ORIGINAL ARTICLE

MEDICATION ADHERENCE IN POST MYOCARDIAL INFARCTION PATIENTS

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Background: Medication non-adherence after acute myocardial infarction is a global problem causing increased morbidity and mortality. This multifaceted problem has not been well studied in our part of the world. Our study aimed to determine the burden of medication non-adherence in post myocardial infarction patients. **Methods:** This cross-sectional study was conducted at National Institute of Cardiovascular disease, Karachi, from December 2016 to June 2017. A total of 350 patients were included at the time of discharge after their first myocardial infarction (MI) of which follow up was completed for 315 patients. Baseline characteristics and discharged drug data were collected for each individual. Patients were called at 7th day, 1 and 3months post discharge and were assessed for the medication adherence using Morisky medication adherence scale. They were stratified accordingly into self-reported high, moderate and low groups. Chi- square test was used to determine significant relationship between variables. The level of significance was set at level of *p*-value ≤0.05. **Results:** Among 315 patients, only 45% patients were adherent to prescribed drugs at 7th day follow up and the adherence further reduces to 19% at 3rd post MI month (*p*-value <0.001). High income, male gender, and presence of partner persistently showed significantly higher medication adherence. Factors like younger age, addiction and advance education showed higher adherence only in early follow up periods. However, presence of comorbidities, intervention and specific diagnosis had no significant impact. The most common stated reasons for non-adherence were forgetfulness and poor understanding of drugs. **Conclusion:** Adherence to prescribed medication in post myocardial infarction patients was found to be strikingly suboptimal, contributed by multiple factors. Modification of these factors would likely improve patient adherence to medication and eventually long-term outcome.

Keywords: Acute myocardial infarction; Medication adherence

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INTRODUCTION

Coronary artery disease (CAD) is one of the leading causes of death and disability worldwide. It is a growing epidemic in South Asia including Pakistan.[1] Studies have shown almost 27% prevalence of coronary artery disease among Pakistanis, equally involving males and females.[2] According to a population based cross sectional study, one out of four adult Pakistani individuals may have coronary artery disease.[2] Similarly, 2014 WHO report suggested 111,367 or 9.87% of total deaths were caused by coronary artery disease in Pakistan.[3]

Post myocardial infarction (MI) morbidity and mortality is mainly determined by risk factors reduction and importantly medication adherence.[4] Post MI medication for the treatment and prevention of future CAD-related events have undergone enormous evidence based evaluation, implying class 1 recommendation for antiplatelets (aspirin, P2Y12 inhibitor), B- blocker, ACE- inhibitor or ARB and lipid lowering agent (statin) in post MI patient, if not contraindicated.[5] These drugs in combination reduces 80% of CAD related mortality.[6] Despite these compelling evidences, post MI adherence to these medication is dismayingly low with studies showing around 40–75% medication adherence depending upon study areas and duration.[7–9]

Non-adherence to medications results in worsening clinical outcomes including repeated hospitalization, recurrent MI, increased healthcare costs, and death.[7,10] Medication costs, polypharmacy of acute coronary syndrome (ACS), fear of medication side effects, low literacy, poor understanding of medication benefit, poor provider patient relationship, unavailability of medicines are the major factors responsible for medication non-adherence.[9,10]

Multiple studies have been conducted in developed countries and a few in developing countries to evaluate the medication adherence in post MI patient and their outcomes.[7–10] Nonadherence in post MI patients has not been well studied in our part of the world. This study aimed to determine the burden of medication non-adherence and consequently to elucidate major factors contributing to it. Targeting these factors could guide initiatives for improving medication adherence which will prove to be worthy in reducing post MI patient's morbidity as well as mortality.

MATERIAL AND METHODS

This was a cross sectional study, conducted at National Institute of Cardiovascular disease, Karachi, from December 2016 to June 2017. This study was approved by the institutional Ethical Review Committee (Reference no: ERC-19/2016). Sample size was calculated using WHO sample size calculator version 2.0, with 95% confidence interval, 5.5% margin of error. A sample size of 284 patients was calculated based on Gonarkar SB *et al* study that showed 33.66% patients had Morisky medication score of 8 at 1st post MI month[8] (Appendix 1). Non-probability consecutive sampling was used.

Three hundred and fifty (350) newly diagnosed myocardial infarction (ST-segment elevation MI or Non-ST segment elevation MI) patients of either gender between 25–80 years of age were initially enrolled in the study at the time of discharge. Patients with mental instability, severe disabling comorbidities or frailty were excluded. A written informed consent was taken from each participant before enrolment (Appendix 2). Information regarding patients' characteristics, comorbidities (hypertension, diabetes mellitus, dyslipidaemia or stroke), employment status, current addiction (within 5 preceding years for at least 2 years), education level, diagnosis, intervention (if performed), and prescribed drugs were gathered at the time of enrolment. Patients were followed through centralized telephonic calls at 7th day, 1 month and 3 months post discharge to evaluate their medication adherence. Follow up was completed for 315 patients which was the final study population. Validated 8 item Morisky Medication adherence scale (MMAS) was used for medication adherence estimation (1 point for each question), and patients were stratified into three groups according to the summed score as self-reported high (score 8), moderate (score 6–7), and low (score <6) medication adherence groups. Patients were considered adherent when they got MMAS score of 8 (high adherence group) while those with score below 8 (moderate and low adherence groups) were classified as non-adherent. Patient with high adherence (i.e., MMAS score 8) for three months were considered persistently medication adherent.

Patient opinion regarding prime reason for their medication non-adherence was asked and categorized into factors as non-affordability, forgetfulness, lack of knowledge, fear of medication side effects, complicated polypharmacy, non-availability, improved health or being bored of medicines. A pre-designed questionnaire was used to collect data of each patient.

The data feeding and analysis was performed on SPSS (Statistical Packages of Social sciences) version 17.0. Clinical characteristics were summarized in terms of frequency and percentages for qualitative variables. Quantitative/continuous variables were expressed as mean with standard deviation. Statistical comparison was performed by using chi-square test and *p*-value ≤0.05 was considered as criteria for significance.

RESULTS

The mean age of our study patients was 54±10 years, with male to female ratio of 3:1. Base line characteristics are shown in table-1.

At early follow up period (7th post discharge day) 142(45%) out of 315 post MI patients were highly adherent to their prescribed medications, while 148(47%) and 25(8%) patients were moderately and poorly adherent to medication, respectively. The adherence to medication declined significantly over time such that at one month follow up, 116 (37%, *p*-value 0.035) and at 3 months follow up, 61 (19%, *p*-value <0.001) patients were reported being highly adherent to medications (Figure-1).

Patient between 25 -50 years of age were more adherent than older patients in initial follow-up at 7th (*p*-value 0.005) day and at 1 month (*p*-value 0.016), however, there was no significant difference among the different age groups at three months (*p*-value 0.323). Medication adherence was significantly and persistently higher among male patients (*p*-value 0.050), in patients with high income (*p*-value 0.034), and among those who were living with partner (*p*-value 0.027). Education level did not show a persistent significant difference in medication adherence. Addiction showed significant difference only at 7th day follow up (*p*-value 0.029). Presence of comorbidities, intervention and specific diagnosis also did not significantly affect the adherence. Table 2–4 shows the association of various factors with medication adherence. The most frequently reported prime reasons for non-adherence were forgetfulness in 39.5% and lack of knowledge in 33.7% patients.

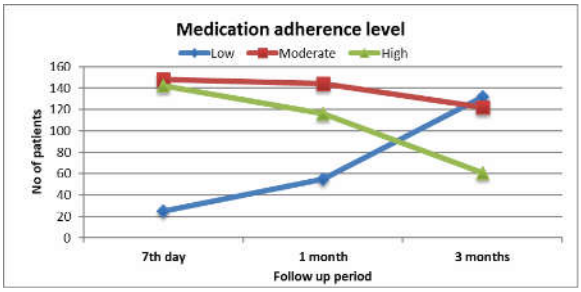

Figure-1: Decline in medication adherence among post myocardial patients across 3 months.

Table-1: Baseline characteristics of patients

	Subject characteristics	Subject (n=315)
Age	25–50	122 (38.73%)
	51–80	193 (61.27%)
Gender	Male	238 (75.56%)
	Female	77 (24.44%)
Education	Illiterate	134 (42.54%)
	Undergraduate	126 (40%)
	Graduate	55 (17.46%)
Income	<20000	257 (81.59%)
	≥ 20000	58 (18.41%)
Comorbid	DM/HTN/Dyslipidaemia	182 (57.78%)
	None	133 (42.22%)
Addiction	Tobacco/Alcohol	165 (52.38%)
	None	150 (47.62%)
Partner	With partner	252 (80%)
	Without partner	63 (20%)
Diagnosis	STEMI	193 (61.27%)
	NSTEMI	122 (38.73%)
Intervention	None	68 (21.59%)
	Early/PPCI	156 (49.52%)
	Elective PCI	91 (28.89%)
Reasons	Knowledge	87 (33.72%)
	Complicated polypharmacy	17 (6.59%)
	Non-affordability	5 (1.94%)
	Non-availability	13 (5.04%)
	Forgetfulness	102 (39.53%)
	Bored	13 (5.04%)
	Improved health	6 (2.33%)
	Side effects	15 (5.81%)

DM=Diabetes mellitus; HTN=Hypertension; STEMI= ST-segment Elevation Myocardial Infarction, NSTEMI=Non-ST- segment Elevation Myocardial Infarction; PPCI = Primary Percutaneous coronary intervention; PCI = Percutaneous coronary intervention

Table-2: Factors associated with medication adherence at 7th Day

Subject characteristics	Non-Adherent (MMAS < 8)	Adherent (MMAS 8)	*p*-value (Chi-Square Test)
Age			
25-50	55 (45.08%)	67 (54.92%)	0.005*
51-80	118 (61.14%)	75 (38.86%)	
Gender			
Male	54 (70.13%)	23 (29.87%)	0.002*
Female	119 (50%)	119 (50%)	
Education			
Illiterate	88 (65.67%)	46 (34.33%)	<0.001*
Undergraduate	66 (52.38%)	60 (47.62%)	
Graduate	19 (34.55%)	36 (65.45%)	
Income			
<20000	149 (57.98%)	108 (42.02%)	0.022*
≥ 20000	24 (41.38%)	34 (58.62%)	
Comorbids			
DM/HTN/Dyslipidemia	106 (58.24%)	76 (41.76%)	0.166
None	67 (50.38%)	66 (49.62%)	
Addiction			
Tobacco/Alcohol	81 (49.09%)	84 (50.91%)	0.029*
None	92 (61.33%)	58 (38.67%)	
Partner			
With partner	127 (50.4%)	125 (49.6%)	0.001*
Without partner	46 (73.02%)	17 (26.98%)	
Diagnosis			
STEMI	103 (53.37%)	90 (46.63%)	0.486
NSTEMI	70 (57.38%)	52 (42.62%)	
Intervention			
None	39 (57.35%)	29 (42.65%)	0.707
Early/PPCI	82 (52.56%)	74 (47.44%)	
Elective PCI	52 (57.14%)	39 (42.86%)	

*Significant at 5% level of significance. DM=Diabetes mellitus; HTN=Hypertension; STEMI= ST-segment Elevation Myocardial Infarction; NSTEMI=Non-ST-segment Elevation Myocardial Infarction; PPCI = Primary Percutaneous coronary intervention; PCI = Percutaneous coronary intervention.

Table-3: Factors associated with medication adherence at 1 month

Subject characteristics	Non-Adherent (MMAS < 8)	Adherent (MMAS 8)	*p*-value (Chi-Square Test)
Age			
25–50	67 (54.92%)	55 (45.08%)	0.016*
51–80	132 (68.39%)	61 (31.61%)	
Gender			
Male	58 (75.32%)	19 (24.68%)	0.011*
Female	141 (59.24%)	97 (40.76%)	
Education			
Illiterate	93 (69.4%)	41 (30.6%)	0.053
Undergraduate	78 (61.9%)	48 (38.1%)	
Graduate	28 (50.91%)	27 (49.09%)	
Income			
<20000	170 (66.15%)	87 (33.85%)	0.021*
≥ 20000	29 (50%)	29 (50%)	
Comorbid			
DM/HTN/Dyslipidaemia	118 (64.84%)	64 (35.16%)	0.475
None	81 (60.9%)	52 (39.1%)	
Addiction			
Tobacco/Alcohol	97 (58.79%)	68 (41.21%)	0.090
None	102 (68%)	48 (32%)	
Partner			
With partner	151 (59.92%)	101 (40.08%)	0.017*
Without partner	48 (76.19%)	15 (23.81%)	
Diagnosis			
STEMI	115 (59.59%)	78 (40.41%)	0.097
NSTEMI	84 (68.85%)	38 (31.15%)	
Intervention			
None	43 (63.24%)	25 (36.76%)	0.465
Early/PPCI	94 (60.26%)	62 (39.74%)	
Elective PCI	62 (68.13%)	29 (31.87%)	

*significant at 5% level of significance. DM=Diabetes mellitus; HTN=Hypertension; STEMI= ST-segment Elevation Myocardial Infarction; NSTEMI=Non-ST-segment Elevation Myocardial Infarction; PPCI = Primary Percutaneous coronary intervention; PCI = Percutaneous coronary intervention.

Table-4: Factors associated with medication adherence at 3 months

Subject characteristics	Non-Adherent (MMAS < 8)	Adherent (MMAS 8)	*p*-value (Chi-Square Test)
Age			
25–50	95 (77.87%)	27 (22.13%)	0.323
51–80	159 (82.38%)	34 (17.62%)	
Gender			
Male	186 (78.15%)	52 (21.85%)	0.050*
Female	68 (88.31%)	9 (11.69%)	
Education			
Illiterate	113 (84.33%)	21 (15.67%)	0.272
Undergraduate	100 (79.37%)	26 (20.63%)	
Graduate	41 (74.55%)	14 (25.45%)	
Income			
<20000	213 (82.88%)	44 (17.12%)	0.034*
≥ 20000	41 (70.69%)	17 (29.31%)	
Comorbid			
DM/HTN/Dyslipidaemia	146 (80.22%)	36 (19.78%)	0.827
None	108 (81.2%)	25 (18.8%)	
Addiction			
Tobacco/Alcohol	128 (77.58%)	37 (22.42%)	0.150
None	126 (84%)	24 (16%)	
Partner			
With partner	197 (78.17%)	55 (21.83%)	0.027*
Without partner	57 (90.48%)	6 (9.52%)	
Diagnosis			
STEMI	151 (78.24%)	42 (21.76%)	0.176
NSTEMI	103 (84.43%)	19 (15.57%)	
Intervention			
None	61 (89.71%)	7 (10.29%)	0.102
Early/PPCI	122 (78.21%)	34 (21.79%)	
Elective PCI	71 (78.02%)	20 (21.98%)	

*significant at 5% level of significance. DM=Diabetes mellitus; HTN=Hypertension; STEMI= ST-segment Elevation Myocardial Infarction; NSTEMI=Non-ST-segment Elevation Myocardial Infarction; PPCI = Primary Percutaneous coronary intervention; PCI = Percutaneous coronary intervention.

DISCUSSION

Medication non-adherence is a global problem that has been investigated for almost 50 years.[11] In post MI period non-adherence to prescribed medication has profound consequences, causing increased morbidity, health care spending and mortality.[10,12–14] On an average, less than 50% of post MI patients remains adherent to medication worldwide, although the prevalence varies widely among different studies.[7–9,14]

Medication adherence is usually defined by patient's intake of their medications as prescribed (e.g., twice daily) and by persistence, related to the medication continuation for the specified duration. Medication adherence can be assessed in a variety of subjective and objective ways. Morisky Medication adherence scale (MMAS) is the most widely used, easy and validated tool for assessing medication adherence.[15] It is a self-reporting tool comprising of 8 items with a dichotomous response (yes/no) for first 7 items and a 5-point Likert response for the last item. Adherence levels are grouped on the basis of summation score as high (score 8), moderate (score 6–7), and low (score <6) adherence.[15]

Our study has shown disappointingly poor adherence to evidence-based medication even in early period following acute myocardial infarction hospitalization. The adherence declined drastically afterwards to only 19% at 3rd post MI month. Multiple factors have been found to be related to medication non-adherence. The impact of patient age on medication adherence varied widely among different studies, however, in our study we found younger subjects to be more adherent to medication than their older counterparts only in early follow up period.[7,8,16–18] Like documented in the past studies, male patients were more adherent to the medicine.[16,17,19] Lack of knowledge, self-ignorance and dependency might be the factors causing non-adherence among females in our part of the world. Similarly, patients in high income groups were more adherent to medicines than the patients with low incomes. This observation is in line with the findings from other studies which suggest that low income does in fact have negative impact on the adherence.[7,8,19] Despite of the availability of drugs from the hospital, financial constraint was still a powerful confounder to medication adherence.

We found that subjects who were living with life partners were more adherent to their prescribed medicine, possibly because of the help and support provided by a spouse; this may be related to the societal and cultural norms. Our result is contradictory to previous studies of Zulling *et al* (2015) and Tantikosoom *et al* (2011) that showed no significant association of marital status with medication adherence.[20,21] Contrary to other studies we could not find any consistent significant association of education level, addiction or presence of comorbidities with medication adherence, implying the interplay of different demographic, social and clinical factors in this part of the world.[8,9,18]

In literature, patients who suffer ST-segment elevation MI are reported to have higher medication adherence, however, in our study there was no significant difference among patients with ST-segment elevation MI (STEMI) or non-ST-segment elevation MI (NSTEMI) in medication adherence.[18] Furthermore, there was no significant impact of post myocardial infarction percutaneous interventions on medication adherence. Forgetfulness was the most frequently stated reason for non-adherence, this finding is consistent with data from the TRANSLATE ACS study.[7] Frequent drug dosing, lack of priority and social stresses might be plausible explanations for this forgetfulness; which can probably be rectified with frequent reminders, educating patients and simplifying the drug regime. Lack of knowledge about the drugs was another often-stated barrier to medication adherence, as seen worldwide.[14,22,23] We found other contributing factors for failure to medication adherence. These include complicated polypharmacy, fear of medication side effects, boredom from persistent use of medicines, medicine non-availability, improved health and non-affordability in order of frequency. These factors are common impediments to medication adherence globally.[7,8,14] Non-affordability might be a more important factor depending on the drug coverage.[8,14,24] A multidisciplinary approach including frequent reminders, improving health literacy, a drug combination pill (polypill) and cost sharing are the promising keys to improve medication adherence and would ultimately guarantee favourable clinical and cost-effective outcomes.[23,24]

Our study has few limitations. The self-reported design of MMAS tool used for medication adherence evaluation may have recall bias, however, self-reported tools have proven accuracy.[15,25] We have only listed single, prime stated determinant of non-adherence for each patient, yet many patients do have multiple coexisting reasons for adherence failure. Lastly, we have not evaluated our patients for post MI depression that may have been an important factor for medication non-adherence.[7,24]

CONCLUSION

Post MI medication adherence is worrisomely poor, even in the early post MI period in our region. There are many potentially modifiable factors contributing

to the medication non-adherence, implying complex interplay of different demographic, social and clinical factors. Collaborative efforts, implementation of new technologies and profound research are needed to remedy this multifaceted phenomenon.

AUTHORS' CONTRIBUTION

All authors have equally contributed to conception, design and data analysis of article. Data was mainly collected by SH. Article revised and approved for final version to be published by ZJ and FQ.

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