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7 Adherence to Medications in Patients with Ischemic Heart Disease in Oman

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16 Abstract

17 **Objectives:** The aim of this study was to evaluate the level of adherence to medications in
18 patients with IHD in Oman and assess the factors influencing it. **Methods:** This was a cross
19 sectional questionnaire-based study among patients with IHD. **Results:** A total of 105 patients
20 (Mean age 49.9±11.1 years; 78.1% male) were recruited. Most of the patients take the
21 medications by themselves (84 or 80%). 77 patients (73.3%) said that over the preceding two
22 weeks, they missed at least three doses. The reasons for missing included forgetting (100%), too
23 many tablets (57%), not effective (48%) and too many times a day (23%). There were no factors
24 that could be identified that made patients prone to not taking medications. **Conclusion:**
25 Medication adherence was low among patients with IHD in Oman with high pill burden the most
26 common reason for non-adherence. Physicians must keep this in mind when patients are
27 reviewed.

28 **Keywords:** Cardiovascular disease, adherence, myocardial infarction.

29

30 **Introduction**

31 Cardiovascular disease are a major cause of morbidity and mortality worldwide. It is estimated
32 that 17.9 million deaths (representing 32% of all deaths) in 2019 were attributed to CVD.¹ A
33 major part of the management of CVD lie in adherence to medications and lifestyle changes with
34 the intention of lowering future cardiovascular events and for symptom control.² Medications are
35 prescribed either as primary prevention for those at high risk for future cardiovascular events or
36 secondary prevention of future events for those who have already sustained a cardiovascular
37 event.

38
39 Current evidence based practice has led to patients with CVD and those at high risk, being
40 initiated on an increasing number of medications. This can affect adherence and as with other
41 chronic illnesses, non-adherence to medication and lifestyle modifications, remains a major
42 issue.³ Studies have demonstrated that adherence is often an issue when given as a long-term
43 preventative strategy rather than for symptom control. This is especially true for hypertensive
44 patients who are often asymptomatic but experience various side effects to medications.⁴
45 The reported rates of adherence with cardiovascular medications range from 30-70%, with
46 patients often not taking all or part of their prescribed medications.⁵ Poor adherence is a major
47 public health issue such that, the World Health Organisation (WHO) in their report on adherence
48 to long term therapies, state that interventions to improve medication adherence might have a far
49 greater impact on the health of the population than any improvement in a specific medical
50 treatment itself.⁶

51
52 There are many factors that are responsible for poor adherence and understanding these factors in
53 a particular population is key to improving medication adherence and ultimately improving
54 patient care and outcomes. The WHO has identified five broad categories of factors that affect
55 adherence: 1) socio-economic factors 2) patient-related, 3) therapy-related, 4) co-morbid
56 conditions, and 5) healthcare system-related.⁶ The first four factors are mainly related to the
57 individual patient and it is important to understand these factors which are very individualised
58 and often related to patient preferences and social and cultural behaviours. These include costs,
59 beliefs regarding medications and treatment, number of pills, side effects of pills, understanding
60 the need for medications, the benefits of it, forgetfulness and overall wellbeing.⁷⁻⁹

61
62 Improving medication adherence helps improve cost savings and helps to put into practice
63 lessons learned from clinical trials and ultimately helps to reduce the burden of chronic
64 illnesses.¹⁰ Early detection of non-adherence can prevent expensive investigations, hospital
65 admissions and unnecessary additional medications and interventions. It is important to ensure
66 high levels of adherence to medications to improve cardiovascular outcomes in the population as
67 a whole.²

68
69 In Oman, IHD is a leading cause of mortality and morbidity accounting for around 35% of all
70 deaths in 2020.¹¹ There is dearth of information regarding adherence to medication in the
71 Middle-east. The aim of this study was to assess the levels of medication adherence in patients
72 with IHD and the patient related factors affecting it in Oman.

73

74 **Methods**

75 This was a cross-sectional study questionnaire based on patients who attended the outpatient
76 clinic at a tertiary hospital in Muscat, Oman. This was performed between January to December
77 2021. Patients aged 18 or over, who were diagnosed to have IHD with a previous MI or
78 undergone PCI for stable angina more than a year earlier were included in the study. Patients had
79 to be independent and fully alert and oriented to be included in the study, They could take
80 medications either by themselves or be given by a carer. Patients who were not able to give
81 consent to the study, or those who had a recent cardiac event or who had a hospitalisation for a
82 cardiovascular event within the preceding 12 months were not included in the study. We chose a
83 sample size of 100 as this is a pilot study.

84

85 The questionnaire was self-developed. It was based in two parts. The first part was about the
86 general demographics of the patients, the number of medications and the total pill burden. The
87 second part of the questionnaire was about their practice of taking medications. It included a
88 question regarding whether they missed more than three doses in the previous two weeks. If they
89 did, they were considered as non-adherent. This was because 3 days out of 14 would work out to
90 an adherence rate of 80% which is the rate accepted by many studies for adequate adherence.

91 This was initially trialled on a few volunteers to adjust the wording, to ensure that there were no

92 difficult or confusing words. The questionnaire was developed in Arabic by native Arabic
93 speaking staff.

94
95 Ethical approval was obtained from the research committee of the Sultan Qaboos University
96 (MREC #1550). All patients gave informed consent before answering the questionnaire.
97 Statistical analysis was performed using SPSS version 21. Data was presented as number (%) or
98 mean \pm standard deviation (SD) or median (Interquartile range- IQR). Data analysis was done by
99 chi-square test or student t-test as appropriate. A p value of <0.05 was considered to be
100 statistically significant.

101

102 **Results**

103 A total of 105 patients (Mean age 49.9 \pm 11.1 years; 82 or 78.1% male) filled in the
104 questionnaires. The patients were taking a median of 9 (interquartile range (IQR) of 6-10) tablets
105 per day. They were taken a median 3 (IQR 2-3) times a day. Most of the patients had a previous
106 MI (100 or 95.2%) with the remaining 5 having chronic stable angina. 87 (82.9%) of patients had
107 a previous PCI, while 12 (11.4%) had previous CABG. Hypertension was the commonest risk
108 factor (97 or 92.4%) followed by diabetes (87 or 82.9%). 14 patients (13.3%) had a previous
109 stroke. Table 1 summarises their demographic features.

110

111 Most of our patients take the medications by themselves (84 or 80%), while for the remaining 21
112 (20%) a family member or carer administers the medications. Twenty-two patients (%%) use a
113 reminder to help them remember to take medications. This includes a phone app for 12 patients,
114 and a family member for 10.

115

116 77 patients (73.3%) said that over the preceding two weeks, they would have missed at least
117 three doses. The main reason given by our patients for not taking medications regularly are that
118 they simply forgot (77 or 100%), while 44(57%) patients felt that there were too many [Table 2].
119 Thirty-seven (48%) felt that they were not effective and 18 didn't take all the medications as
120 prescribed as it was too many times a day (23%). A further 41 (39%) said that they stop taking
121 the tablets when they feel well. A majority of patients (80 or 76.2%) felt that taking tablets was a
122 burden and 63 (60%) said that they sometimes do not take tablets while travelling.

123

124 Table 3 summarises the differences between those who missed more than 3 doses of tablets over
125 the previous 2 weeks with those who said they never missed a single dose. There was no
126 difference between the two groups. There was no difference in age, gender, educational status, or
127 the number of pills or the number of times a day. The cardiovascular risk factors were similar,
128 apart from those who had a previous stroke had a higher number of those who missed tablets (p-
129 0.01). Although there did not appear to be any difference between the two groups, by binary
130 logistic regression, the only factor that predicted non-adherence was the number of pills taken
131 daily (Odds ratio 1.26, 95% confidence interval 1.001-1.059, p=0.04)

132

133 **Discussion**

134 The rates of non-adherence were high in our group, with more than three-quarters of those
135 surveyed saying that they had missed multiple doses over the previous two weeks. The findings
136 are similar to those from other studies. Adherence to medications in CVD is low worldwide.
137 In a meta-analysis of around 20 observational studies involving more than 300,000 patients with
138 CVD, it was estimated that the prevalence of poor adherence was as high as 43%.¹² For
139 individual risk factors that rate can be even higher. It has been demonstrated that at the end of
140 end of 6 months one-third of patients discontinue their antihypertensive medications, and only
141 around half of all patients persist with their initial therapy at one year.⁴

142

143 The rates of adherence for primary prevention of CVD are generally lower than those for
144 secondary prevention. Patients who have suffered a myocardial infarction or a stroke are more
145 likely to take their medication regularly than those who have not suffered an event.¹² However,
146 even for those on secondary prevention, adherence is sub-optimal as demonstrated on a study on
147 4591 post MI patients, where around 18% of patients did not collect their prescriptions even once
148 in the four months following the MI.¹³ In a separate cohort of 22,379 post-ACS patients, 60%
149 discontinued their statin medication within 2 years of hospitalization.¹⁴

150

151 There are many factors that affect adherence to medications.⁵ These include physician/healthcare
152 related factors, patient factors and socio-economic factors. Healthcare factors include busy
153 outpatient consultations, pill burden, access to pharmacies and ease of refills and costs. Patient

154 factors include socio-economic factors such as affordability, access to health care, social
155 circumstances, forgetfulness, and understanding of the disease process.¹⁵

156
157 Beliefs regarding medications, the disease process and its management are an important part and
158 determinant of medication adherence. It has been shown that these beliefs play an important part
159 in medication adherence even among people of middle-eastern origin who live in Australia.¹⁶

160 Beliefs regarding medications include the importance and usefulness of taking medications, and
161 the concern regarding the illness. Horne et al, into one of four subgroups according to their
162 attitudes towards medication; Sceptical (low necessity, high concerns), Ambivalent (high
163 necessity, high concerns), Indifferent (low necessity, low concerns), and Accepting (high
164 necessity, low concerns).¹⁷ The sceptical and ambivalent patients have been shown to have low
165 adherence rates as compared to the other two groups.^{16,18} Education is therefore an important part
166 of ensuring adherence and empowering the patient to take care of their own health by explaining
167 the need for adherence and the benefits. In our cohort of patients, we did not specifically study
168 the beliefs of the patients, though we had asked them whether or not they felt the medications
169 were effective.

170
171 Other cultural factors such as the use of traditional medicine, which is high in Oman, could also
172 play a role in non-adherence.¹⁹ In this study Al-Riyami et al found that a high proportion of
173 people prefer to take herbal medications and undergo traditional practices to taking medications
174 for chronic illnesses. Scicchitano et al have described the role of “functional foods” or
175 “nutraceuticals” in cardiovascular disease.²⁰ Functional foods are described as any food or food
176 ingredient that may provide a health benefit beyond the traditional nutrients it contains,²¹ while
177 nutraceuticals have been defined as food (or part of a food) that provides medical or health
178 benefits, including the prevention and/or treatment of a disease.²² This concept might explain the
179 benefits of herbal diets and the willingness of the population to try these remedies rather than
180 modern medications and thereby affecting adherence.

181
182 The findings of our study are also in keeping with data from the middle east, where adherence
183 rates ranging from 1.4-88% have been demonstrated in a variety of conditions.²³ A previous
184 study from Oman on patients with hypertension also revealed that less than 50% of the patients

185 were adherent to medications.²⁴ Al-Qasem et al performed a systemic review of studies from the
186 middle east and found that the reasons reported by patients for non-adherence in the Middle East
187 are similar to those reported in the international literature.²³ However, some of the reasons
188 mentioned were unique to the middle-east such as patient dissatisfaction and/or lack of trust in
189 health care providers and lack of social support. Poor physician support and explanations and
190 lack of understanding of the need for taking medications has also been described previously from
191 the region.²⁵

192
193 In our study, we could not identify any factor that could predict non-adherence apart from the
194 number of pills. The age, gender, educational status, or marital status did not affect adherence.
195 The use of aids or whether the patient self-medicated or whether it was given by a carer did not
196 affect adherence. It is possible that the small sample size was not able to differentiate between
197 those who were adherent and those who were not. The mean age of our patients was 49 years
198 with only a small proportion of patients above 60 years. This could explain why age did not
199 appear to be a contributing factor. Previous studies on adherence to medications for other
200 conditions in the region demonstrated that gender, educational status affected adherence, with
201 female patients and those with lower educational achievement had poorer adherence. In our
202 study we did not demonstrate any difference, possibly again due to the small sample size and
203 general over all poor adherence among all groups.^{23;26;27}

204
205 The only factor that predicted low adherence was the pill burden. Most patients with IHD are on
206 a large number of pills for secondary prevention. After coronary intervention, or on adequate
207 medical therapy, many patients have adequate control of symptoms which then becomes a
208 determinant of poor adherence.^{8;13;14;28} The average number of pills per patient in our study was
209 around 9 which is a large number. A large proportion of patients felt that they were taking too
210 many tablets and felt burdened by it. It is therefore important for physicians to review patients'
211 medications at each visit to ensure that patients are not on any medications that they do not need
212 to be on, such as stopping dual antiplatelet therapy after one year (if indicated). The use of
213 combination pills reduces the pill burden and has been demonstrated to improve adherence in
214 patients with CVD with improved clinical outcomes.²⁹ Perhaps local health authorities should
215 consider using more combination pills in routine practice.

216

217 Assessment of medication adherence is not easy There are many questionnaires that are validated
218 for a variety of conditions.¹⁵ However, all of them have their own advantages and disadvantages
219 and has been described elsewhere. We did not use any of these questionnaires, but instead chose
220 to directly ask the patients whether or not they missed any doses in the previous two weeks.
221 Although direct questioning has its limitations, we felt this would help us explore reasons behind
222 non-adherence.³⁰

223

224 There were a few limitations to our study. Medication adherence is very variable over time, with
225 patients having periods of strict adherence followed by periods of mild to severe nonadherence.³¹
226 Our study only investigated a snapshot of the two weeks preceding the questionnaire. This is
227 therefore not representative of their overall long-term adherence. This study was performed in
228 the outpatient setting of a tertiary hospital in Muscat, Oman which is a large city. The results are
229 not generalisable to the whole of Oman and the rural areas. Access to health care, beliefs
230 traditions and customs are different in the different parts of Oman, along with different social
231 and economic conditions, all of which play a role in medication adherence and have not been
232 fully assessed in this study. Another limitation was the lack of follow up. It would have been
233 useful to have additionally studied the effects of intervention and co-operation between primary
234 and secondary care on the levels of medication adherence as this has been previously
235 demonstrated to be useful in an Italian population.³²

236

237 Our study was limited to Omani population and the adherence rates among the expat population
238 might be different due to the different socio-economic conditions. Our study sample size was
239 small. This study was conducted just when social restrictions related to the COVID pandemic
240 were being lifted. Access to healthcare and patients was still not as free as prior to the pandemic.
241 However, this is the first study of its type on adherence to medications among patients with IHD
242 from Oman. Larger studies are required to fully assess the barriers to optimal medication
243 adherence among patients with IHD from different parts of Oman.

244

245 **Conclusion**

246 The rates of medication non-adherence in patients with IHD is high in Oman. Number of pills
247 was the major determinant of non-adherence. Lowering pill burden and frequent review of
248 medications, use of combination pills must be considered in these patients. Additionally, more
249 needs to be done to assess the needs of each individual patient in order to improve their
250 understanding of the disease and to improve overall adherence.

251
252 **Conflicts of Interest**

253 The authors declare no conflict of interests.

254
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256 No funding was received for this study.

257
258 **Authors' Contribution**

259 AA, QA, MA, HA were involved in collection of data and contributing to writing the
260 manuscript. SKN-data analysis and manuscript writing. All authors approved the final version of
261 the manuscript.

262
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350

351 **Table 1:** Demographics of the participants.

	Number (n=105)	percentage
Age	49.9 ± 11.1 years	
Sex		
<i>Male</i>	82	78.1%
<i>Female</i>	23	21.9%
Marital status		
<i>Never married</i>	7	6.7%
<i>Married</i>	81	77.1%
<i>Separated</i>	17	16.2%
Educational status		
<i>Less than Primary school</i>	35	33.7%
<i>Secondary school</i>	49	46.7%
<i>Graduate or more</i>	21	20%
Diabetes	87	82.9%
Hypertension	97	92.4%
Smoker	46	43.8%
Previous stroke	46	43.8%
Previous MI	100	95.2%
Previous CABG	12	11.4%
Previous PCI	87	82.9%

352 *MI = myocardial infarction; CABG = coronary artery bypass grafting; PCI = percutaneous*
 353 *coronary intervention.*

354
355

Table 2: Reasons for non-compliance.

	Number (n=77)	Percentage
Just forget to take	57	74.02%
Too many tablets	44	57.1%
Too many side effects	18	23.3%
Not effective	37	48.1%
Many times a day	15	19.4%

356
357

Table 3: Differences between those who missed tablets and those who did not.

	Those who did not miss (n=28)	Those who missed more than 3 doses in last two weeks (n=77)	p-value
Age (years)	49.01 ± 10.1	50.2 ± 11.5	0.61*
Gender			
<i>Male</i>	23 (82.1%)	59(76.6%)	0.60
<i>Female</i>	5(17.9%)	18(23.4%)	
Marital status			
<i>Married</i>	21(75%)	60(77.9%)	0.54
<i>Single/Divorced/Widowed</i>	7(25%)	17(22.1%)	
Educational status			
<i>Primary school or less</i>	9(32.1%)	26(33.7%)	0.7
<i>Completed secondary school</i>	12(42.8%)	37(48.1%)	
<i>Postgraduate studies</i>	7(25%)	14(18.1%)	
Number of pills	8(5-10)	9(6-10)	0.24*
Number of times per day	3(2.5-3)	3(3-3)	0.9*
Diabetes	21(75%)	66(85.7%)	0.19
Hypertension	26(92.8%)	71(92.2%)	0.91
Smoker	11(39.2%)	35(45.4%)	0.67
Previous cva	0	14(18.1%)	0.01
Previous CABG	1(3.5%)	11(14.2%)	0.12
Previous PCI	21	66(85.7%)	0.19
Who gives the pills			
<i>Self</i>	22(78.5%)	62(80.5%)	0.52
<i>Carer</i>	6(21.5%)	15(19.5%)	
Use reminder	7(25%)	15(19.5%)	0.53

358 CVA = cerebrovascular accident; PCI = percutaneous coronary intervention; CABG =
359 coronary artery bypass grafting.
360 Analysis by chi-square test apart from *students t-test and **Mann Whitney U test.