Assessment of adherence to cardiovascular medicines in rural population: An observational study in patients attending a tertiary care hospital

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ABSTRACT

Introduction: Nonadherence to cardiovascular medicines is a major concern. It increases the morbidity and mortality of cardiovascular patients. The work was conducted to evaluate the adherence to cardiovascular medicines in patients of rural India.

Methods: The study was conducted in the Department of Medicine involving rural patients with essential hypertension (HTN), congestive cardiac failure (CCF), and ischemic heart disease (IHD) over 12 months period. Patients were prescribed with cardiovascular medicines at the initial visit and adherence to medicines was assessed in the subsequent visit. Four items Morisky’s Medication Adherence Scale (MMAS-4) was used for assessing medication adherence. Patients were considered adherent to medication if they answered negatively to all four questions.

Results: Overall adherence to medication was 20.83%, 28.37% and 32% in HTN, CCF, and IHD patients, respectively. Nonadherence was highest in patients of HTN. Among the four reasons of nonadherence assessed by MMAS-4, carelessness was the most common and forgetfulness was the least common cause of nonadherence in all the three groups of patients.

Conclusion: Patients of rural India adhere poorly to cardiovascular medicines. Nonadherence should be considered as a public health problem. Strategies for detecting the level of adherence of cardiovascular medicines, its barriers, and subsequent interventions should be developed by policy-makers to reduce morbidity and mortality due to cardiovascular disorders.

KEY WORDS: Cardiovascular medicines, congestive cardiac failure, essential hypertension, ischemic heart disease
Methods

The study was carried out over a 12-month period in the Department of Medicine of a tertiary care teaching hospital. Both male and female patients (age ≥25 years) with essential HTN, CCF and IHD attending the outpatient clinic or admitted in indoor were selected for the study. The center is situated amidst the rural areas, and patients attending only from rural areas were included in the study. Patients with co-morbid conditions such as type II diabetes mellitus, chronic liver and kidney diseases, chronic obstructive pulmonary diseases, malignancy, and collagen vascular diseases were excluded from the study. Secondary HTN cases were also excluded. Adherence to dietary restriction and lifestyle modification was not assessed in the study. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 and Institutional Ethics Committee permission was obtained prior to conducting the study. Written consent was obtained from all patients for being included in the study.

HTN was diagnosed by physical examination after exclusion of secondary causes like Cushing syndrome, pheochromocytoma, kidney disorder, renal artery stenosis, etc. Diagnosis of CCF was established on the basis of history, physical examination, and echocardiographic findings. Patients who had CCF due to acute myocardial infarction (AMI) were excluded from the study. IHD was diagnosed from a history of angina and past AMI, electrocardiogram features, treadmill test, echocardiography (regional wall motion abnormality), and angiography. IHD patients, who refused angioplasty and coronary artery bypass grafting and preferred medical therapy, were included in the study.

Patients were prescribed with appropriate medicines at the initial visit and adherence to medicines was assessed in the subsequent visit. Initially, 185, 82, and 129 patients of HTN, CCF and IHD were selected, respectively. However, finally 120, 60, and 100 patients of HTN, CCF and IHD were assessed for adherence, respectively, as others failed to return at the follow-up visit.

Four items Morisky’s Medication Adherence Scale (MMAS-4) was used for assessing medication adherence in HTN, CCF and IHD patients. Four questions of MMAS-4 addressed the fundamental reasons of nonadherence such as forgetting, carelessness, stopping the medicine when feeling better or starting the medicine when feeling worse. Patients were considered adherent to medication if they answered negatively to all four questions.

Statistical method: Simple statistical methods were used for data analysis. Mean values, standard deviations, and percentages were used for data representation. GraphPad QuickCalcs online statistical calculator (GraphPad Software Inc., La Jolla, California, USA) was used for data analysis.

Results

All patients in the study were from the rural area and majority were from lower socioeconomic status with poor education level [Table 1]. Mean age of the patients suffering from HTN, CCF and IHD were 43.47 ± 9.26 years, 50.02 ± 10.55 years, and 54.71 ± 5.57 years, respectively. Male patients out-numbered the female patients. Family size was large (more than five members) and education level was <10th grade in majority of patients of all three groups.

Morisky’s scale revealed that overall rates of adherence to medication were 20.83%, 28.37%, and 32% in HTN, CCF and IHD patients, respectively [Table 2]. Nonadherence was highest in patients with HTN.

Ninety HTN patients (75%) were on single antihypertensive (amlodipine 48.33%, angiotensin converting enzyme inhibitors [ACEI]/angiotensin receptor blockers [ARBs] 12.50%, beta-blockers 7.50%, diuretics 6.67%), and 30 HTN patients (25%) were on combination antihypertensives (amlodipine + ACEI/ARBs 8.33%, amlodipine + beta-blockers 5%, amlodipine + diuretics 3.33%, ACEI/ARBs + beta-blockers 1.67%, ACEI/ARBs + diuretics 6.67%). Adherence was seen in 20.83% patients (25 cases) of HTN (21 patients on single antihypertensive and four patients with combination therapy).

### Table 1: Demographic profile of study populations of patients with HTN, CCF and IHD

| Parameters | HTN (n=120) | CCF (n=60) | IHD (n=100) |
|------------|-------------|------------|-------------|
| Age (±SD)  | 43.47±9.26 years | 50.02±10.55 years | 54.71±5.57 years |
| Gender-male:female | 68:52 | 36:24 | 59:41 |
| Education groups (%) | | | |
| Illiterate | 12.50 | 13.33 | 11 |
| Primary (up to fourth standard) | 50.83 | 45 | 51 |
| Secondary (up to 10th standard) | 17.50 | 21.67 | 19 |
| Higher secondary (up to 12th standard) | 12.50 | 11.67 | 12 |
| Graduates and above | 6.67 | 8.33 | 7 |
| Family size (±SD) | 5.90±1.64 | 5.77±1.62 | 5.81±1.65 |
| Socioeconomic status | | | |
| Higher (family income ≥INR 5000/month):lower | 16:104 | 8:52 | 14:86 |
| (family income <INR 5000/month) | | | |

HTN=Hypertension, CCF=Congestive cardiac failure, IHD=Ischemic heart disease, SD=Standard deviation, INR=Indian Rupee
Table 2: Assessment of medication adherence in HTN, CCF and IHD patients by Morisky’s instrument

| Morisky’s instrument (MMAS-4) | Cardiovascular diseases |
|-------------------------------|------------------------|
| Questionnaires                | HTN (n=120) | CCF (n=60) | IHD (n=100) |
| 1. Do you ever forget to take your medication? | 58 (48.33) | 23 (38.33) | 37 (37) |
| 2. Are you careless at times about taking your medication? | 88 (73.33) | 37 (61.67) | 58 (58) |
| 3. When you feel better, do you sometimes stop taking your medication? | 83 (69.16) | 35 (58.33) | 57 (57) |
| 4. Sometimes, if you feel worse when take your medicine do you stop taking it? | 75 (62.5) | 27 (45) | 42 (42) |
| Number of patients who said “no” to all four questions were considered adherent to medications | 25 (20.83) | 17 (28.37) | 32 (32) |

MMAS-4=Four items Morisky’s Medication Adherence Scale, HTN=Hypertension, CCF=Congestive cardiac failure, IHD=Ischemic heart disease

C Cf and I HD patients were on multiple medications. CCF patients were on loop diuretics (100%), spironolactone (40%), ACEI/ARBs (83.33%), beta-blockers (53.33%) and digoxin (31.67%). Adherence to CCF medications was seen in 28.37% (17 cases). IHD patients were on aspirin (76%), beta-blockers (30%), ACEI/ARBs (82%), statin (100%), and nitrates (55%) in different combinations. Adherence to IHD medications was seen in 32% (32 cases).

Among the four reasons of nonadherence assessed by MMAS-4, carelessness was the most common and forgetfulness was the least common cause of nonadherence in all the three groups of patients, i.e. HTN, CCF and IHD (Table 2).

Discussion

Adherence to medication is the extent to which a person takes medicines as prescribed by the health care provider. It is a key factor for effectiveness of pharmacological therapy. Nonadherence to medication leads to increased morbidity and mortality. Several measurement tools for medication adherence are available. Objective measures of adherence include pharmacy refill records and pill counts. In medication event monitoring system, a microprocessor attached to medicine bottle lid records the occurrence and time of each opening. Subjective methods, such as a questionnaire, interview, or diary are commonly used to measure adherence. These methods are flexible and practical but are less reliable than objective methods. We interviewed the patients with validated questionnaires of Morisky’s instrument that has been used in many adherence studies.

Our study revealed that HTN, IHD, and CCF patients adhere poorly to cardiovascular medicines (20–32%). There are only few studies of adherence to antihypertensive medication from India, but no Indian studies are found on medication adherence of IHD and CCF patients.[6-11]

Different Indian studies revealed different levels of adherence to antihypertensive medication. Rural studies are also present but are fewer in number. In a study among slum dwellers in Kolkata, the prevalence of antihypertensive adherence over a recall period of 1 week was 73%. High adherence was observed in hypertensive patients of long duration (≥5 years), patients getting free drugs, having a small family (≤ four family members) and high income. Patients, who were satisfied with the current treatment and perceived current blood pressure to be under control, were adherent to treatment.[10] In a survey from Bangalore, nonadherence to antihypertensive medication was found in 49.67% of patients. Belief, access, and recall barriers were reported by 39.14%, 82.57%, and 62.17% patients, respectively. Patients (78.62%) had difficulty to pay for medication and 54.93% had difficulty to get a refill on time.[3] In a study from Mangalore, 45.8% of the participants had a low level of adherence to anti-hypertensive medication. The absence of side-effects, provision of free medication and regular checkups were associated with good adherence.[8] In a Coimbatore-based study, the most prevalent causes of noncompliance were side effects of drugs (74%), forgetfulness (72%), thinking medication not effective (21%), and medications too expensive (19%). After 6 months, compliance increased significantly from 0% to 95.4% with interventions such as patient education, repeated counseling and reminder by a pharmacist.[9] In a rural Indian study from Loni, Ghaziabad, compliance to antihypertensive medication was better with combination therapy in comparison to monotherapy and with an economic approach.[10] In another rural Indian study of Mysore district of Karnataka, belief and recall barriers were prevalent to antihypertensive medication and pharmacist intervention was effective in reducing these barriers.[11] Adherence to antihypertensive medication is associated with significantly lower total healthcare costs, the rate of hospitalizations and emergency department visits.[12] In our study, adherence to antihypertensive medication was very poor in rural patients, and it was only 20.83%. Carelessness was the most common reason for nonadherence to antihypertensive medication, and it was seen in 73.33% patients. Nonadherence rate in our study is higher than other Indian studies. It reflects the poor medication adherence in the region. Place of residence is a contributing factor of medication nonadherence, patients recruited in urban studies being relatively more adherent.[7,8]

Adherence rates for CCF medication in different observational studies are different. In an Asian study from Yemen, overall nonadherence to CCF medication was 54.2%, and adherence to diuretics, digoxin, and beta-blockers were 46%, 29%, and 8%, respectively.[13] In a study of residents of Olmsted County, Minnesota, proportions of CCF patients with poor adherence were 19%, 19%, and 13% for beta-blockers, ACEI/ARBs and statins, respectively. Patients with poor adherence experienced more cost-related issues.[14] A study from a university hospital in Rio Grande do Sul, Brazil revealed a higher level of...
adherence to pharmacological treatment (47%) in comparison to nonpharmacological treatment (18%).\[15\] Availability of data of adherence to CCF medication in India is not available. Nonadherence to CCF medication in our study from rural India is higher than other above mentioned non-Indian studies. Only 28.37% CCF patients in our study were adherent to medication. Carelessness was seen in 61.67% patients and forgetfulness was seen in 38.33% cases of CCF. In our study, 58.33% and 45% CCF patients used to stop medicines when feeling better or used to stop medicines when feeling worse respectively.

Nonadherence to medication is common among coronary artery disease (CAD) patients. In an observational study from London, medication nonadherence of postacute coronary syndrome (ACS) patients was 20%, 54%, and 53% at 2 weeks, 6 months and 12 months, respectively. Nonadherence was mainly unintentional.\[16\] In an US based study, muscle pain was the primary reason for discontinuation of statin (60%) in CAD patients, followed by cost (16%) and then a perceived lack of efficacy (13%).\[17\] In a multicenter study involving post-ACS patients, more than 9% of aspirin-treated patients discontinued therapy early and remained off treatment. Common reasons for early discontinuation of aspirin were a patient refusal, bleeding and other side effects and physician's preference.\[18\] In a multicenter analysis from the USA of more than 17,000 post-ACS patients who had health insurance and prescription drug coverage, only 45% were adherent to beta-blockers by 1 year, and the highest decrease in adherence occurred between 30 and 90 days.\[19\] In another study from Ontario province of Canada, adherence to statin therapy in post-ACS patients was poor. The 2-year adherence rate was only 40%.\[20\] In another US-based study, a multifaceted intervention comprising pharmacist-led medication reconciliation and tailoring, patient education, collaborative care between pharmacist and clinician and voice messaging increased adherence to medication in the year after ACS hospital discharge. Patients on intervention were more adherent to clopidogrel, statins, and ACEI/ARBs but not to beta-blockers.\[21\] In our study, IHD patients had highest medication adherence (32%) among the three groups of patients with cardiovascular diseases. Patients of IHD and CCF are more symptomatic (because of angina, breathlessness, and edema) than HTN patients which may explain the higher medication adherence rates of these patients in comparison to HTN patients. These patients, being more symptomatic, are easily motivated. Furthermore, symptom relief possibly increases their faith in medication.

There are few limitations of our study. As this is not a community-based study, it does not reflect the original status of the community. We used the MMAS-4 which detects only the patient’s factors of adherence (such as forgetfulness, carelessness, patient’s perception/belief of the disease and its treatment requirement). Other contributors of nonadherence were not assessed. No single valid instrument of medication adherence measurement is yet developed that assesses all the World Health Organization defined factors of nonadherence (socioeconomic, health care system, therapy, patient, and condition-related factors).

As no instrument can detect all barriers, detection of barriers should be individualized when needed with through evaluation. When barriers are identified, appropriate interventions should be taken, and it should also be individualized when required. Behavioral and informational interventions by health care professionals and collaborative relationship between patient and provider may improve patient’s adherence to medication.\[22\]

**Conclusion**

Patients of rural India adhere poorly to cardiovascular medicines. Nonadherence should be attended to with due concern that it deserves. However, this issue is under-addressed as a public health problem and has received the little intervention. It is important to develop strategies for detecting the level of adherence of cardiovascular medicines; the barriers to adherence and the subsequent interventions thereof.

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**Conflicts of Interest**

There are no conflicts of interest.

**References**

1. Chowdhury R, Khan H, Heydon E, Shroufi A, Fahimi S, Moore C, et al. Adherence to cardiovascular therapy: A meta-analysis of prevalence and clinical consequences. Eur Heart J 2013;34:2940-8.
2. Barolletti S, Dell’Orfano H. Medication adherence in cardiovascular disease. Circulation 2010;121:1455-8.
3. Kulkarni SP, Alexander KP, Lytle B, Heiss G, Peterson ED. Long-term adherence with cardiovascular drug regimens. Am Heart J 2006;151:185-91.
4. Bowry AD, Shrank WH, Lee JL, Stedman M, Choudhry NK. A systematic review of adherence to cardiovascular medications in resource-limited settings. J Gen Intern Med 2011;26:1479-91.
5. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 1986;24:67-74.
6. Bhandari S, Sarma PS, Thankappan KR. Adherence to antihypertensive treatment and its determinants among urban slum dwellers in Kolkata, India. Asia Pac J Public Health 2015;27:NP74-84.
7. Dennis T, Meera NK, Binny K, Sekhar MS, Kishore G, Sasidharan S. Medication adherence and associated barriers in hypertension management in India. CVD Prev Control 2011;6:9-13.
8. Kumar N, Unnikrishnan B, Thapar R, Mittra P, Kulkarni V, Holla R, et al. Factors associated with adherence to antihypertensive treatment among patients attending a tertiary care hospital in Mangalore, South India. Int J Curr Res Rev 2014;6:77-85.
9. Palanisamy S, Sumathy A. Intervention to improve patient adherence with antihypertensive medications at a tertiary care teaching hospital. Int J Pharm Technol Res 2009;1:369-74.
10. Kale S, Patil A, Mandlecha RH. Compliance and adverse drug effects of antihypertensives in rural India. J Clin Diag Res 2011;5:775-9.
11. Sathvik BS, Karbasappa M, Nagavi BG. Self-reported medication adherence pattern of rural Indian patients with hypertension. Asian J Pharma Clin Res 2013;6 Suppl 1:49-52.
12. Pittman DG, Tao Z, Chen W, Stetlin GD. Antihypertensive medication adherence and subsequent healthcare utilization and costs. Am J Manag Care 2010;16:588-76.
13. Akshali KM, Daniel PS, Nochu AM, Sirajdeen SA. Patient medication adherence and physician prescribing among congestive heart failure patients of Yemen. Indian J Pharm Sci 2013;75:557-62.
14. Dunlay SM, Eveleth JM, Shah ND, McNallan SM, Roger VL. Medication adherence among community-dwelling patients with heart failure. Mayo Clin Proc 2011;86:273-81.
15. De Castro RA, Aliti GB, Linhares JC, Rabelo ER. Adherence of patients with heart failure to pharmacological and non-pharmacological treatment in a teaching hospital. Rev Gaucha Enferm 2010;31:225-31.
16. Molloy GJ, Messerli-Bürgy N, Hutton G, Wikman A, Perkins-Porras L, Steptoe A. Intentional and unintentional non-adherence to medications following an acute coronary syndrome: A longitudinal study. J Psychosom Res 2014;76:430-2.
17. Wei MY, Ito MK, Cohen JD, Brinton EA, Jacobson TA. Predictors of statin adherence,
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switching, and discontinuation in the USAGE survey: Understanding the use of statins in America and gaps in patient education. J Clin Lipidol 2013;7:472-83.

18. Newby LK, Bhapkar MV, White HD, Moliterno DJ, LaPointe NM, Kandzari DE, et al. Aspirin use post-acute coronary syndromes: Intolerance, bleeding and discontinuation. J Thromb Thrombolysis 2003;16:119-28.

19. Kramer JM, Hammill B, Anstrom KJ, Fetterolf D, Snyder R, Charde JP, et al. National evaluation of adherence to beta-blocker therapy for 1 year after acute myocardial infarction in patients with commercial health insurance. Am Heart J 2006;152:454.e1-8.

20. Jackevicius CA, Mamdani M, Tu JV. Adherence with statin therapy in elderly patients with and without acute coronary syndromes. JAMA 2002;288:462-7.

21. Ho PM, Lambert-Kerzner A, Carey EP, Fahdi IE, Bryson CL, Melnyk SD, et al. Multifaceted intervention to improve medication adherence and secondary prevention measures after acute coronary syndrome hospital discharge: A randomized clinical trial. JAMA Intern Med 2014;174:186-93.

22. Mansoor SM, Krass I, Aslani P. Multiprofessional interventions to improve patient adherence to cardiovascular medications. J Cardiovasc Pharmacol Ther 2013;18:19-30.