Non-Adherence to the Guideline Recommended Pharmacologic Therapy in Patients with Reduced Left Ventricle (LV) Ejection Fraction (HFrEF)

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Abstract-
The aim of the present study was to ascertain how closely heart failure patients with reduced ejection fraction (HFrEF) adhere to the pharmaceutical therapy that is advised by guidelines. Total 137 patients were taken for the proposed research study. According to the Morisky medication adherence score, 36.5% of the participants in our study were found to have insufficient adherence. Age (elderly), cognitive impairment, the use of multiple medications and monthly income were significant contributors to non-adherence. Every piece of data was acquired using a pre-made proforma. Patients were asked questions on their drug adherence using the eight-question Morisky tool. Following that, it was divided into two categories: appropriate adherence (score 6 or above) and insufficient compliance (score 5 or below). In patients with heart failure, satisfactory adherence to the pharmaceutical therapy prescribed by guidelines was noted in 63.5 percent of cases. 63.5 percent of participants in this study were found to have good adherence to their prescription regimens (Morisky score of 6 or above). Nonetheless, it was noted that 36.5 percent of the HFrEF patients in our study had inadequate adherence. Increasing drug adherence requires regular patient counselling and the care they receive.

Keywords: pharmaceutical therapy adherence by guidelines, heart failure, and drug adherence.

I. INTRODUCTION

Ventricular dysfunction is a condition associated with heart failure (HF). Both ventricles may be affected simultaneously or independently; left ventricular (LV) failure results in exhaustion and dyspnea, whereas right ventricular (RV) failure results in a buildup of fluid in the abdomen and peripheral tissues (Kocabaş et al., 2020). Echocardiography, plasma natriuretic peptides levels, and chest X-rays confirm the first clinical diagnosis (Kocabaş et al., 2023). According to Lawson et al. (2016), treatment options include specialized implantable pacemakers/defibrillators as well as additional components, diuretic medications, angiotensin-converting enzyme (ACE) inhibiting agents, anticoagulants, angiotensin II receptor blockers, beta-blocking medications aldosterone inhibitors, sodium-glucose cotransporter-2 inhibiting agents, neprilysin inhibitors, sinus node inhibiting agents, and adjustment of the causes of heart failure syndrome. Cardiac-related rise of arterial or systemic arterial pressures might result in organ obstruction in heart failure, and the cardiac system may not pump enough blood to tissues for their metabolic needs. Defects in either or both of the systolic or diastolic functions might cause this illness. There are variations in the external matrix's collagen production in addition to alterations in cardiac function, which may be the underlying aberration (Hood et al., 2018; Ruppar et al., 2016; Ekman et al., 2017). Heart failure (HF) can also be brought on by cardiac anatomical defects (such as congenital malformations or valvular illnesses), irregular rhythms (such as an abnormally fast heart rate), and excessive metabolic needs (such as those brought on by thyrotoxicosis). Nonetheless, during the course of 15 years, the percentage of people with heart failure using beta-blocker medications in European nations has risen from 37 percent to 91 percent (Wang et al., 2023). Patients with heart failure (HF) who do not follow guidelines when receiving medical therapy are more likely to experience increasing symptoms, more frequent hospitalizations, and early mortality. Additionally, non-adherence puts individuals at risk for needless treatments, tests (such as medical imaging, and laboratory tests), and surgical operations (such as cardiac organ transplantation, device medical treatment, and more.) (Bitar et al., 2019). These risks also have a substantial financial impact on economies due to preventable hospital stays, wasted resources, and complications of disease (Krueger et al., 2018). According to Gupta et al. (2021), there is a variation in the estimated prevalence of non-adherence to heart failure drugs from 55 percent to 60 percent among cohorts (Ødegaard et al., 2022; Voors et al., 2016). For patients, carers, and those making decisions to grasp targets for the successful execution of guideline-directed medical therapy (GDMT), research on drug compliance and persistence is crucial (Spreafico et al., 2020; Williams et al., 2019; Burns et al., 2019). In real life, treatments that increase adherence and tenacity may have a greater influence on heart failure outcomes than novel medications. However, the constraints of many patient databases, such as poor follow-up or insufficient cross-linkage, or the fact that they rely on highly chosen populations of patients, frequently make it difficult to conduct research on real-world patient populations. Therefore, the current study's goal is to ascertain how closely heart failure patients with reduced ejection fraction (HFrEF) adhere to the pharmaceutical therapy that is advised by guidelines.

II. MATERIAL AND METHODS

The research comprised known cases of patients who had reduced ejection fraction (HFrEF) that arrived at the Indus Hospital. The Morisky medication adherence scale was used to assess their compliance with prescribed medicine and the main causes of non-

adherence. The study's foundation was a cross-sectional care analysis. adults who have been 18 years of age or older and have had an echocardiogram showing a left ventricular (LV) ejection fraction (EF) of no more than forty percent for over thirty days. The study comprised patients whose doctors had prescribed medications for HFrEF. Patients were asked questions on their drug adherence using the eight-question Morisky tool. Following that, it was divided into two categories: appropriate adherence (score 6 or above) and inadequate compliance (score five or below). SPSS version 26 was used to analyze the data. Based on normalcy, the mean ± SD or median was calculated for age, level of education, medication duration, and monthly earnings. For every categorical variable, including marital status and gender, the percentage and frequency were calculated. Workplace, known co-occurring conditions, addiction (Naswar, Pan, gutka, etc.), smoking habits (smoker or non-smoker), prescription medications, and medication compliance.

III. RESULTS

In this study, 137 patients with left ventricular (LV) ejection fraction (EF) of no more than 40 percent on echocardiography and medications recommended for HFrEF by their healthcare providers were included. 52 (37.96 %) and 85 (62.04 %) of the participants were female. Of those receiving treatment, 88 percent were married. The ladies were almost all housewives. The following tables display the patients' profession and level of education. Only 19 of the patients (13.9 percent) were smokers, and 80.3 percent of patients had co-morbid conditions. The most prevalent comorbid, seen in more than fifty percent of cases, was hypertension and diabetes. In terms of drugs, the most regularly consumed categories were diuretics (85.4 percent), statins (93.4 percent), ACEIs (78.1 percent), and beta blockers (97.8 percent). Adherence to the pharmaceutical therapy prescribed by the guidelines for individuals with heart failure and a lower ejection fraction. 63.5 percent of heart failure patients showed adequate compliance with the pharmaceutical therapy prescribed by the guidelines, while 36.5 percent showed a lack of compliance or non-adherence.

In contrast to older patients, young people have been shown to be more adherent; mean family size, length of medication use, and years of schooling did not significantly affect this finding. Compared to patients with lower incomes, those with greater incomes were more devoted. The percentage of non-adherence was statistically not significant about marital status, occupation, or education, but it was substantially greater in patients who were widowed or separated. In summary, neither the rate of non-adherence among smokers nor non-smokers nor among patients with concomitant conditions was statistically significant. With the exception of Angiotensin-Converting Enzyme Inhibitors (ACEI), the rate of non-adherence to recommended medicine was likewise not statistically significant. There are several reasons why patients do not follow guidelines when receiving therapy, but the most frequent one is Issues with affordability.

Mean Median, Mode, Standard Deviation and SEM of Demographic Information of Patients

Statistics		Age in years	Gender	Occupation	Education	Marital Status	Smoking Status
N	Valid	137	137	137	137	137	137
	Missing	0	0	0	0	0	0
Mean		56.88	1.38	9.97	2.92	2.17	1.86
Std. Error of Mean		1.000	.042	.325	.097	.053	.030
Median		56.00	1.00	11.00	3.00	2.00	2.00
Mode		50	1	13	3	2	2
Std. Deviation		11.705	.487	3.806	1.131	.625	.347
Variance		137.016	.237	14.484	1.280	.391	.120

Statistical Analysis of Demographics

Age in years		
	Frequency	Percent
25-40	2	1.5
41-50	14	10.2
51-60	53	38.7
61-70	48	35.0
71-80	16	11.7
91-100	4	2.9
Total	137	100.0
Gender		
Male	85	62.0
Female	52	38.0
Total	137	100.0
Occupation		
Managers	1	.7
Technicians and associate Professional	6	4.4
Clerical support workers	7	5.1
Service and sales workers	10	7.3
Skilled Agriculture, Forestry and Fishery workers	13	9.5
Craft and related trade workers	14	10.2
Plant and machine operators	1	.7
Elementary occupations	2	1.5
Unemployed	15	10.9
Housewife	50	36.5
Retired/ Pensioner	18	13.1
Total	137	100.0
Education		
Illiterate	16	11.7
1-8	34	24.8
9-10	43	31.4
11-12	33	24.1
>12	11	8.0
Total	137	100.0
Marital Status		
Single	2	1.5
Married	120	87.6
Widowed	10	7.3
Separated	5	3.6
Total	137	100.0
Single	2	1.5

Total	137	100.0
Monthly Income		
10000	15	10.9
100000	1	.7
15000	15	10.9
20000	17	12.4
25000	21	15.3
28000	1	.7
30000	11	8.0
35000	5	3.6
40000	1	.7
50000	3	2.2
None	47	33.6
Total	137	100.0

Demographic Characteristics of Respondents

Statistics	Mean	Std. Error of Mean	Median	Mode	Std. Deviation	Variance
A8- Smoking status	1.86	0.03	2	2	0.347	0.12
A9- Number of Cigarettes/days						
A10- Other Addictions						
A12- Comorbid	1.81	0.034	2	2	0.395	0.156
A13- Co-morbid (choice=1. HTN)	1.45	0.043	1	1	0.499	0.249
A13- Co-morbid (choice=2. DM)	1.45	0.043	1	1	0.5	0.25
A13- Co-morbid (choice=3. CKD)	1.85	0.03	2	2	0.354	0.126
A13- Co-morbid (choice=66.Other)	1	0	1	1	0	0
4- Other Co-morbid						

Smoking Status of the Patients with other Comorbidities

Smoking Status		
	Frequency	**Percent**
Yes	19	13.9
No	118	86.1
Total	137	100.0
A9- Number of Cigarettes per day		
0	118	86.1
10	4	2.9
12	1	.7
20	4	2.9
5	8	5.8
8	2	1.5
Total	137	100.0
A10- Other Addictions		
	129	94.2
-	2	1.5
beetle nut	2	1.5
Beetle nut	1	.7

Niswar	3	2.2
Total	137	100.0
A12- Comorbid		
No	26	19.0
Yes	112	81.1
Total	137	100.0
A13- Co-morbid (choice=1. HTN)		
Yes	76	55.5
No	61	44.5
Total	137	100.0
A13- Co-morbid (choice=2. DM)		
Yes	75	54.7
No	62	45.3
Total	137	100.0
A13- Co-morbid (choice=3.CKD)		
Yes	20	14.6
No	117	85.4
Total	137	100.0
A13- Co-morbid (choice=66.Other)		
Yes	23	16.8
No	114	83.2
Total	137	100.0
A14- Other Co-morbid		
	114	83.2
A. Fib	1	.7
Asthma	1	.7
BPH	2	1.5
BPH, CVA	1	.7
CA bladder	1	.7
CKD, MVR	1	.7
CLD	2	1.5
COPD	2	1.5
CVA	6	4.4
Dyslipidemia	2	1.5
Epilepsy	1	.7
hypothyroid	1	.7
ovarian CA	1	.7
Systemic Sclerosis, Thyroid Nodule	1	.7
Total	137	100.0

Mean Median, Mode, Standard Deviation and SEM of Medications

		Beta blockers	ACEI	ARNI	Aldosterone antagonist	Statin	Diuretics	All	A17- Others
N	Valid	137	137	137	137	137	137	137	137
	Missing	0	0	0	0	0	0	0	0
Mean		.98	.78	.04	.28	.93	.85	.42	
Std. Error of Mean		.013	.035	.016	.038	.021	.030	.042	
Median		1.00	1.00	.00	.00	1.00	1.00	.00	
Mode		1	1	0	0	1	1	0	
Std. Deviation		.147	.415	.188	.449	.249	.354	.496	
Variance		.022	.172	.035	.202	.062	.126	.246	

Prescribed Medications

Beta blockers		
	Frequency	Percent
No	3	2.2
Yes	134	97.8
Total	137	100.0
ACEI		
No	30	21.9
Yes	107	78.1
Total	137	100.0
ARNI		
No	132	96.4
Yes	5	3.6
Total	137	100.0
Aldosterone antagonist		
No	99	72.3
Yes	38	27.7
Total	137	100.0
Statin		
No	9	6.6
Yes	128	93.4
Total	137	100.0
Diuretics		
No	20	14.6
Yes	117	85.4
Total	137	100.0
A17 Other		
	79	57.7
Ascard	7	8.0
Ascard, Amlodipine	1	.7
Ascard, Clopidogrel	6	4.4
Ascard, Clopidogrel, Hydralazine	1	.7
Ascard, Clopidogrel, Hydralazine, Amiodarone	1	.7
Ascard, Clopidogrel, Hydralazine, Monis	1	.7
Ascard, Clopidogre, sustac	1	.7
Ascard, Hydralazine, Nitrates, Metolazone	1	.7
ascard, Sustac	2	1.5
Ascard, warfarin	1	.7
ascard, ranzole	1	.7
Calcium channel blocker	1	.7
Cardinet	1	.7
Clopidogrel	2	1.5
DAPA	6	3.2
Dapa, Lowplat plus	1	.7
Dapa, Vestral MR, Insulin	1	.7
Hydralazine	3	2.2
Hydralazine, sustac	1	.7
hydralazine, ascard	2	1.5
Hydralazine, Nitrate	4	1.2
Hydralazine, Sustac	1	.7
Hydralzine	1	.7
Ivatab	1	.7
lophos, Ascard	1	.7
Metolazone, Calcium channel blocker	1	.7

monis	1	.7
Ranola, Lowplat, Thyroxine	1	.7
Xcept / Ca channel blockers / Norvasc	1	.7
Total	137	100.0

Comparing the Adherence Rate to the Suggested Pharmacological Therapy Based on Comorbidities and Smoking

Variables	Adherence To the Guideline Recommended Pharmacological Therapy		Total	P-Value
	Adequate n=87	Inadequate n=50		
Smoking Status			19	**0.973**
Yes	12(63.2%)	7(36.8%)	118	
No	75(63.6%)	43(36.4%)		
Other Addiction				
Beetle Nut	1(33.3%)	2(66.7%)	3	0.999
Niswar	1 (33.3%)	2(66.7%)	3	0.999
Comorbid	69 (62.7%)	41(37.3%)	110	0.534
Hypertension	46(60.5%)	30(39.5%)	76	0.477
Diabetic Mellitus	43(57.3%)	32(42.7%)	75	0.099
CKD	14(70%)	6(30%)	20	0.620
Others	14(60.9%)	9(39.1)	23	0.468

Comparing the Prescribed Medication's Adherence Percentage to the Guideline-Recommended Pharmacological Therapy

Prescribed Medications	Adherence To the Guideline Recommended Pharmacological Therapy		Total	P-Value
	Adequate n=87	Inadequate n=50		
Beta blockers	84(62.7%)	50(37.3%)	134	0.184
ACEI/ARB	62(57.9%)	45(42.1%)	107	0.011
ARNI+ARB	3(60%)	2(40%)	5	0.868
Aldosterone antagonist	24(63.2%)	14(36.8%)	38	0.958
Statin	81(63.3%)	47(36.7%)	128	0.838
Diuretics	73(62.4%)	44(37.6%)	117	0.514
Ascard	22(75.9%)	7(24.1%)	29	0.119
Hydralazine	13(76.5%)	4(23.5%)	17	0.235
Clopidogrel	10(83.3%)	2(16.7%)	12	0.210
DAPA	6(75%)	2(25%)	8	0.710
Nitrates	3(60%)	2(40%)	5	0.999
Others	8(80%)	2(20%)	10	0.326

IV. DISCUSSION

The degree to which an individual takes medicine as directed by their healthcare professional is known as adherence to medications. According to Yancy et al. (2013), non-adherence is often an undetected issue that healthcare professionals and patients fail to acknowledge. The degree to which a person's behavior of taking drugs, following a dietary plan, and/or implementing changes in lifestyle coincides with accepted recommendations from a medical professional is how the World Health Organization describes adherence to ongoing treatment (Usuda et al., 2021). A variety of techniques, including pill counting, firsthand observation, caretaker reports, physician ratings and self-reports, and medicine used for the previous seven days, can be used to assess compliance with medications (Willenheimer et al., 2005). A variety of factors such as the disease status and individuals' educational backgrounds, the objective of adherence assessment varies by country (Shah et al., 2017). The mean age of the participants in this study was $56.89 \pm N11.74$ years, while they were taking medicine for an average duration of 2.41 ± 3.44 years. Of them, 62.04 percent were men and 37.96 percent were women. The study conducted by Yancy et al. (2017) found that the mean age of the respondents was 46.25 ± 17.04 and that more than fifty percent of them were female (57.1 %).

In this study, 63.5 percent of heart failure individuals (Morisky medication adherence score 6 or above) showed adequate adherence to the guideline-recommended pharmaceutical therapy, while 36.5 percent showed inadequate adherence or non-adherence (Morisky medication adherence score). The Ponikowski et al. (2016) study's outcome also shows that 64.86 percent of individuals took their medications as directed. This statistic differs significantly from a study done in Yemen in 2013, where 54.2 percent of the subjects did not take the medication, they were given as recommended, and the Canadian city of Toronto in 2013, where 43 percent of participants did not take their prescribed medicine as recommended. In a 2015 systematic analysis research, 57 percent of the individuals in the untreated group following the 6-week trial's intervention were included. The shift in non-adherence could be attributed to the creation of knowledge and follow-up data through the many media outlets available in our nation. Several characteristics associated with heart failure (HF) were discovered, including the patient's awareness of the illness, socioeconomic situation, education level, client-provider relationship, and the varying acute and chronic characteristics of HF (Sliwa et al., 2004). However, these domains are intricate and interconnected, and there is still a lack of knowledge to distinguish particular elements linked to improved medication compliance that can direct the creation of effective, workable interventions.

I. The key components of self-care as well as adherence to medicine and self-care behavior must be health behaviors, knowledge about medications, and self-monitoring of the signs and symptoms of the condition (Fang, 2005). Numerous factors can influence a patient's adherence to medications. According to Packer (2015), the World Health Organization (WHO) has classified the following characteristics: socioeconomic status, factors linked to the health care providers and system in place, factors connected to disease, characteristics associated with therapy, and aspects related to patients.

II. CONCLUSION

According to the Morisky medication adherence score (below 6), 36.5% of the participants in our study were found to have insufficient adherence. Age (elderly), cognitive impairment, the use of multiple medications and monthly income were significant contributors to non-adherence. Inadequate adherence is linked to worsening health, faster illness progression, and higher death rates. A multifaceted strategy is needed to combat the issue of inadequate adherence. Counselling patients and their carers and providing education to medical staff about the advantages of sticking to medication therapy are essential. The government, charities, and social service providers all play crucial roles in providing the underprivileged patient population with social and financial support. A nationwide study with a sizable sample size will help us create an affordable approach for widespread adherence to drugs.

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