failure, the prescribing as well as utilisation rates generally appears to be low leading to subtherapeutic outcome. In addition to recognising the fact, adequate multimodel interventions focusing on the gaps could be instituted to realise prescribing and utilisation targets.

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